ANAEMIA in a COUNTRY PRACTICE

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It has been said of general practitioners that they rely, largely, on a physical examination and not on a blood examination for the diagnosis of blood diseases ("Textbook of Medical Treatment", Dunlop, Davidson & McNee, p.p.395, 396). In this way serious errors in diagnosis and treatment of blood diseases arise.

Clearly, when anaemia is suspected, it is the duty of every general practitioner to see that a blood examination is carried out before commencing treatment. A recent survey, however, has shown that only 8 to 10 per cent of general practitioners do their own blood counts (Hadfield, S.J.,(1953) British Medical Journal, 2, 697 and Supplement, p.120).

In contrast to town practice, there is usually no direct access to a pathological department in country practice. To treat his anaemic patients properly, the country practitioner is thus compelled to do blood examinations himself. It may be argued that this is too great a responsibility for the general practitioner to undertake alone as, even to the experienced haematologist, the interpretation of anaemia is often difficult.

It is the purpose of this paper to show that a reasonable degree of accuracy in the diagnosis and treatment of anaemia is possible in general practice. My experiences, in a country practice of approximately 3,200 patients in the diagnosis and treatment of blood diseases during the period 1944-1952, are described.

An initial blood count was performed at home in all patients suspected of being anaemic. Only when the diagnosis or the origin of the anaemia was in doubt were patients referred to hospital for further investigation.

METHOD.

Oxalated tubes were prepared by Wintrobe's method as described by Whitby & Britton ("Disorders of the Blood", 1950, p.625). To a 5 c.c. test-tube were added 0.2 c.c. of a solution of 2% potassium oxalate and 0.2 c.c. of a solution of 3% ammonium oxalate. The test-tube containing this mixture was placed in the oven of an electric cooker which had been previously heated to a temperature of just under 200° F. The oven was turned off as soon as the mixture was placed in it and, while cooling, evaporated the latter to dryness leaving a white flaky deposit of oxalate. This process took approximately 12 hours and is open to criticism, as too high a temperature during evaporation causes dissocation of the ammonium salt (Whitby, L., 1939, "Practical Procedures", p.102).

Blood samples were obtained from patients by withdrawing 5 c.c. of blood from an arm vein and transferring the blood to an oxalated tube. This method is very useful in general practice as it allows the practitioner to test the specimen when most convenient to him.

Haemoglobin estimations were performed by the Sahli method, the haemoglobin being estimated after

the mixture of blood and N/10 HCl. had stood for ten minutes, as recommended by Britton ("Modern Diagnosis", 1940, p.220).

In performing the erythrocyte and leucocyte counts, the coverslip was pressed into intimate contact with the supporting columns of the counting slide so that Newton's rings were visible. This is recommended by the Standing Committee on Laboratory Methods of the University of Glasgow ("Notes on Clinical Laboratory Methods", 1952, p.45).

To check the accuracy of my methods, and the anti-coagulant properties of the oxalated test-tubes, I carried out blood tests in 1944 on 17 males and 9 females, all of whom had a healthy appearance but were suffering from minor complaints for which they were attending my surgery.

A haemoglobin estimation, a red cell count and a packed cell volume estimation were performed in each of these "normals". For the packed cell volume estimation a Wintrobe's haematocrit tube was filled with oxalated blood and centrifuged, for 45 minutes to 1 hour, on a covered electric centrifuge capable of reaching a centrifugal speed of 3,000 r.p.m. uncovered and unloaded.

MALES:

Case No.	Hb% (Sahli)	R.B.C. per cubic mm.	Packed cell volume per cent.
1.	86	5,090,000	48 c.c.
2.	84	4,710,000	45 c.c.
3.	84	4,770,000	46 c.c.
4.	95	4,980,000	49 c.c.
5.	80	4,210,000	47 c.c.
6.	94	4,210,000	49 c.c.
7.	80	5,210,000	48 c.c.
8.	90	4,390,000	42 c.c.
9.	90	4,390,000	47 c.c.
10.	80	4,460,000	48 c.c.
11.	80	4,470,000	43 c.c.
12.	82	5,040,000	50 c.c.
13.	80	5,000,000	48 c.c.
14.	90	4,490,000	48 c.c.
15.	90	5,040,000	50 c.c.
16.	88	4,510,000	43 c.c.
17.	82	4,680,000	45 c.c.

FEMALES:

1.	80	4,390,000	47 c.c.
2.	80	4,790,000	45 c.c.
3.	80	4,690,000	45 c.c.
4.	80	4,630,000	44 c.c.
5.	80	4,270,000	45 c.c.
6.	85	4,280,000	46 c.c.
7.	80	4,350,000	44 c.c.
8.	86	4,600,000	44 c.c.
9.	80	4,120,000	43 c.c.

The above findings gave a range of Haemoglobin (Sahli) of 80% to 95% with an average for men of 85.58% and for women of 81.22%. Thus the figure of 85% Hb. was considered to be normal for my haemoglobinometer and equal to 14.8 gramms Haemoglobin. All haemoglobin estimations in anaemic patients, performed on my Sahli haemoglobinometer, were therefore

adjusted to 100% = 14.8 gramms haemoglobin which is the average normal. In all the cases described in this paper, the haemoglobin (Hb.) is expressed in this "corrected" form.

In the above series, the red cell count (R.B.C.) was within normal limits, with a range of 4,120,000 per cubic mm. to 5,210,000 per cubic mm., and an average of 4,606,538 erythrocytes per cubic mm.

The packed cell volume estimation (P.C.V.) in the series ranged from 42 c.c. per cent to 50 c.c. per cent, with an average for men of 46.8 c.c. and an average for women of 44.7 c.c. The normal P.C.V. for men is 47 c.c. and that for women is 42 c.c. (Whitby, L. & Britton, C.J.C. 1950, "Disorders of the Blood", p.p. 51, 54, 60).

Diagnosis of Anaemia: Anaemia was considered to be present if a patient had a haemoglobin under 80% or a red cell count under 4,000,000 per c.mm. or a packed cell volume below 40 c.c. per cent. Using these standards, I encountered 170 patients with anaemia during the period 1944-52.

Classification of Anaemia: (1) The Blood Film. A blood film was performed in all severe anaemias and was more informative than indices or absolute

values in determining the type of anaemia present. In the more moderate anaemias, cell shape and size could be judged from their appearance in the counting chamber while the red cell count was being performed ("Notes on Clinical Laboratory Methods", 1952, University of Glasgow, p.46). This saved much time and if this milder type of anaemia did not respond rapidly to treatment with iron, then a blood film was performed.

(2) The Colour Index - This is the haemoglobin percentage (calculated from 14.8 g. Hb. = 100%) divided by the red cell percentage (calculated from 5,000,000 red cells per c.mm. = 100%) and is normally equal to 1 (Whitby, L. & Britton, C.J.C., 1950, "Disorders of the Blood", p.58). It used to be taught that a colour index of less than 1 signified iron deficiency and that a "high" colour index, i.e. greater than 1, occurred only in macrocytic anaemias (Osler, W., 1938, "Principles and Practice of Medicine", p.p.911, 919). This dictum I found unreliable, as in 157 patients with normocytic or microcytic anaemias, over 50 per cent had a colour index greater than 1, e.g.

Colour Index	No. of Patients
Under 1	72
1 to 1.1	31
1.1 to 1.2	25
1.2 to 1.3	15
1.3 to 1.4	8
1.4 to 1.5	6
	157

As expected, 13 patients with definite macrocytic blood pictures all had a "high" colour index whilst under treatment, although one patient with pernicious anaemia had a "low" colour index (less than 1) when first seen. This is due to the macrocytic cells being only partially filled with haemoglobin when an iron deficiency is present in addition to pernicious anaemia (Whitby, L. & Britton, C.J.C., 1950 "Disorders of the Blood", p.56). For example, a male, A.F. aged 71 years had lemon yellow icterus and signs of subacute combined degeneration when first seen on 17.9.44. His blood film showed macrocytosis, anisocytosis, poikilocytosis and polychromasia and the blood count was Hb. = 25%, R.B.C. = 1,400,000, W.B.C. = 2,600 and Colour Index = .89. He was maintained on liver therapy for eight years and died on 23.6.52 from chronic nephritis with oedema. On 11.9.46 he had a slight relapse due to inadequate maintenance therapy with liver. His blood showed P.C.V. = 34, Hb. = 88%, R.B.C. = 2,290,000

and the Colour Index = 1.95 was on this occasion in keeping with the other findings of pernicious anaemia. (3) The Packed Cell Volume - This is the volume of packed red cells per 100 c.c. of blood and is obtained by centrifugalising an exact quantity of venous blood to which an anti-coagulant has been added until such time as the packed volume of cells is constant. This investigation was performed in 113 of the 170 anaemic patients. It was of use in confirming the presence of anaemia, as only 3 of the patients examined had a packed cell volume above 42 c.c. which is the lowest normal figure (Whitby, L. & Britton, C.J.C., 1950, "Disorders of the Blood", p.p. 60, 655), e.g.

Packed Cell Volume (c.c.)	No. of cases
43 to 44	3
40 to 42	17
30 to 39	71
20 to 29	19
Under 20	3
	113

The haematocrit was also helpful in distinguishing the pale serum commonly seen in severe iron deficiency anaemias from the icteric serum commonly seen in pernicious anaemia, due to the low icterus index in the former and the raised icterus index in the latter (Whitby, L. & Britton, C.J.C., 1950, "Disorders of

the Blood", p.p. 202, 215).

(4) Mean Corpuscular Volume (M.C.V.) - This is the volume of packed red cells in c.c. per litre of blood divided by the red cells in millions per c.mm. The normal range is 78 to 94 cubic microns. An M.C.V. below this range would, in theory, suggest microcytosis and an M.C.V. above this range would indicate macrocytosis (Whitby, L. & Britton, C.J.C., 1950, "Disorders of the Blood", p.60). I found that the M.C.V. was raised above the normal range in all of nine cases of macrocytic anaemia and coincided with blood film appearances, but in the iron deficiency anaemias the M.C.V. was occasionally very misleading, e.g.,

Macrocytic Anaemias:-

Case	Diagnosis	HB. %	R.B.C. per c.mm.	P.C.V. in c.c.%	M.C.V. in c. microns
1.	Pernicious Anaemia	70	2,300,000	34	147
2.	Pernicious Anaemia	88	2,290,000	34	148
3.	Pernicious Anaemia	94	2,540,000	37.5	147
4.	Pernicious Anaemia	94	3,740,000	42	112
5.	Pernicious Anaemia	47	1,130,000	24	212
6.	Pernicious Anaemia	74	2,750,000	39	141
7.	Pernicious Anaemia	58	2,080,000	27	129
8.	Myxoedema	76	1,970,000	37	187
9.	Undiagnosed (Pemphigus foliaceus)	58	1,400,000	25	178

Iron Deficiency Anaemias:-

1.	Menorrhagia	43	3,210,000	22	68
2.	Pregnancy	49	3,280,000	23	70
3.	T.B. salpingitis	52	4,110,000	33	80
4.	Monocytic leukemia	47	1,890,000	22	116
5.	Pregnancy	56	2,320,000	28	116
6.	Abortion	49	1,580,000	21	132

In the latter table, cases 1, 2 and 3 show a mean corpuscular volume in keeping with the actual cell size as judged from microscopical appearance, but in cases 4, 5 and 6 the M.C.V. gives a false impression of macrocytosis which did not exist.

It is interesting to consider the discrepancies I observed between blood film appearances and the estimations of colour index and mean corpuscular volume, in view of the modern trend to discard both these latter values as worthless. The explanation of the inaccuracy of the colour index and the mean corpuscular volume is, according to Discombe (British Medical Journal, 1954, I, 327) because they depend on the red cell count in their calculation. Discombe thinks that the red cell count should be abandoned as it is, for various reasons, a grossly inaccurate estimation even when performed by experts. Discombe advises for a full blood examination - (1) an Hb. estimation performed on a colorimeter; (2) a packed cell volume estimation and (3) a blood film. He diagnoses macrocytic anaemia from the blood film, and iron deficiency from mean corpuscular haemoglobin concentration obtained by the calculation:-

$$\frac{\text{Hb. in grams per 100 c.c.}}{\text{Packed cell volume in c.c. per 100 c.c.}} \times 100.$$

The normal range is 32-38 per cent and figures below 32% indicate iron deficiency.

It is thus obvious that for really accurate blood examination, a laboratory equipped with a colorimeter, as well as a centrifuge, is essential.

Where the practitioner has access to such a laboratory it is, clearly, advisable for him to have all his blood examinations done there. In country practice, where this is impossible, it is still the responsibility of the practitioner to detect anaemia and it is here that there is still a use for the Sahli haemoglobinometer and the blood counting pipettes. Using the method already described I was satisfied that a reasonable degree of accuracy in diagnosis of anaemia was obtained in my series of cases, and it was gratifying to find that my estimations compared favourably with those of the haematologists, on the occasions when my anaemic patients required hospital treatment.

MACROCYTIC ANAEMIAS.

There were 13 patients encountered with definite macrocytic anaemia during the years 1944-52, e.g.,

Pernicious anaemia	9 patients
Myxoedema	2 "
Leuco-erythroblastic anaemia	1 "
Undiagnosed	1 "

The Diagnosis of Pernicious Anaemia (P.A.):-

According to Whitby & Britton, to establish the diagnosis of P.A., the following signs must be present ("Disorders of the Blood", 1950, p.p. 218, 220).

1. A macrocytic anaemia
2. Glossitis
3. Central Nervous System Changes (subacute combined degeneration)
4. A raised icterus index (lemon yellow appearance of skin and serum)
5. Urine containing excess urobilinogen
6. Faeces negative for occult blood
7. Achlorhydria (after histamine)
8. A reticulocyte response after starting liver therapy (demonstrated by Cresyl blue staining of blood film).

The above investigations are all within the scope of the general practitioner but, in addition, three further investigations now seem necessary for a complete diagnosis.

9. A barium meal X-ray examination to eliminate gastric carcinoma. The association of P.A. and gastric carcinoma has been observed by Bourne (British Medical Journal, 1948, 1, 92) and Mosbech & Videbaek (British Medical Journal, 1950, 2, 390). Scott (British Medical Journal, 1950, 2, 159) recommends a Ba. meal X-ray once a year for all P.A. cases.

10. A "megaloblastic" bone-marrow. Davis & Brown (Practitioner, March 1952, p.224) indicate the need for sternal puncture to distinguish the macrocytic anaemia of pernicious anaemia which has a megaloblastic bone marrow, from the macrocytic anaemias with normoblastic bone marrow reaction, seen occasionally in haemolytic syndromes, leukemias, aplasia, scurvy and myxoedema.

11. Faecal fat estimation. Conway (British Medical Journal, 1952, 1, p.1098) discovered latent steatorrhoea in four comparatively young adult patients with blood pictures and marrow reactions similar to those occurring in pernicious anaemia, all of whom had been wrongly diagnosed as cases of pernicious anaemia several years previously at the Western Infirmary, Glasgow. An abnormally high faecal fat content distinguishes such cases from true pernicious anaemia. According to Discombe (British Medical Journal, 1954, 1, 386) 90% of ingested fat is absorbed and only 10% excreted. Steatorrhoea is present if more than 10% of ingested fat is excreted in the faeces.

The latter three investigations can only be performed in hospital and as they are of considerable importance one must question whether or not it is advisable to diagnose pernicious anaemia without hospital confirmation of the diagnosis. The following case is an example of pernicious anaemia diagnosed and treated at home and shows that a fairly complete examination is possible.

CASE 1. R.Y., male aged 61 years, was seen by me in March, 1952 when he was confined to bed with fatigue of three months duration. He complained

of retching and a sore tongue. He had cardiac failure with oedema and there was lemon yellow icterus of his skin, extreme pallor of conjunctival and buccal mucosa and a marked glossitis. Blood examination showed Hb. = 52%, R.B.C. = 1,650,000, W.B.C. = 2,200 with an icteric serum. The film showed pronounced macrocytosis with also anisocytosis, poikilocytosis and polychromasia. The urine contained an excess of urobilinogen, giving a deep red colour with Ehrlich's aldehyde reagent (Notes on Clinical Laboratory Methods, 1952, p.p. 24, 25). The faeces were negative for occult blood to both guaiacum and benzidine tests. The gastric juice showed a total achlorhydria, with Topfer's reagent, after the injection of 0.5 mgm. histamine subcutaneously. On the fifth day of treatment with liver, there was a reticulocytosis of 15 per cent. This patient made an excellent recovery and is now well controlled with regular liver therapy and blood counts (under the supervision of Dr. J.F.C. Waterston of Lochwinnoch).

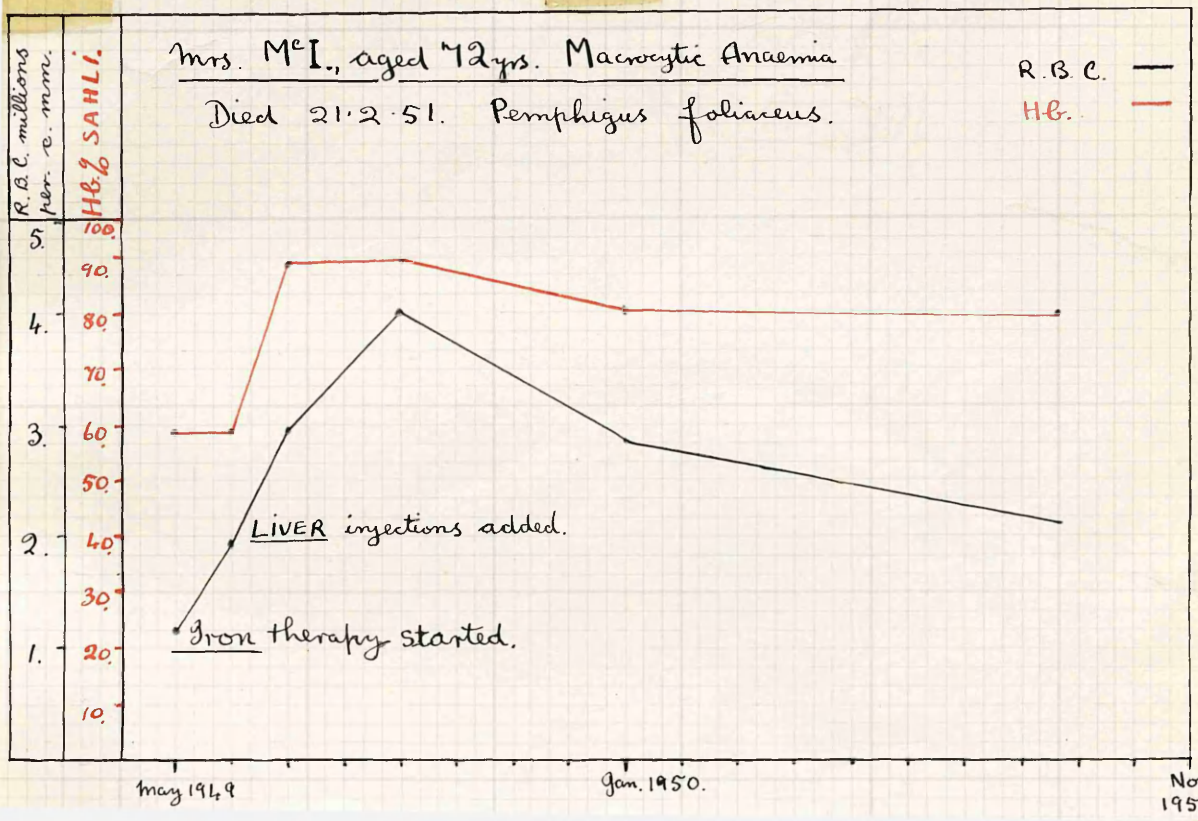
Not all macrocytic anaemias were so straightforward, however, as on several occasions I encountered patients with severe anaemia showing macrocytosis, which did not respond to liver therapy.

In these cases a bone marrow biopsy would have been a decided advantage before starting treatment as this would probably have revealed either a megaloblastic anaemia likely to respond to liver, or a normoblastic reaction in which case liver therapy would be useless. Because this information was lacking, errors in the diagnosis and treatment of macrocytic anaemias arose, which are illustrated by the following cases:-

CASE 2. W.A., male aged 66 years, complained on 5.3.46 of fatigue of one year's duration. He had a good appetite and had not lost weight. Physical examination was negative apart from obvious pallor and anaemia. P.C.V. = 22, serum clear, Hb. = 37%, R.B.C. = 2,300,000. The colour index = .8 and the M.C.V. = 95 cubic microns were against the diagnosis of macrocytic anaemia, but the blood film showed some macrocytosis, anisocytosis, polychromasia and an occasional normoblast. The absence of icterus in the serum was against the diagnosis of pernicious anaemia. Pulmonary tuberculosis was eliminated by a negative X-ray examination before starting treatment with liver. This was necessary as the patient's brother with whom he lived (they had slept in the

same bed for many years) had just been diagnosed as an advanced case of pulmonary tuberculosis. The patient did not respond to liver therapy. His reticulocyte count on the first, second, third and fifth days after the start of liver therapy was less than 1 per cent and on 27.3.46 the blood showed no improvement with P.C.V. = 22, serum clear, Hb. = 42%, R.B.C. = 2,770,000. The patient was now referred to the Western Infirmary, Glasgow, where, after initial negative barium meal x-ray examinations, an extensive carcinoma of the stomach was finally demonstrated. He died on 20th June 1946.

CASE 3. Mrs. Mc.I., aged 72 years, was seen in May, 1949 with a severe anaemia. Physical examination was negative but there was a history of bleeding piles. The blood was P.C.V. = 25, serum faintly icteric, Hb. = 58%, R.B.C. = 1,400,000, and W.B.C. = 5,000. The film, as in Case 2, showed some macrocytosis which was not so pronounced as that seen in pernicious anaemia. There was also anisocytosis but no poikilocytosis and no polychromasia. On this occasion a trial course of iron and ammonium citrate (gr. 30 t.i.d.) was given but, although the patient had no bleeding from her haemorrhoids, the anaemia


Mrs. McI., aged 72yrs. Macrocytic Anaemia
Died 21·2·51. Pemphigus foliaceus.
R.B.C. millions per c. mm.
HB % SAHLI.
R.B.C.
H.B.
5.
4.
3.
2.
1.
100
90
80
70
60
50
40
30
20
10
LIVER injections added.
Iron therapy started.
May 1949
Jan. 1950.
Nov. 1950

did not respond. After four weeks of iron therapy the blood in June, 1949 was P.C.V. = 28, serum icteric, Hb. = 58%, R.B.C. = 1,920,000 with colour index = 1.7 and M.C.V. = 145 cubic microns. Liver therapy was now commenced and the initial response was encouraging. By September, 1949 the P.C.V. = 42, the serum was now clear, Hb. = 88% and R.B.C. = 4,010,000. At this point the faeces were negative for occult blood and a test meal showed achlorhydria with Topfer's reagent, after histamine. This patient had responded to liver therapy like a case of pernicious anaemia although the blood film at no time showed the pronounced macrocytosis characteristic of that condition. In December, 1949 however, the patient's condition commenced to deteriorate and the blood showed a fall despite regular and intensive liver therapy and because of this she was admitted to the Western Infirmary, Glasgow, where a post-haemorrhagic anaemia was diagnosed, probably due to bleeding piles. By September, 1950 despite further liver and iron therapy, the blood had dropped to Hb.=76%, R.B.C. = 2,180,000, and W.B.C. = 5,200. The patient now developed a generalised vesicular skin eruption with severe toxaemia and died in the Southern General Hospital,

Glasgow in February, 1951. The skin disease was diagnosed by Dr. James Sommerville as pemphigus foliaceus. At autopsy no abnormality was found apart from "a fatty right ventricle".

These two cases show how much one is working in the dark in the diagnosis and treatment of macrocytic anaemias when the state of the bone marrow is not known. In the absence of this information one cannot be certain of interpreting correctly the varying degree of macrocytosis seen in blood films of severe anaemias. This macrocytosis could be due to (1) megaloblastic marrow reaction; (2) macro-normoblastic erythropoiesis or (3) to a relatively large number of circulating reticulocytes. The latter could be demonstrated by counter-staining with cresyl blue after Leishman's stain (Whitby & Britton, 1950, p.639).

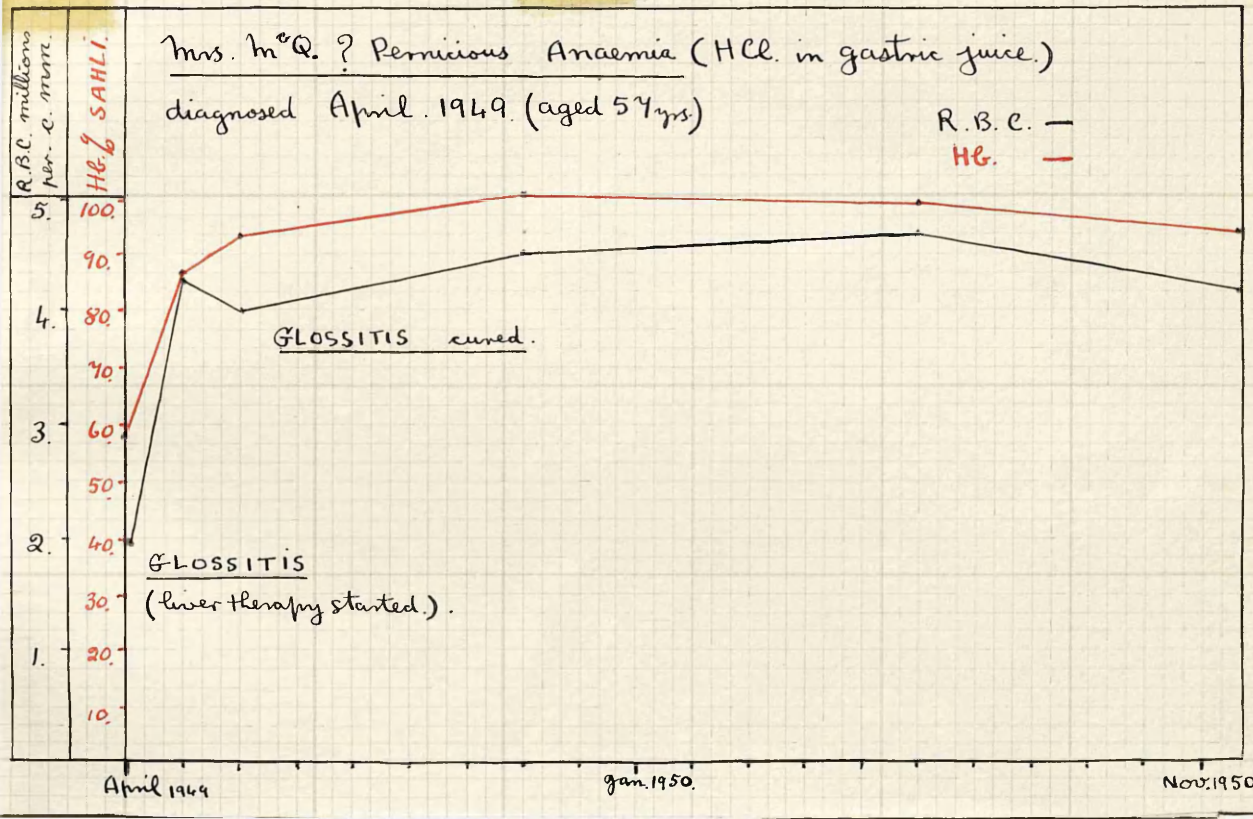
Several other problems arose in the interpretation of severe anaemias showing macrocytosis, e.g.,

CASE 4. Showed leuco-erythroblastic anaemia. Mrs. I., a widow aged 80 years, was confined to bed in January, 1951 with sickness, loss of appetite and extreme weakness, and pain in her chest and back. Examination showed emaciation, pallor, an enlarged

liver and tenderness over ribs and vertebrae. The blood was Hb. = 47%, R.B.C. = 1,113,000 and W.B.C. = 16,800. The film was mainly normocytic but showed some macrocytosis, anisocytosis, poikilocytosis and polychromasia. Primitive red cells were present which resembled early and late normoblasts and there was a relative lymphocytosis, the differential white cell count being neutrophil polymorphs 16%, small lymphocytes 48%, large lymphocytes 30% and monocytes 6%. The bone tenderness, enlarged liver, the fact that the anaemia was not predominantly macrocytic, the leucocytosis and the primitive red cells seen in the blood film were suggestive of malignant disease with bone involvement producing a leuco-erythroblastic anaemia. I informed the patient's relatives that she probably had cancer, but they decided against her removal to hospital for confirmation of this diagnosis and she died at home a few weeks after my initial examination on 20.2.51.

CASE 5. Showed an anaemia identical with pernicious anaemia but without achlorhydria. Mrs. McQ., aged 57 years, was seen in April, 1949 complaining of fatigue, nausea and a sore tongue. Examination

showed a slightly jaundiced woman with pallor of buccal mucosa and glossitis. The faeces were negative for occult blood but a test meal showed free hydrochloric acid after histamine. The blood showed P.C.V. = 27, the serum was icteric, Hb. = 58%, R.B.C. = 2,050,000, W.B.C. = 2,800 and the blood film showed pronounced macrocytosis with polychromasia, anisocytosis, poikilocytosis and multi-lobed polymorphs. On treatment with liver this patient gained strength rapidly and her jaundice and glossitis disappeared. After eight weeks on liver treatment the blood was, in June 1949, P.C.V. = 42, serum was now clear, Hb. = 94%, and R.B.C. = 4,030,000. Since then this patient has been receiving liver therapy regularly and her blood has never had a red cell count below 4 millions per c.mm. She is still (1953) in good health. The finding of free HCl. in the gastric juice is a distinctly rare occurrence in pernicious anaemia (Whitby & Britton, 1950, p.220). Askey (Year Book of General Medicine, 1944), investigated 47 similar cases and found that none was a true case of Addisonian pernicious anaemia. A possible explanation of this case may be that Topfer's reagent was used to test for free HCl.


Mrs. McQ. ? Pernicious Anaemia (HCl. in gastric juice.)
diagnosed April. 1949. (aged 57 yrs.)
R.B.C. millions per c. mm.
Hg. % SAHLI.
R.B.C. —
Hg. —
5.
4.
3.
2.
1.
100.
90.
80.
70.
60.
50.
40.
30.
20.
10.
GLOSSITIS cured.
GLOSSITIS
(liver therapy started.).
April 1949
Jan. 1950.
Nov. 1950

in the gastric juice of this patient. This indicator turns from orange to red in the presence of free HCl. but may also do so when HCl. is absent. This error occurs when a relatively large amount of organic acid is present in the gastric secretions. The more specific Gunzberg test was not performed on this patient's gastric juice. This test consists of heating, in a crucible, small quantities of phloroglucin and vanillin together with 1 c.c. of absolute alcohol and 1 drop of filtered gastric juice. A red colour appears if free HCl. is present (Panton, P.N. and Marrack, J.R., 1945, "Clinical Pathology", page 330, 331).

CASE 6. Showed how misleading the "gastric crisis" in pernicious anaemia could be. In December, 1942 I was called to see a widow, Mrs. C., aged 72 years, who was believed to be dying of cancer of the stomach. The patient had just arrived by ambulance from a neighbouring town to be nursed, during the last stages of her illness, by a relative who lived in my area. A few weeks earlier this patient had been examined at the Out-Patient Department of the Western Infirmary, Glasgow, where the diagnosis of gastric cancer had been presumed. The patient had been

considered too weak for X-ray confirmation of this diagnosis.

She gave a history of increasing fatigue during the previous year and of nausea and vomiting for two months, associated with rapid loss of weight. At first glance she looked a typical case of advanced cancer of the stomach. She was extremely emaciated, dehydrated and collapsed. She was retching repeatedly and could swallow only sips of water. There was pallor of conjunctival and buccal mucosa, and she was also slightly jaundiced. There was epigastric tenderness in the region of the pylorus. I informed the patient's relatives that there seemed little I could do apart from treating the anaemia which was obviously present. After examining the blood, however, it seemed possible that an error in diagnosis had been made. The blood film showed a grossly macrocytic picture with anisocytosis, poikilocytosis and polychromasia and the red cell count was in the region of one million per c.mm. (the figures of this initial blood count were not kept). A trial course of liver therapy was commenced and a most spectacular recovery resulted. The patient's sickness and nausea rapidly disappeared

and she gained weight and strength so quickly that she was able to be out of bed after four weeks. She was no longer jaundiced and her epigastric tenderness had gone. Subsequent examination showed a tendency to arteriosclerosis with radial arteries palpable and tortuous, B.P. 120/80, urine sp. gr. 1015 with a trace of albumin but no casts; faeces negative for occult blood and test meal showing achlorhydria, with both Gunzberg and Topfer's reagents, after histamine. This patient, now aged 84 years, is still leading an active outdoor life (1954) having been on maintenance liver therapy for the past 12 years.

The relationship of pernicious anaemia to cancer of the stomach should always be kept in mind as the following case shows:-

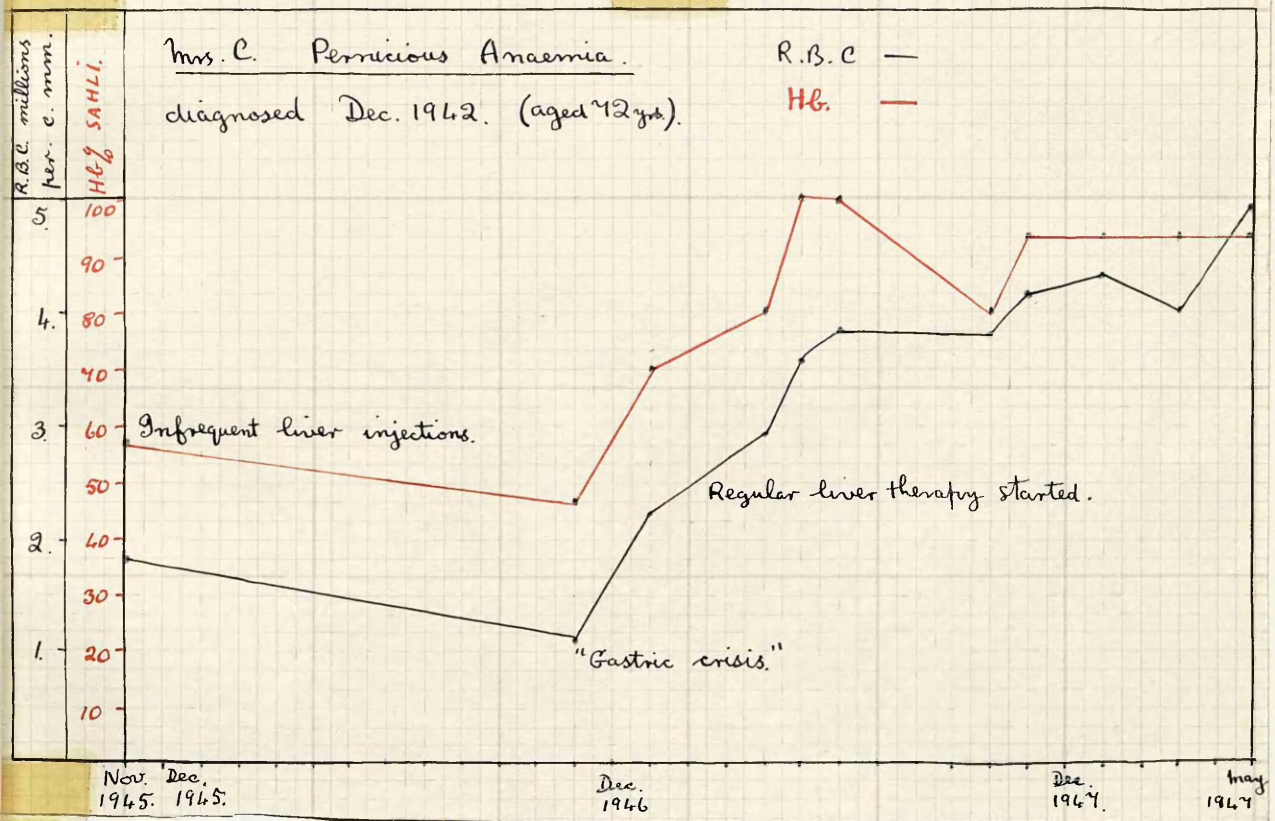
CASE 7. A spinster, M.K., aged 58 years, complained in September, 1943 of extreme fatigue. She had, a short time before, been nursing her mother who died from cancer of the rectum, and was very worried in case she had contracted this disease herself. Physical examination (including rectal examination) showed no abnormality apart from a faint lemon yellow icterus of her skin and blood examination showed a

pronounced macrocytic anaemia (the figures of the initial blood examination in this case have been lost). I referred this patient to the late Mr. J. Scoular Buchanan at the Western Infirmary, Glasgow. Mr. Buchanan could find no evidence of malignancy and recommended treatment for the anaemia. Liver therapy was commenced immediately and the patient responded rapidly, being able shortly to resume work as a french polisher. A test meal was performed subsequently and showed achlorhydria, after histamine, to both Gunzberg's and Topfer's reagents. She was maintained, well and at work, on liver therapy for 10 years until 1953 when she developed cancer of the stomach from which she died in March, 1954. (I am indebted to Dr. J.F.C. Waterston of Lochwinnoch for this latter information). This is the only instance of a case of pernicious anaemia developing cancer of the stomach that I have encountered.

THE TREATMENT of PERNICIOUS ANAEMIA.

A count of at least 5 million per c.mm. and not less than 4,500,000 is the ideal to be aimed at in maintenance treatment of P.A. (Whitby & Britton, "Disorders of the Blood", 1950, p.236), but Blackburn et al (British Medical Journal, 1952, II, p.245) have demonstrated that this ideal is seldom achieved in practice. They observed very low blood levels in cases of P.A. referred by general practitioners in Sheffield to the Sheffield Royal Infirmary for a check blood count. In addition, these haematologists had twenty two cases of P.A. under observation for some years at a blood clinic at Sheffield Royal Infirmary. In spite of regular liver therapy, none of these cases had a blood count over 5 million and two patients had a count under 4 million.

My early attempts at the management of pernicious anaemia in practice were disappointing. Indeed, the treatment of Mrs. C., my first case of P.A., (Case 6 above) is a good example of how not to treat pernicious anaemia. Diagnosed as P.A. in 1942, this patient seemed reasonably well on irregular liver therapy until October, 1945 when she had a relapse. Her blood then was P.C.V. = 34, Hb. = 58%,


Mrs. C. Pernicious Anaemia.
diagnosed Dec. 1942. (aged 42 yrs).
R.B.C —
Hb. —
R.B.C. millions per. c. mm.
Hb% SAHLI.
5
4.
3.
2.
1.
100
90
80
70
60
50
40
30
20
10
Infrequent liver injections.
Regular liver therapy started.
"Gastric crisis."
Nov. 1945.
Dec. 1945.
Dec. 1946
Dec. 1947.
May 1947

R.B.C. = 1,730,000, W.B.C. = 2,400. A year later in October, 1946 she had a return of her initial symptoms of vomiting and collapse. The blood was now P.C.V. = 24, serum icteric, Hb. = 47%, R.B.C. = 1,130,000, colour index = 2.1 and M.C.V. = 212 cubic microns with film grossly macrocytic. Since 1946 further relapse has been prevented by regular blood examination performed by myself, and regular liver therapy administered by the district nurse. This patient also showed how difficult it is to treat adequately the arteriosclerotic patient with P.A. (Whitby & Britton, 1950, p.232), as it was not until December, 1947, after fourteen months intensive liver therapy, that a satisfactory count was obtained in this case. The blood was then P.C.V. = 43, Hb. = 94%, R.B.C. 4,230,000. Since then the count has remained above 4 million with a maintenance dose of 2 c.c. anahaemin fortnightly.

The need for careful control of pernicious anaemia cases in practice to prevent serious relapse was further impressed upon me by encountering the following patient in August, 1944. R.B., a male aged 53 years, had been diagnosed at the Western Infirmary, Glasgow in 1940 as a case of pernicious anaemia. Since then he had been under the care of

a general practitioner in Glasgow. He had never had a check blood count and had been told to come to his doctor's surgery for a liver injection "whenever he felt tired". He complained to me of excessive fatigue, sore tongue, dyspnoea on exertion, cough with white frothy sputum and "pins and needles" in his arms and legs. Examination showed a well marked glossitis, congestion of lung bases and central nervous system changes in the form of absent abdominal reflexes, exaggerated knee jerks and impaired touch sensation. The blood was Hb. = 98%, R.B.C. = 3,400,000, W.B.C. = 1,400 and colour index = 1.4. The film showed a macrocytic anaemia with anisocytosis, polychromasia and multilobed polymorphs. His gastric juice, after histamine injection, showed total achlorhydria to both Gunzberg and Topfer's reagents. Since 1944 this patient has visited me regularly for blood counts and has remained well and at work to date (1953) on regular liver therapy. There has been no recurrence of glossitis or fatigue since 1944.

Further experience of maintenance therapy in P.A. cases was similar to that of Blackburn, mentioned above. In spite of regular supervision and treatment it was extremely difficult to obtain satisfactory

blood counts as the following table shows. It illustrates the blood count in four cases of pernicious anaemia during a four year period of observation. The four patients had been receiving liver treatment previously.

Cases 3 and 4 have been described previously in detail and Case 2 has been mentioned already as an example of iron deficiency in pernicious anaemia. Case I, S.M., male aged 46 years, was a foundry worker who had obvious melaena in March, 1944. His blood showed Hb. = 56%, R.B.C. = 1,540,000 and W.B.C. = 1,000. The blood film was mainly normocytic with some macrocytosis, anisocytosis and scanty multi-lobed polymorphs. The anaemia responded to liver and iron, and barium meal x-ray examinations at Glasgow Royal Infirmary in May and November 1944 were normal. In December, 1944 the patient had a haematemesis and his blood was Hb. = 61%, R.B.C. = 1,300,000 and W.B.C. = 1,000. The film again showed some degree of macrocytosis. The patient was now investigated in the Glasgow Western Infirmary. Barium meal x-ray was again normal and he was treated as a case of pernicious anaemia, relatively huge doses of parenteral liver being necessary before the blood

responded. Test meals were performed both in hospital and at home. The latter, after histamine injection, showed total achlorhydria to both Gunzberg and Topfer's reagents.

Several tests of faeces have since been negative for occult blood, and the patient has remained well and at work for the past ten years on regular liver therapy.

Case 2. A.F., male aged 71 years, complained of extreme fatigue in September, 1944. He showed pallor and lemon yellow icterus of his skin. His left leg was slightly spastic. His blood showed Hb. = 27%, R.B.C. = 1,400,000 and W.B.C. = 2,600. The film showed gross macrocytosis, anisocytosis, poikilocytosis and polychromasia. The test meal, after histamine, showed total achlorhydria to both Gunzberg and Topfer tests and the faeces were negative for occult blood to both guaiacum and benzidine tests. The B.P. 160/80 and the urine showing a trace of albumin and a low specific gravity of 1010 were significant also, as this patient had been treated in 1929 for "kidney trouble" at Glasgow Royal Infirmary. He became rapidly well on liver therapy and his pallor and jaundice disappeared although some

spasticity persisted in his left leg, which suggested that subacute combined degeneration of the spinal cord was present. This patient died on 23.6.52 of chronic nephritis with oedema.

P.A. Maintenance Therapy with Liver Extract.

Case No.		1945	1946	1947	1948
1. S.M.	Range	3,480,000 to 4,300,000	2,650,000 to 3,360,000	2,300,000 to 5,100,000	4,390,000 to 4,830,000
	Average	3,760,000	3,790,000	3,930,000	4,620,000
2. A.F.	Range	3,070,000 to 4,500,000	2,290,000 to 3,630,000	3,970,000 to 5,420,000	4,240,000 to 5,010,000
	Average	3,790,000	3,090,000	4,510,000	4,590,000
3. R.B.	Range	3,940,000 to 4,500,000	2,540,000 to 3,750,000	2,530,000 to 5,100,000	4,240,000 to 5,830,000
	Average	4,230,000	3,050,000	3,900,000	4,930,000
4. M.K.	Range	3,500,000 to 4,600,000	3,260,000 to 3,690,000	3,310,000 to 4,910,000	4,310,000 to 5,050,000
	Average	4,010,000	3,470,000	4,120,000	4,750,000

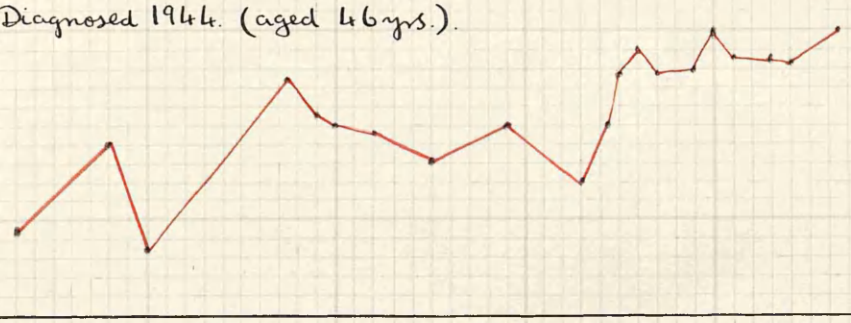
All four cases were inadequately controlled in the first three years of observation. Towards the end of the third year (1947) all four patients received relatively huge doses of anahaemin liver extract in an attempt to boost the marrow response (but Cases

P.A. Maintenance Therapy with Liver.

R.B.C. in millions per cubic millimetre.

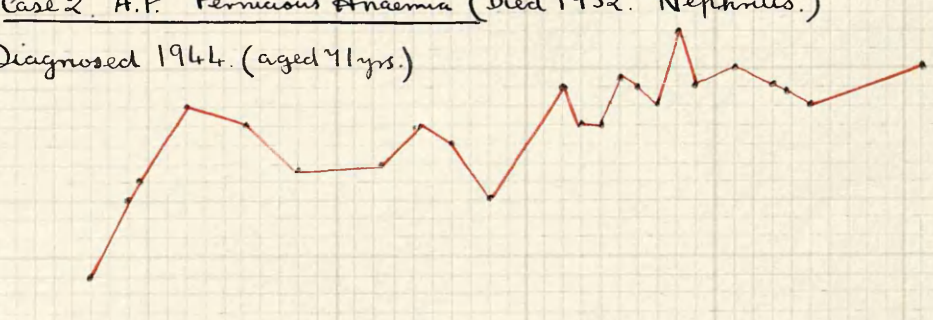
Case 1. S.M. Pernicious anaemia.

Diagnosed 1944. (aged 46 yrs.).



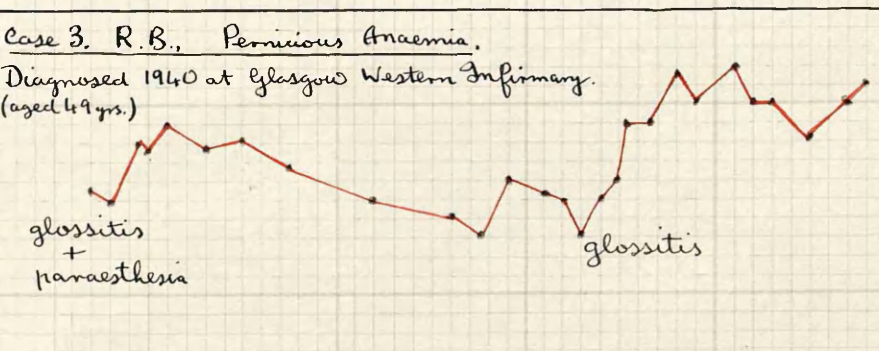
Case 2. A.F. Pernicious Anaemia (Died 1952. Nephritis.)

Diagnosed 1944. (aged 41 yrs.)



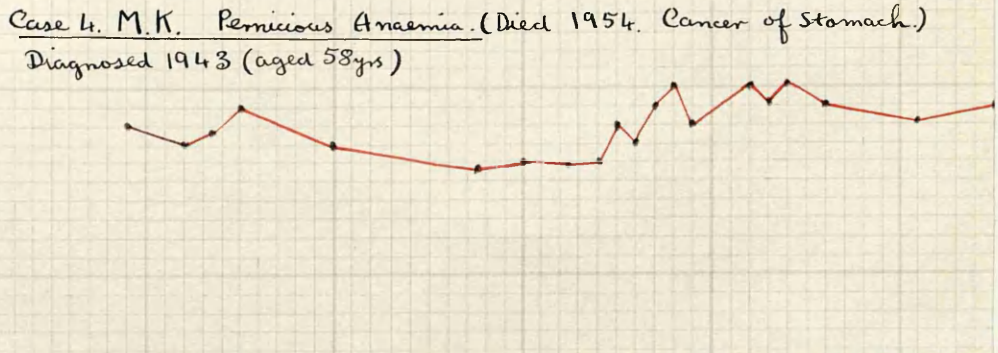
Case 3. R.B., Pernicious Anaemia.

Diagnosed 1940 at Glasgow Western Infirmary. (aged 49 yrs.)



Case 4. M.K. Pernicious Anaemia. (Died 1954. Cancer of Stomach.)

Diagnosed 1943 (aged 58 yrs)



Dec. 1943. | Dec. 1944. | Dec. 1945. | Dec. 1946. | Dec. 1947. | Dec. 1948.

3 and 4 required oral proteolysed liver in addition) before the blood counts remained above 4 million per cubic mm. Since then, normal maintenance doses of 2 c.c. anahaemin fortnightly have been sufficient to maintain the blood at this level in the four patients.

CONCLUSION:- The interpretation in general practice of anaemias showing macrocytosis is extremely difficult. To determine whether or not liver therapy is indicated in such cases, the diagnosis of macrocytic anaemia should be confirmed in hospital by a trained haematologist and the bone marrow reaction ascertained by marrow biopsy.

Although it is possible to diagnose cases of P.A. in practice with a reasonable degree of accuracy, the maintenance treatment of these patients demands the greatest care and can probably be best accomplished by referring all P.A. cases to blood clinics, which they should attend regularly for the rest of their lives.

IRON DEFICIENCY ANAEMIAS.

There were 157 cases of iron deficiency anaemias consisting of 130 females and 27 males. The etiology was as follows:-

Group 1. Anaemia during menstrual life

	No. of Patients
Uterine haemorrhage	58
Tuberculosis	9
Valvular disease of heart	7
Pregnancy	7
Miscellaneous conditions	12
	93

Group 2. Anaemia after the menopause

Malignant disease	10
Tuberculosis	4
Miscellaneous conditions	9
Etiology uncertain	14
	37

Group 3. Anaemia in men

Malignant disease	8
Tuberculosis	4
Haematemesis (simple)	4
Miscellaneous conditions	9
Etiology uncertain	2
	27

The tables indicate that uterine haemorrhage was the commonest cause of iron deficiency anaemia. Cancer and tuberculosis were the two main factors in the production of secondary anaemias. The

origin of the anaemia in 16 patients (14 females and 2 males) was uncertain. These will be discussed later under the appropriate sections.

Symptoms of Iron Deficiency Anaemia:-

(1) Fatigue was a constant symptom. It was surprising to find how long patients could tolerate fatigue before seeking advice. An outstanding example of this was A.W., a male aged 68 years, whose extreme pallor I had observed in the street for several months before he sought my advice. On 18.5.48 he came to my surgery complaining of fatigue and shortness of breath. He had a severe microcytic anaemia with the lowest haemoglobin I have encountered in a male in general practice, e.g. P.C.V. = 20, serum pale, watery, Hb. = 24%, R.B.C. = 2,060,000 and W.B.C. = 2,400. His faeces were positive for occult blood to both guaiacum and benzidine tests. His melaena continued but he refused to go to hospital and developed a large epigastric mass. He died within a year of seeking medical advice.

(2) Dyspepsia occurred in 29 patients with iron deficiency anaemia. In 23 patients, however, the anaemia was not the sole cause of dyspepsia, e.g.,

Disease	No. of Patients
Idiopathic hypochromic anaemia	6
Duodenal ulcer	5
Cancer of stomach	8
Tuberculosis	2
Pyloric stenosis	2
Uterine fibroid	1
Ovarian cyst	1
Rosacea	1
Anorexia nervosa	1
Chronic nephritis	1
Meningitis	1
	29

It is of interest to record that in both patients with pelvic complaints (fibroid and ovarian cyst) the removal of the tumour cured a very troublesome dyspepsia, presumably by lessening the tendency to menorrhagia and anaemia.

(3) Dysphagia was uncommon. Only two patients complained seriously of dysphagia (Plummer-Vinson Syndrome). Both patients responded well to iron therapy but in one of them slight dysphagia was still present two years after correction of the anaemia.

(4) Glossitis - A mild painless glossitis was common but only one patient had painful glossitis. This was present in one of the two patients with dysphagia and anaemia. The glossitis disappeared rapidly with the commencement of iron therapy for the anaemia.

(5) Paraesthesiae - Only one patient had a severe

neuritis. This took the form of severe tingling pains in the arms and legs. This patient had also pulmonary tuberculosis and diabetes mellitus. The diabetes was probably the cause of the neuritis.

(6) Fever due solely to anaemia was not observed. Fever did occur in Mrs. G., aged 46 years, who had a severe anaemia due to menopausal haemorrhage. In October, 1948 the blood was Hb. = 47%, R.B.C. = 3,780,000, W.B.C. - 3,800. During treatment with iron and rest in bed, this patient was fevered and had slight tremor of her hands. After four weeks rest the blood was normal, P.C.V. = 44, Hb. = 86%, R.B.C. = 4,766,000, but on being allowed out of bed the patient still showed tremor of her limbs. This patient later developed Parkinsonism. She had a further uterine haemorrhage in 1950 and was given an X-ray induction of the menopause at the Samaritan Hospital, Glasgow, where the condition of metropathia haemorrhagica was diagnosed. She died on 2.6.53.

The Degree of Anaemia present in 157 patients with iron deficiency anaemia can be judged from the following tables. The haemoglobin levels were the lowest recorded in each patient and are corrected to 100% = 14.8 g.Hb.

Haemoglobin %	No. of Patients
90 to 100	4
80 " 89	51
70 " 79	38
60 " 69	19
50 " 59	22
40 " 49	11
30 " 39	8
20 " 29	4
	157

The red cell counts corresponding to the lowest haemoglobin recorded in each case were per cubic millimetre:-

R.B.C.	No. of Patients
4.5 million to 5 million	11
4 " " 4.49 "	21
3.5 " " 3.99 "	55
3 " " 3.49 "	38
2.5 " " 2.99 "	15
2 " " 2.49 "	12
1.5 " " 1.99	4
1 " " 1.49 "	1
	157

The lowest haemoglobin recorded in a female was 22%, and in a male was 24%. The lowest recorded red cell count was, in a female, 1,480,000 per c.mm. and in a male, 1,560,000 per c.mm. In 32 patients the red cell count was above 4 million per c.mm. and was presumably due to a compensatory increase of erythrocytes, a common finding in chronic microcytic iron deficiency anaemias (Whitby & Britton, 1950, "Disorders of the Blood", p.201).

Both tables indicate that the majority of the patients had only a mild degree of anaemia. This finding is, on a small scale, in keeping with that of Davidson & Fullerton, who have previously indicated how common iron deficiency anaemia is. They found 50% of working class women in Aberdeen (1935) and Edinburgh (1943) had subnormal haemoglobin levels and 15% had severe anaemia ("Textbook of Medical Treatment", Dunlop, Davidson & McNee, 1946, p.398).

The Treatment of Iron Deficiency Anaemia:-

In anaemias resulting from uterine or other haemorrhage a rapid response to the administration of iron in full doses is to be expected in the absence of secondary disease or renewed bleeding. Normally there should be a rise in the patient's haemoglobin of 1 per cent each day provided inhibitory factors such as sepsis, toxaemia or haemorrhage are absent (Dunlop, Davidson & McNee, "Textbook of Medical Treatment", 1946, p.405). In this series of iron deficiency anaemias, the observation of response of haemoglobin level to iron therapy was of considerable value in distinguishing uncomplicated anaemias from those associated with infection or malignant disease, e.g.,

Case 1. Mrs. R., aged 38 years, with severe post-partum haemorrhage due to an abortion when four months pregnant.

Date	Hb.%	R.B.C. per c.mm.	P.C.V.	Rate of Rise in Haemoglobin %
22.5.47	49	1,580,000	21	45% Hb. in 36 days
27.6.47	94	4,460,000	-	

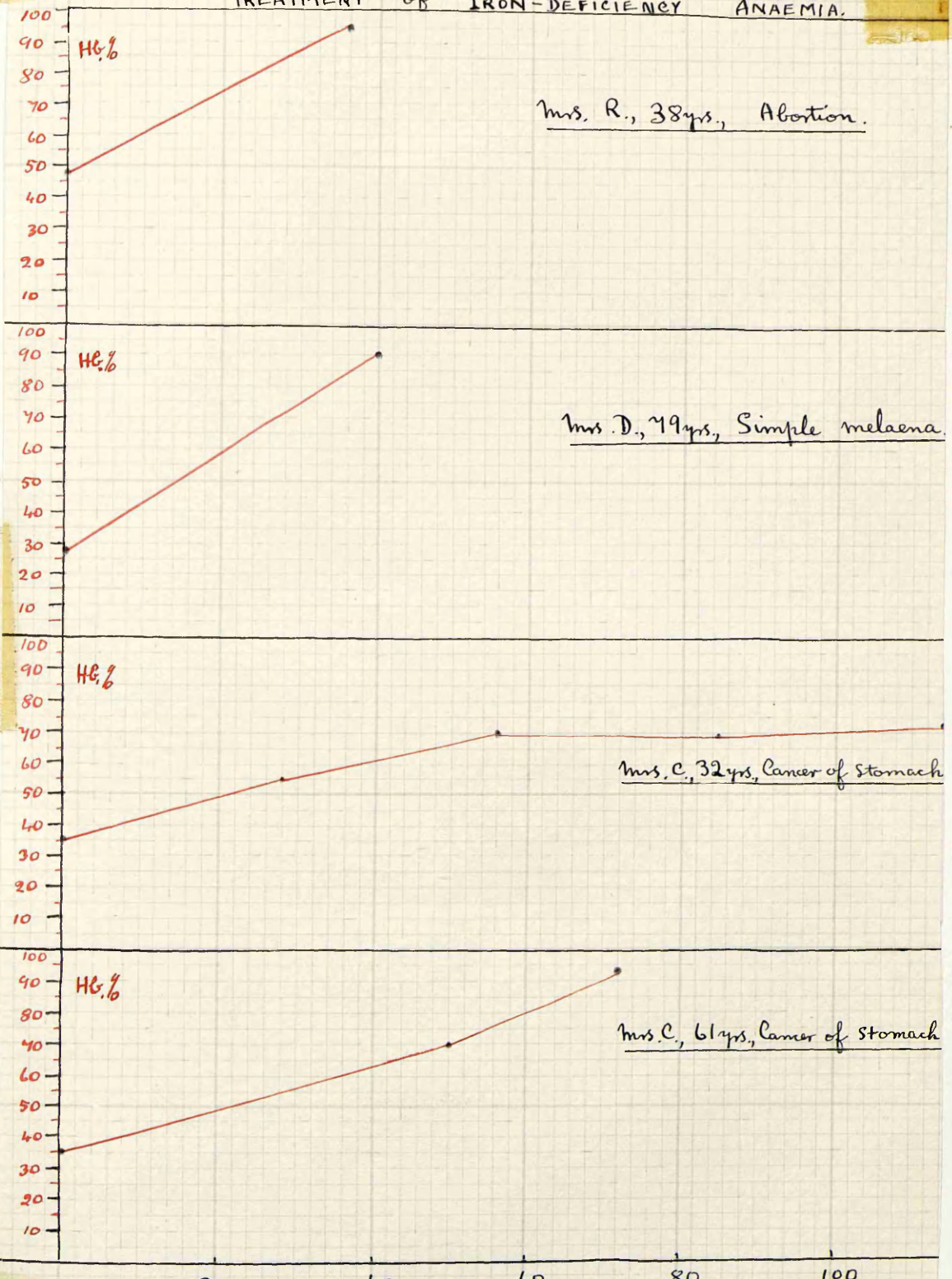
This represents a rapid recovery from anaemia at a rate of over 1% Hb. for each day of treatment with iron. A year later this patient had another abortion, e.g.,

Date	Hb.%	R.B.C. per c.mm.	P.C.V.	Rate of Rise in Haemoglobin %
8.8.48	68	3,130,000	31	26% Hb. in 23 days
31.8.48	94	-	-	

Thus this patient demonstrates a normal response to iron therapy on two occasions.

Case 2. Mrs. D., aged 79 years, had, in April, 1947, an anaemia due to a large gastro-intestinal haemorrhage. There was no evidence of malignant disease and the patient lived for four years after the haemorrhage. The haemorrhage may have been due to arteriosclerosis. The B.P. was 120/80, but there was chronic nephritis with a pale urine of specific gravity 1010 and containing a trace of albumin. A most remarkable recovery resulted from iron therapy, being much more than 1% Hb. rise per day of treatment.

TREATMENT of IRON-DEFICIENCY ANAEMIA.



Date	Hb.%	R.B.C. per c.mm.	P.C.V.	Rate of Rise in Haemoglobin %
9.4.47	29	2,150,000	21	59% Hb. in 39 days
18.5.47	88	4,100,000	44	

This case suggests that a normal response to iron occurs irrespective of the age of the patient. Arteriosclerosis was not an inhibiting factor.

By contrast, the following two patients showed a sluggish response to iron therapy. In both patients this observation was the first indication of the presence of serious disease.

Case 3. Mrs. C., aged 32 years, had a severe anaemia, the origin of which was obscure. There was no menorrhagia and physical examination and per vaginam examination were normal. The response of her anaemia was watched as follows:-

Date	Hb.%	R.B.C. per c.mm.	P.C.V.	Rate of Rise in Haemoglobin %
1.6.46	37	3,460,000	24	Less than 1% Hb. per day of treatment with iron
29.6.46	54	-	-	
26.7.46	70	-	-	
24.8.46	68	-	-	
21.9.46	72	3,780,000	40	

In September, 1946 this patient complained for the first time of sickness and "acid mouthfuls". She was referred to the Out-Patient Department of the Western Infirmary, Glasgow, where she was diagnosed as a case of microcytic anaemia with achlorhydria. In November, 1946 her sickness became much worse and

she was admitted to the wards of the above hospital. Although her barium meal x-ray was normal, a laparotomy performed on 21.11.46 showed an inoperable carcinoma of the stomach.

Case 4. Mrs. C., aged 61 years, had a severe anaemia on 29.1.48. There was no history of bleeding per vaginam and the faeces were negative for occult blood. Her appetite was good and she had not lost weight. Physical examination was entirely negative. In view of the severity of the anaemia, which was Hb. = 35% P.C.V. = 24, R.B.C. = 3,240,000 with pale clear serum and film microcytic, this patient was admitted at once to the Western Infirmary, Glasgow. She was discharged from hospital on 25.2.48 with the diagnosis of achlorhydria and simple microcytic anaemia. The table indicates the sluggish response of the blood, which followed the administration of iron:-

Date	Hb.%	R.B.C. per c.mm.	P.C.V.	Rate of Rise in Haemoglobin %
29.1.48	35	3,240,000	24	Less than 1% Hb. per day of treatment with iron
19.3.48	70	3,240,000	-	
10.4.48	88	4,280,000	-	

The final blood count above, although adequate, was achieved after a very sluggish rise in haemoglobin. In June, 1948 this patient complained for the first time of epigastric pains and sickness, and I found the faeces to be positive for occult blood to guaiacum and

benzidine tests. She was re-examined at the Western Infirmary, Glasgow, and now found to have an inoperable carcinoma of the stomach.

ANAEMIA DURING MENSTRUAL LIFE:- This was the most common type of anaemia encountered, there being 93 cases of anaemia in women during the child-bearing age, e.g.

Disease	No. of Patients
Idiopathic hypochromic anaemia	38
Anaemia associated with pelvic abnormality	20
"Secondary" anaemias	28
Pregnancy anaemias	7
	93

The diagnosis of idiopathic hypochromic anaemia is presumed in the 38 patients mentioned above, as there was no pelvic abnormality present nor any other condition which might cause anaemia. The main factors in producing anaemia in these patients would appear to be (1) menstruation and pregnancy; (2) diet deficient in iron and (3) defective absorption of iron caused by a tendency to achlorhydria (Dunlop, Davidson & McNee, "Textbook of Medical Treatment", 1946, p.398). A marked tendency to "chronic anaemia" was observed in this group of patients, e.g. 13 of the 38 patients with idiopathic hypochromic anaemia

were found to be still anaemic when examined at intervals of one to three years after the initial blood count. Regular courses of iron in large doses would appear to be necessary to prevent relapse in these patients. The following two cases show this tendency to chronic anaemia.

Case 1. Mrs. G., aged 40 years, para 2, was seen on 24.9.46 with complaint of fatigue and dizziness. She had menorrhagia, with menstrual periods regular, every three weeks but lasting six days. There was no pelvic abnormality. The blood was P.C.V. = 33, Hb. = 76% and R.B.C. 3,610,000. The patient took iron for three months and a year later, on 2.7.47, felt well and had a normal blood count of P.C.V. = 40, Hb. = 94% and R.B.C. = 4,010,000. After another year this patient's fatigue and dizziness returned and on 12.11.48 she was again anaemic with P.C.V. = 38, Hb. = 76% and R.B.C. = 4,060,000. She was given iron again but on 8.4.49 she was still anaemic with haemoglobin of 77%.

Case 2. Mrs. A., aged 31 years, para 2, complained of fatigue on 16.4.50. There was no pelvic abnormality and no menorrhagia but menstruation was irregular and infrequent, occurring approximately every seven weeks

and lasting six days. The blood was P.C.V. = 32, Hb. = 51% and R.B.C. = 3,140,000. After two months on iron, P.C.V. = 33, Hb. = 58% and R.B.C. = 3,470,000. A very poor response suggested either that the patient was having heavier menstruation or was not taking her iron prescription. A year later on 2.6.51, this patient felt and looked better. Her menstruation was now regular, every 28 days, lasted four days and had normal loss. She was, however, still anaemic with Hb. = 70% and R.B.C. = 3,000,000.

ANAEMIA DUE TO SEVERE MENORRHAGIA occurred in 20 menstruating women. This was due to fibroid of uterus in five patients, abortion in four patients, ovarian cyst in one patient and ectopic pregnancy in one patient. In the other nine patients, there was no pelvic abnormality. The latter were probably cases of idiopathic hypochromic anaemia, as menorrhagia is commonly associated with this condition. Such cases deserve a trial with large doses of iron which sometimes stop the menorrhagia by correcting the anaemia. This saves the patient a journey to hospital for a D. & C. operation (Dunlop, Davidson & McNee "Textbook of Medical Treatment", 1946, p.400).

The following case of menorrhagia was successfully treated with iron. The patient, Mrs. K., aged 37 years, para 5, had very heavy, irregular menstruation lasting ten days and recurring every two or three weeks. Per vaginam examination was normal. She had dyspnoea on exertion and was very pale. On 25.4.46, blood examination showed P.C.V. = 22, Hb. = 44%, R.B.C. = 3,210,000, serum clear and cells microcytic. There was a rapid response to iron as on 28.5.46 the Hb. = 82%, and on 9.7.46 the Hb. reached 94%. The patient felt well but a year later had a relapse with return of anaemia and also koilonychia. On 20.7.47 the P.C.V. = 27, Hb. = 53% and R.B.C. = 3,520,000. The patient was advised to have curettage but refused, owing to her domestic and family commitments and resumed iron, taking 27 grains of ferrous sulphate daily. On 24.2.48 she had again recovered, with menstruation regular, every 28 days, lasting four days, with normal loss. Her Hb. = 94% and R.B.C. = 4,740,000. She has remained well since then and her koilonychia has disappeared.

ANAEMIA AND MENOPAUSAL HAEMORRHAGE occurred in seven patients who were thought to be at or near the

menopause, as shown in the following table:-

Case No.	Age	Pelvic Examination	Diagnosis	Treatment
1.	46	P.V. normal	Idiopathic hypochromic anaemia	X-rays
2.	39	P.V. normal	do.	Iron
3.	48	P.V. & D.&C. normal	do.	X-rays
4.	44	do.	do.	do.
5.	48	Fibrosis of uterus	Fibrosis of uterus	Dilatation & curettage
6.	48	Metropathia haemorrhagica	Metropathia	X-rays
7.	46	P.V. normal	Idiopathic hypochromic anaemia	Iron

From the above table it would appear that X-ray induction of the menopause is the best treatment for haemorrhage at the menopause as iron was given to all the above patients and was successful in curing the anaemia in only one patient (Case 2). In Case 7 the bleeding was arrested, but the actual conclusion of the menopause was not observed by me in either case 2 or case 7.

ANAEMIA OF PREGNANCY:- The exact total of pregnancies during the seven year period is not known but from the start of the National Health Service in July, 1948 to July, 1951 there were 111 pregnancies giving a yearly average of 37 cases confined at home. On this basis

the total number of pregnancies supervised in eight years from 1944 to 1952 would be in the region of 296 cases. During the whole period a maternity services scheme operated which provided each expectant mother with the services of both doctor and district nurse during pregnancy and at the confinement.

All expectant mothers were given "fersolate" tablets routinely and as most patients started iron therapy early in pregnancy, this may explain the small number (7) of anaemic patients encountered. Blood counts were only done in patients who, from their pale appearance or symptoms of fatigue, suggested anaemia. Only 6 cases of anaemia are described in the following table and they were all of the "hypochromic" or iron deficiency type. A seventh case was detected in the early months of pregnancy but was not fully investigated as the patient was confined elsewhere. In all 6 patients, pallor was a marked feature.

Case No.	Age	No. of Pregnancy	When first seen	Hb.%	R.B.C.	W.B.C.	P.C.V. %
1.	40	6th	6 months	76	2,960,000	-	39
2.	29	2nd	7½ "	56	2,320,000	8,000	28
3.	28	2nd	8 "	77	3,230,000	-	35
4.	30	3rd	6 "	68	3,430,000	-	34
5.	42	6th	7 "	49	3,240,000	5,400	23
6.	31	2nd	in labour	70	2,850,000	11,400	-

It is significant that all 6 patients were multiparous and that all were seen for the first time late in pregnancy, as Benstead & Theobold (British Medical Journal, 1952, 1, 407) have shown that anaemia of pregnancy is preventable by continuous administration of iron during pregnancy and is not, as was previously held, (Whitby & Britton, 1950, "Disorders of the Blood", p.286) mainly due to a physiological increase in plasma volume. Benstead and Theobold have shown that pregnancy anaemia is often due to a pre-existing iron deficiency anaemia from menstrual bleeding, frequent pregnancies or diet deficient in iron. Case 2 above, Mrs. S., first seen in 1948 with pregnancy anaemia, had a similar anaemia detected in a subsequent pregnancy in 1952, and was still anaemic three months after the birth. The anaemia was microcytic, e.g.,

Date	Hb.%	R.B.C.	P.C.V.	Time in relation to pregnancy
11.8.48	56	2,320,000	28	7½ months pregnant
17.9.48	57	3,670,000	33	5th day of puerperium
24.4.52	70	3,000,000	-	5th week of puerperium
3.6.52	70	2,850,000	-	3 months post-natal

It was discovered that this patient was not taking the iron preparation which had been prescribed for her. Thus this case seems to demonstrate the main causes

of pregnancy anaemias, namely, a tendency to idiopathic hypochromic anaemia, repeated pregnancies and inadequate intake of iron.

Toxaemia of Pregnancy occurred in association with the most severe anaemia of pregnancy encountered (Case 5). This assocation has been referred to by Benstead & Theobold (British Medical Journal, 1, 410) but Magee & Milligan on the other hand (British Medical Journal, 1951, 2, 1307), found no relation between Hb. levels and Blood Pressure readings in pregnancy. Case 5 above, Mrs. D., had a B.P. = 160/110 with heavy albuminuria and gross oedema. She was confined prematurely at 36th week on 20.4.46, in hospital, and three months after her return home was still anaemic. A year later, however, her blood count was normal and her blood pressure also was normal:-

Date	Hb.%	R.B.C.	P.C.V.	Time in relation to pregnancy
8.4.46	49	3,280,000	23	7 months pregnant
20.7.46	80	3,600,000	38	3 months post-natal
25.7.47	92	4,680,000	44	15 months post-natal

Macrocytic anaemia was not detected in any of the patients and this coincides with the observation of Klopper & Ventura (British Medical Journal, 1951, 2, 1252) that pernicious anaemia of pregnancy is a rare disease in Great Britain. Case 6, however,

showed some macrocytosis and anisocytosis although the film was normocytic mainly. This patient, Mrs. B., was given folic acid and Fe, in view of the observation of Davis & Brown that some cases of pregnancy anaemia may have a normocytic peripheral blood and a megaloblastic marrow (Practitioner, March 1952, p.229). The response of this patient to folic acid was disappointing although macrocytes were no longer seen in the peripheral blood in the 8th week of the puerperium, e.g.

Date	Hb.%	R.B.C.	P.C.V.	Time in relation to pregnancy
21.4.52	70	2,850,000	-	2nd week of puerperium
3.6.52	82	3,200,000	-	8th week of puerperium

At this stage persistent pyrexia, a leucocytosis of 11,400 and troublesome cough led to an X-ray examination of the patient, when bilateral apical pulmonary tuberculosis was diagnosed.

ANAEMIA AFTER THE MENOPAUSE:- Anaemia was detected in 37 females who had passed the menopause. In 23 of these patients anaemia was associated with the following conditions which were obvious contributing factors:-

Malignant disease	9 patients
Tuberculosis	4 "
Haematemesis (simple)	4 "
Pyloric stenosis	2 "
Chronic nephritis	2 "
Vaginal haemorrhage (simple)	1 "
Osteosclerosis	1 "

In 14 other patients the explanation of the anaemia was less obvious. These included 4 patients with hypertension, 2 patients with mitral stenosis, one patient with probable cholecytisis (with abnormal cholecystogram) and one patient who died of an obscure meningitis. Possible explanations of anaemia in these 14 patients are:-

(1) Persistence of Idiopathic hypochromic anaemia:- This is unlikely as this type of anaemia tends to spontaneous correction after the menopause (Whitby & Britton, "Disorders of the Blood", 1950, p.196). This was observed in one patient, Mrs. B., who had, as a result of intolerance of iron, remained anaemic during the last 14 years of her menstrual life. She had been treated without success at Glasgow Royal Infirmary and at home. In 1942, when aged 46 years, she required an X-ray induction of the menopause for menorrhagia. Her blood was then Hb. = 57%, R.B.C. = 3,230,000. Six years later in 1948, the blood was normal, Hb. = 94%, R.B.C. = 4,930,000 and P.C.V. = 45.

(2) Undetected haemorrhage:- An attack of melaena may pass unnoticed by the patient who may not consult her doctor until some time afterwards. This is a possible explanation of the following case where the

patient recovered quickly from her anaemia and has remained well ever since. The origin of the anaemia remains uncertain. The patient, Miss C., aged 70 years, was seen on 20.9.48 with a severe anaemia. Physical examination was negative apart from hypertension, B.P. = 200/130. The urine was normal and the faeces were negative for occult blood. Blood examination was P.C.V. = 28, serum clear, Hb. = 41%, R.B.C. = 3,290,000, W.B.C. = 3,000. She was given iron and ammonium citrate, and on 2.11.48, P.C.V. = 45, R.B.C. = 4,300,000 and Hb. = 82%. She has remained well during the past 5 years, her haemoglobin reaching 100% by May, 1949.

(3) Arteriosclerosis:- Although arteriosclerosis is common in elderly patients of either sex, it does not of itself seem to cause anaemia. This has been demonstrated by Hobson & Blackburn who discovered only 9 males and 16 females with anaemia in a group of 246 female and 177 male, old age pensioners living in Sheffield (British Medical Journal, 1953, 1, 647).

(4) Undetected malignant disease or chronic inflammation:- There was no evidence of either malignant disease or chronic inflammation in any of the 14 patients with post-menopausal anaemia of unknown origin, but it must

be remembered that those conditions are easily missed in elderly patients owing to a tendency to chronicity.

(5) Inadequate Diet:- An oral iron intake of 4 to 10 mgm. is necessary for most menstruating women in their daily diet, to prevent anaemia (Dunlop, Davidson & McNee, "Textbook of Medical Treatment", 1946, p.p.398,403). After the menopause the need for iron is much less, but dietary deficiency seemed, partly, responsible for the anaemia detected in Mrs. McL., aged 77 years. She had, for the previous 10 years, been taking a diet for blood pressure which consisted of bread, butter, potatoes and milk puddings with, occasionally, some porridge or soup. The patient had always been thin, but on 17.4.52 she was confined to bed with exhaustion due to anaemia and congestive cardiac failure with oedema. There was marked wasting, particularly of the buttocks, but no evidence of organic disease was detected. Pigmentation of the forearms and the back of the neck was present and there was slight clubbing of the fingers. The B.P. = 120/80, the urine was normal, the sputum was negative for tubercle bacilli and the faeces were negative for occult blood. A pronounced microcytic anaemia was present, Hb. = 32%,

R.B.C. = 3,030,000 and W.B.C. = 4,000. With oral iron and injections of liver extract the blood rose, by 3.6.52, to Hb. = 63%, R.B.C. = 4,550,000 and W.B.C. = 7,200. The patient was now able to get out of bed. A year later she was able to do her own housework but she was still thin and still showed pigmentation and anaemia. Her blood was, on 3.4.53, P.C.V. = 37, Hb. = 70%, R.B.C. = 3,860,000 and W.B.C. = 5,200.

(6) Defective Absorption of Iron:- Conway (British Medical Journal, 1952, I, p.1098) and Davis & Brown ("Practitioner", March 1952, p.227) discuss "malabsorption syndrome" as a cause of anaemia, and stress that the typical pale, frothy, offensive stool of steatorrhoea may be absent and that the condition may be missed unless faecal fat estimations are carried out. Conway has described cases of latent steatorrhoea in which pigmentation of the skin and clubbing of the fingers were present. In addition to the patient with inadequate diet, just described, there were two other patients in my practice with emaciation of long standing, both of whom showed pigmentation and anaemia.

Case 1. Miss D., a retired nurse, aged 69 years, had previously suffered from idiopathic hypochromic anaemia

at the age of 43 years. This was treated by the late Dr. Walter K. Hunter without success as the patient could not tolerate iron. She had improved, however, after artificial (X-ray) induction of the menopause but remained pale and thin. She had flatulent dyspepsia and a tendency to diarrhoea with yellow mucoid stools. Physical examination showed slight emaciation, pallor of the skin and buccal mucosa, and patchy brown pigmentation of the forearms and back of the hands. The urine was normal. She took a normal diet, apart from fried foods, which she avoided. Her blood on 12.4.51 showed a microcytic anaemia, Hb. = 45%, R.B.C. = 3,580,000 and W.B.C. = 2,200. In spite of this she felt reasonably well. She was given iron orally but could only tolerate small doses as normal dosage produced intense epigastric pain and diarrhoea. A year later on 16.6.52 she felt quite well but was still thin and pale and showed the same pigmentation of her forearms. The blood had improved with iron and was Hb. = 80%, R.B.C. = 4,070,000 and W.B.C. = 3,000.

Case 2. Mrs. McC., aged 64 years, was seen in January, 1946. She was tired but able to lead a normal life. She gave a history of anaemia since

1938 and of attacks of diarrhoea for the past 20 years. A blood test which I performed in 1938, whilst still a student, showed Hb. = 82%, R.B.C. = 3,468,000. Her faeces were described by her relatives as being like "sand" and very offensive. Her diet was a normal one. Physical examination showed a very pale, thin woman with patchy brown pigmentation of the forearms. A normocytic anaemia was present on 15.1.46, e.g. Hb. = 70%, R.B.C. = 2,480,000 and P.C.V. = 34, with serum clear. Iron was prescribed but this caused diarrhoea and was abandoned by the patient. A year later on 12.7.47 she was still anaemic but had no complaint, e.g. Hb. = 46%, R.B.C. = 2,940,000 and P.C.V. = 32. Three years later on 25.1.50 this patient collapsed with vomiting and diarrhoea. Her anaemia was little different from the two previous occasions, being Hb. = 64%, R.B.C. = 2,530,000 and W.B.C. = 2,800. The faeces were negative for occult blood. Suspecting malignancy, I asked this patient to enter hospital but she refused. She was now given liver injections as a last resort and rapidly regained her strength. Her vomiting and diarrhoea ceased and she gained 1½ stones in weight, enjoying a full diet. The liver therapy did not appear to affect the anaemia in any way, as a

year later on 23.1.51 the Hb. = 82% and the R.B.C. = 3,800,000. This patient had a further attack of vomiting and diarrhoea with collapse in December, 1951 after being off liver therapy for six months. She recovered with liver therapy. Since I last saw this patient, she has been examined at the Western Infirmary, Glasgow (March, 1953). I am indebted to Dr. J.F.C. Waterston for the information that no evidence of malignant disease was found. This case remains undiagnosed (?malabsorption syndrome) and the patient is again leading a normal life.

IRON DEFICIENCY ANAEMIA IN MEN:- There were 27 cases of this type. In 22 patients there was an obvious explanation of the anaemia, e.g.

Pulmonary tuberculosis	4 cases
Malignant disease	8 "
Haematemesis	4 "
Thrombophlebitis	1 "
Addison's disease	1 "
Splenic anaemia	1 "
Chronic lymphatic leukemia	1 "
Severe epistaxis (hypertension)	1 "
B.T. malaria	1 "

In the remaining 5 patients the cause of anaemia was less certain but in each there was a possible explanation, e.g.

Case No.	Age	Hb.%	R.B.C. per c.mm.	W.B.C. per c.mm.	P.C.V.%
1.	73	82	3,170,000	4,000	36
2.	81	35	2,550,000	2,000	23
3.	15	68	3,780,000	11,600	-
4.	18	70	4,280,000	-	38
5.	60	84	4,070,000	-	39

On 5.1.47, Case I gave a history of coronary thrombosis 13 years previously. His B.P. = 98/70 mm.Hg. and his urine contained albumin. He died of myocardial failure, without oedema but with marked pallor probably due to peripheral circulatory failure, on 6.3.47.

Case 2 had a severe microcytic anaemia on 19.4.50 but died before any investigation could be carried out. In view of his age (81 years) malignant disease seems probable.

Case 3 was a boy aged 15 years who had, several years previously, undergone numerous tendon-splitting operations for spastic diplegia. His anaemia (18.11.50) which may have been a chronic post-operative one, responded to iron therapy.

Case 4 was a boy of 18 years with mitral stenosis resulting from rheumatic fever in childhood. This anaemia also responded to iron (20.1.46).

The last patient, Case 5, was an old case of duodenal ulcer and his anaemia may have resulted from occasional melaena although the faeces, when tested, were negative for occult blood. His anaemia responded to iron (12.5.46).

Thus, no case occurred in 27 men which could be classified as idiopathic hypochromic anaemia, and this is in keeping with the opinion expressed by Whitby & Britton ("Diseases of the Blood", 1950, p.196) that this is a rare occurrence in the male.

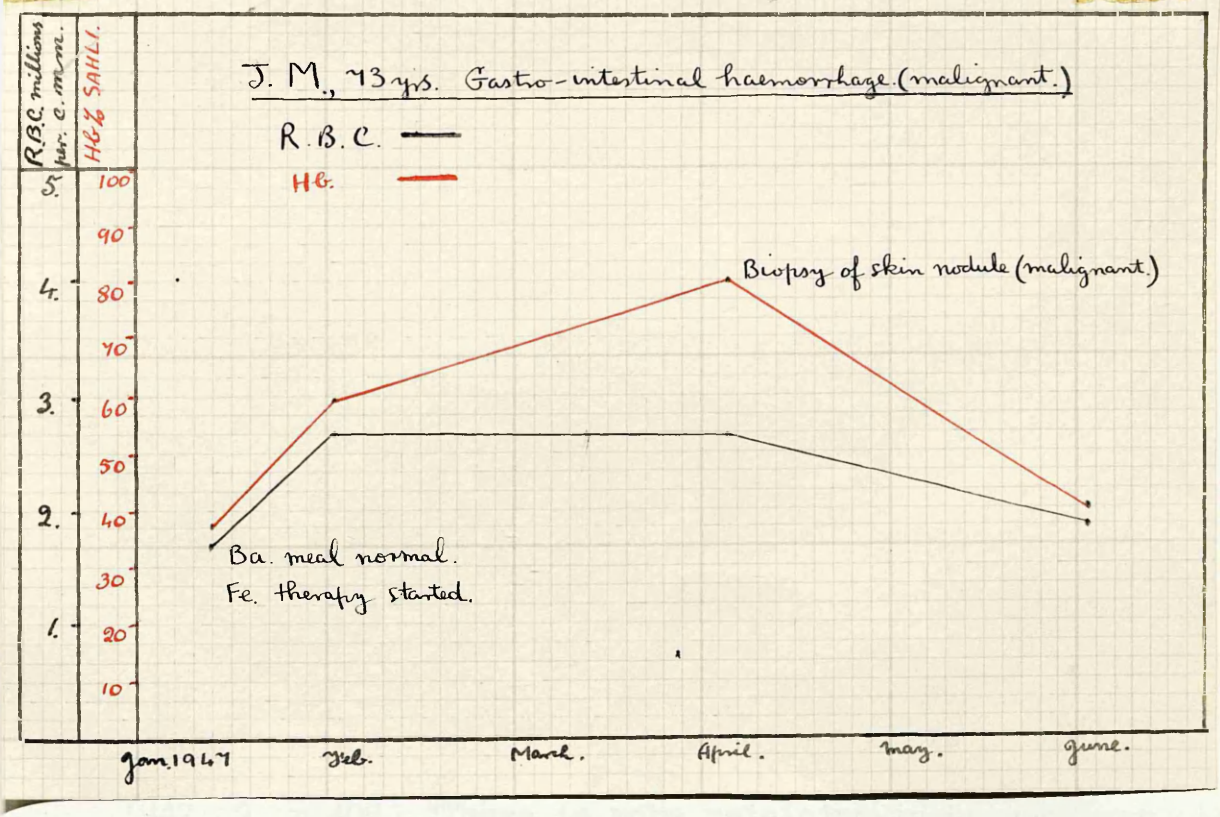
CANCER:- Anaemia was detected in 18 cases of malignant disease. In 13 patients hospital investigation confirmed the diagnosis of cancer. In the 5 others, hospital investigation was refused but the diagnosis was obvious on clinical grounds alone.

	Case No.	Age	Site	Anaemia of diagnostic value
FEMALES:	1.	60	Pelvic colon	Yes
	2.	32	Stomach	Yes
	3.	61	Stomach	Yes
	4.	60	Breast	No
	5.	79	Pelvic colon	No
	6.	65	Stomach	No
	7.	79	Breast	No
	8.	65	Uterus	No
	9.	50	Uterus	No
	10.	60	Stomach	No
MALES:	11.	66	Stomach	Yes
	12.	73	Stomach	Yes
	13.	68	Stomach	Yes
	14.	80	Stomach	Yes
	15.	65	Melanoma of leg	No
	16.	70	Transverse colon	No
	17.	60	Lung	No
	18.	75	Bladder	No

In seven patients the anaemia appeared early in the course of the disease, before definite localising signs enabled a diagnosis to be made. In the remaining eleven patients, the anaemia was not of diagnostic importance as the disease had been confirmed in these cases before the anaemia appeared. It is significant that anaemia appeared early in six cases

of stomach cancer and in one case of cancer of the pelvic colon as it has been stressed in the booklet of the British Empire Cancer Campaign ("The Early Diagnosis of Cancer", 1953, p.6) that anaemia, as an early sign of cancer, occurs most commonly in cancer of the stomach and colon. It was noticed, also, in six of these patients with early anaemia that there was a very poor response to oral treatment with iron, i.e. a rise of haemoglobin of less than 1% per day of treatment with iron. This observation was of great importance in Cases 2, 3, 11 and 12, as all 4 patients had initially negative barium meal x-ray examinations, and all four, on re-examination later, were found to have inoperable cancer of the stomach. This was surprising in view of the claim of Swynnerton & Truelove (British Medical Journal, 1952, I, p.287) that 90.5% of 297 patients with cancer of the stomach had abnormal barium meals when first examined.

Case 12 illustrates how difficult it is to make an early diagnosis of cancer of the stomach, e.g. this patient, J.M., aged 73 years, complained of dyspepsia in July, 1946. There was no evidence of wasting and barium meal x-ray examination was normal. In January,


J. M., 73 yrs. Gastro-intestinal haemorrhage (malignant.)
R.B.C.
HB.
Biopsy of skin nodule (malignant.)
Ba. meal normal.
Fe. therapy started.
R.B.C. millions per c.m.m.
HB % SAHLI.
5.
4.
3.
2.
1.
100
90
80
70
60
50
40
30
20
10
Jan. 1947
Feb.
March.
April.
May.
June.

1947 the patient collapsed with haematemesis and melaena. Physical examination was again negative, apart from anaemia. This was confirmed by a consultant physician, and treatment with iron for the anaemia commenced. The response proved sluggish.

Date	Hb.%	R.B.C. per c.mm.	P.C.V.%
12.1.47	36	1,690,000	18
2.2.47	58	2,640,000	28
4.4.47	76	2,630,000	36
2.6.47	41	1,890,000	20

In April, 1947 a small hard nodule appeared in the subcutaneous tissue of the left scapular area. I excised this nodule and on examination at the Pathology Department of the Western Infirmary, Glasgow, it was found to be a deposit of secondary carcinoma.

These cases suggest that in the early diagnosis of cancer of the stomach, any patient with dyspepsia and an unexplained symptomless anaemia must be regarded with suspicion and this would seem to justify an exploratory laparotomy. In this connection, Sir Heneage Ogilvie has remarked (British Medical Journal, 1947, 2, p.407) "There is more rejoicing in heaven over the one laparotomy that fails to find cancer than over the ninety-and-nine (positive) ones that find it too late".

HAEMATEMESIS AND MELAENA:- Gastro-Intestinal haemorrhage was the cause of anaemia in 8 females and 8 males, e.g.

FEMALES:

Case No.	Age	Diagnosis	Obvious Haemorrhage	Occult Melaena
1.	79	Chronic nephritis	Yes	-
2.	65	Hypertension	Yes	-
3.	74	Arteriosclerosis	-	Yes
4.	74	Cause unknown	-	Yes
5.	61	Cancer of stomach	-	Yes
6.	60	Hypertension	Yes	-
7.	45	Rosacea	Yes	-
8.	40	Not investigated (left district)	Yes	-
MALES:				
9.	40	Duodenal ulcer	Yes	-
10.	45	Duodenal ulcer	Yes	-
11.	54	Uraemia (?Amyloid)	Yes	-
12.	73	Cancer of stomach	Yes	-
13.	70	Cause unknown	Yes	-
14.	68	Cancer of stomach	-	Yes
15.	65	Duodenal ulcer	Yes	-
16.	80	Cancer of stomach	-	Yes

As the table indicates, bleeding was obvious in 11 patients. In the remaining 5 patients, occult blood was detected in the faeces by the guaiacum and benzidine tests after excluding meat and vegetables from the diet of the patients for three days prior to the tests (Price, 1944, "Textbook of Medicine", p.615).

In only 7 of the 16 cases was the source of bleeding clearly established. These were Cases 5, 12, 14 and 16 with gastric carcinoma and Cases 9, 10 and 15 with duodenal ulcer.

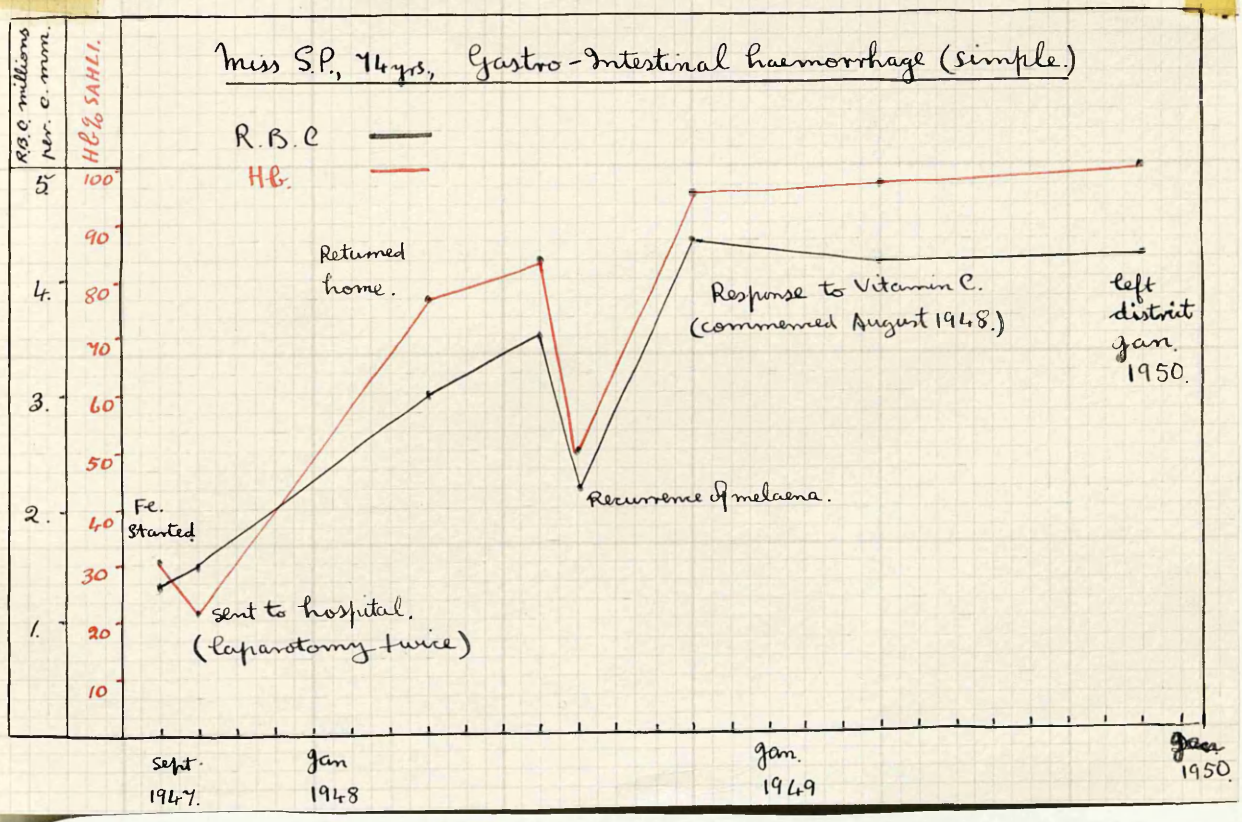
In 6 of the remaining 9 cases, hospital or specialist investigation failed to discover the origin of the haematemesis or melaena. (Cases 1, 8 and 11 did not have hospital investigation). Dyspepsia was present, however, in 2 of the 9 patients, cases 3 and 7, and it is possible from the ages of the patients that malignant disease was present in the former and peptic ulcer in the latter.

There are many possible explanations of bleeding in these undiagnosed cases. Acute rapidly healing ulcers are a likely cause in the younger patients, while it seems probable that localised arteriosclerosis of gastric vessels (Avery Jones, British Medical Journal, 1947, 2, p.444) and/or ascorbic acid deficiency may have been responsible for haemorrhage in some of the older patients. For example, Case 4 above, S.P., a spinster aged 74 years, was seen in September, 1947 with a very severe anaemia, Hb. = 29%, R.B.C. = 1,340,000, W.B.C. = 7,000 and P.C.V. = 15. The serum was watery clear and the blood film showed some anisocytosis and some macrocytosis. The faeces, at this time, were negative for occult blood. The patient did not respond to iron therapy or to liver injections and was admitted in October, 1947 to the

Western Infirmary, Glasgow, where melaena was detected. Barium meal and barium enema and test meal were normal. Laparotomy was performed on 26.11.47 when no abnormality was seen excepting a slightly enlarged spleen which was removed. As melaena continued, a further laparotomy was performed on 9.12.47. Again no abnormality was seen but a Meckel's diverticulum was excised. This patient returned home, still with melaena, on 13.2.48. She was given, regularly, oral iron therapy consisting of iron and ammonium citrate gr. 30 t.i.d., but on 14.4.48 the faeces were still positive for occult blood and Hb. = 76%, R.B.C. = 3,010,000 per c.mm. Further melaena occurred in August, 1948 and at this point, ascorbic acid 50 mgm. t.i.d. was added to the treatment and from then on the patient's blood count and her general health improved, e.g.

Date	Hb.%	P.C.V.%	R.B.C. per c.mm.	
17.7.48	82	41	3,500,000	
11.8.48	47	27	2,200,000	(recurrence of melaena)
19.11.48	92	45	4,330,000	
27. 4.49	96	-	4,040,000	
25.11.49	100	-	4,180,000	

This patient who had been confined to bed for over a year was now able to get up. In December, 1949, she left the relative who had been nursing her in my


Miss S.P., 14 yrs., Gastro-Intestinal haemorrhage (simple.)
R.B.C.
Hb.
R.B.C. millions per c. mm.
Hb% SAHLI.
5
4.
3.
2.
1.
100
90
80
70
60
50
40
30
20
10
Returned home.
Response to Vitamin C. (commenced August 1948.)
left district Jan. 1950.
Fe. started
sent to hospital. (Laparotomy twice)
Recurrence of melaena.
Sept. 1947.
Jan 1948
Jan. 1949
Jan. 1950.

district and returned to her own home in Glasgow. She is still alive (1953) at the age of 80 years. In view of her age and the response to ascorbic acid, it would appear that arteriosclerosis and Vitamin C. deficiency have been important factors in producing the gastro-intestinal haemorrhage in this case.

The occurrence of dehydration uraemia in cases dying after haematemesis, about the 8th to the 16th day, has been described by Avery Jones (British Medical Journal, 1947, 2, 444). Uraemia (Blood urea = 212 m.gm.%) was detected in Case 11. This man, J.M. aged 54 years, who had, 20 years previously, recovered from tuberculosis of larynx and lungs in Bridge of Weir Sanatorium, took a severe haematemesis on 14.8.46. His Hb. = 35%, P.C.V. = 17, R.B.C. = 2,060,000 and W.B.C. = 6,000. He appeared to be making an excellent recovery when he suddenly developed a transient aphasia three weeks after his haemorrhage. His blood pressure was 240/140 mm.Hg. and his urine was loaded with albumin. The raised blood urea was detected by a titration method which I found of great value in my practice (Using mercuric chloride 5%, sodium carbonate 20% and trichloracetic acid 10%)

and the diagnosis of uraemia established. This diagnosis was confirmed by a medical consultant who visited the patient. In view of the previous tuberculous disease, the gross albuminuria and the interval of three weeks after the haematemesis, it is possible that the uraemia was not due to the haematemesis in this case and that amyloid disease may have produced both. The patient died in coma four weeks after his haematemesis.

RETICULO-ENDOTHELIAL DISEASES:- There were 4 Cases in the period 1944-52.

Case 1. Acute Lymphatic Leukemia:- The patient was a boy, A.McK., aged 7 years, who developed symptoms of mediastinal obstruction following a chest "cold". There was enlargement of cervical, axillary and inguinal glands. The diagnosis of acute lymphatic leukemia was made in the Royal Hospital for Sick Children, Glasgow, where the child died on 23.5.48 after a four weeks' illness.

Case 2. Chronic Lymphatic Leukemia:- This case was investigated at home. A male, A.F., aged 67 years, was seen in 1947 with enlarged cervical, axillary and inguinal glands. In November, 1947 a provisional diagnosis of Hodgkin's disease was made by a consultant. In May, 1948, however, although there was no leucocytosis the differential white cell count showed a relative lymphocytosis and I excised a cervical gland which was examined at the Pathology Department of the Western Infirmary, Glasgow. The gland consisted entirely of large lymphocytes. During the next two years, the white cell count remained reasonably normal and the relative lymphocytosis constant, e.g.

Date	W.B.C.	Lymphocytes (small)	Lymphocytes (large)	Polymorphs Neutro-phils	Polymorphs Eosino-phils	Monocytes
May 1948	8,600	32%	19%	42%	0	7%
17.11.48	6,200	15%	39%	34%	2%	10%
14. 1.50	5,400	48%	20%	24%	0	8%
16. 7.50	8,200	-	-	-	-	-
26. 9.50	12,600	-	-	-	-	-
5.12.50	9,600	28%	50%	10%	2%	10%

By January, 1950, the patient had developed a normocytic anaemia, Hb. = 80%, R.B.C. = 3,680,000, P.C.V. = 37 and his spleen was enlarged and palpable below the left costal margin. By December, 1950 the anaemia had increased, despite liver injections and iron, to Hb. = 58% and R.B.C. = 2,300,000. The patient now suffered a pathological fracture of his lumbar spine by falling on a stair. X-rays showed leukemic infiltrations in the vertebrae. On the advice of a medical specialist, this patient received no irradiation therapy, and this decision seemed justified as the patient was able to get about, wearing a special jacket to support his spine, until shortly before his death on 1.4.54, having survived 7 years.

Case 3. Monocytic Leukemia:- Mrs. D. aged 34 years, was seen in May, 1948 complaining of excessive fatigue. There was no loss of weight or excessive menorrhagia. There was no glandular or splenic enlargement and the patient did not look anaemic. A surprising degree

of anaemia was, however, present and this did not respond to iron, e.g.

Date	Hb.%	R.B.C.	W.B.C.	P.C.V.
30.5.48	60	2,660,000	7,000	29
4.7.48	47	1,890,000	-	22

In view of this deterioration, the patient was investigated in the Western Infirmary, Glasgow, where the diagnosis of monocytic leukemia was established in September, 1948. Thereafter the patient was nursed at home and sent up at intervals to hospital for blood transfusions, whenever the haemoglobin fell to 40%. This patient survived in this manner for about ten months, but the white cell count gradually rose and reached 80,000 per c.mm., shortly before her death. A differential count of nucleated cells on 9.1.49 showed monocytes = 42%, polymorphs = 36%, large lymphocytes = 3%, small lymphocytes = 10%, myelocytes = 1% and normoblasts = 8%. A distressing feature of the terminal stages of the illness was the development of sloughing stomatitis and carbuncles of the scalp. She died on 4.3.49.

Case 4. Splenic Anaemia:- A male, J.R., aged 66 years, complained in June, 1950 of fatigue, anorexia and loss of weight of several months' duration. There was extreme pallor of skin and buccal mucosa,

and a large mass was palpable in the left hypochondrium. Blood examination showed Hb. = 58%, R.B.C. = 4,140,000, W.B.C. 8,800 and P.C.V. = 32. The film showed a definite microcytic anaemia. He was admitted at once to the Western Infirmary, Glasgow, where splenic anaemia was diagnosed. He was treated with iron orally without response and he died within a year of diagnosis.

TUBERCULOSIS.

Anaemia was detected in 19 patients (14 females and 5 males) suffering from tuberculosis, as shown in the following table:-

FEMALES:

Case No.	Age (years)	Site	Hb.%	R.B.C. per c.mm.	W.B.C. per c.mm.	P.C.V.	Deaths (1944-52)
1.	40	Rectum	89	4,500,000	4,000	-	-
2.	44	Lungs	72	2,550,000	4,200	-	-
3.	60	Spine	52	3,330,000	5,400	32	Died
4.	72	Lungs	72	3,790,000	9,000	36	Died
5.	40	Lungs & Spine	62	3,570,000	-	32	-
6.	42	Lungs	52	3,450,000	7,000	30	-
7.	70	Lungs	58	3,520,000	-	31	Died
8.	26	Lungs	70	3,860,000	8,000	30	-
9.	43	Lungs	82	3,850,000	20,000	35	Died
10.	17	Pelvis	52	4,110,000	7,400	33	-
11.	46	Face (Lupus)	35	2,320,000	2,000	23	-
12.	53	Lungs	82	4,500,000	3,600	-	-
13.	31	Lungs	70	2,850,000	11,400	-	-
14.	30	Lungs	84	4,050,000	4,000	37	Died

MALES:

15.	59	Lungs	76	3,000,000	-	42	Died
16.	54	Lungs	35	2,000,000	6,000	17	Died
17.	29	Lungs	76	3,910,000	17,000	38	Died
18.	18	Lungs	42	2,170,000	-	21	-
19.	60	Lungs	70	3,490,000	6,400	-	Died

The diagnosis of tuberculosis was confirmed in all pulmonary cases, except Cases 2 and 4, by X-ray examination or sputum tests. Both Cases 2 and 4 had haemoptysis and clinical signs of pulmonary tuberculosis.

According to Clegg (British Medical Journal, 1954, I, 267) a progressive hypochromic anaemia is the most

constant alteration seen in the blood in pulmonary tuberculosis, and this reacts well to adequate treatment.

In the cases under my care, this anaemia was of little diagnostic value as, with the exception of Case 3, the diagnosis was known or suspected in all cases before a blood examination was carried out.

In case 3, however, an anaemia proving unresponsive to iron therapy led to the patient's admission to hospital where a Pott's abscess of the spine was discovered.

With regard to prognosis, the detection of anaemia proved of little value as most of the patients had other factors contributing to the anaemia, e.g. Cases 5, 6 and 8 had menorrhagia with no pelvic abnormality and could have been cases of idiopathic hypochromic anaemia. Cases 10 and 11 had menorrhagia due, respectively, to tuberculous pyosalpynx and uterine fibroid, while Case 13 was complicated by anaemia of pregnancy. Similarly, in the males, there were other sources of anaemia, e.g. Case 17 had a lipoid nephrosis with fatty casts in the urine and a terminal uraemia. In Case 16, anaemia was caused by a huge haematemesis associated with heavy

albuminuria and uraemia. In Case 18, anaemia was directly due to a severe haemoptysis and in Case 19, a positive sputum was associated with a radiographic picture highly suggestive of bronchial carcinoma.

It was noticed, however, that where the anaemia appeared to be due to tuberculosis alone, the prognosis was not good. This was the case with patients Nos. 3, 4, 7, 9, 14 and 15, all of whom died.

A guide to prognosis was also obtained by the response of the anaemia to iron therapy, as a normal response seemed to indicate healing and a poor response indicated activity or deterioration, e.g. Case 3, Mrs. McI. aged 60 years with spinal tuberculosis, showed no response to iron and died later.

Date	Hb.%	R.B.C. per c.mm.	W.B.C. per c.mm.	P.C.V.
13.6.45	88	2,850,000	2,600	-
17.9.45	82	3,500,000	-	-
7.10.45	52	3,330,000	5,400	32

By contrast, Case 18 showed a rapid response to iron therapy. This was a boy of 18 years who took a severe haemoptysis on New Year's Day, 1948. He had previously had a left thoracoplasty (1947).

Date	Hb.%	R.B.C. per c.mm.	W.B.C. per c.mm.	P.C.V.
3.1.48	42	2,170,000	-	21
18.2.48	92	4,960,000	-	-

This patient was x-rayed in March, 1948 and found to be well with no evidence of active disease. He has remained well.

Finally, leucocytosis occurred in case 4 (W.B.C. = 9,000), case 9 (W.B.C. = 20,000) and case 17 (W.B.C. = 17,000), all of whom died.

Case 13 (W.B.C. = 11,400) improved with sanatorium treatment but still has bilateral pulmonary tuberculosis.

Leucocytosis was absent, however, in other patients with active disease and could not be regarded as an accurate guide to prognosis in this condition.

ANAEMIA AND HEART DISEASE.

"Heart Disease is occasionally accompanied by secondary anaemia due to local infection or haemorrhage" (Lewis, "Diseases of the Heart", 1943, p.35).

Anaemia was detected in 10 patients with valvular disease of the heart, as shown in the following table:-

FEMALES:

Case No.	Age (years)	Lesions	Hb.%	R.B.C. per c.mm.	P.C.V.
1.	60	Mitral stenosis	70	3,280,000	-
2.	21	Mitral stenosis	76	5,100,000	-
3.	65	Mitral stenosis	82	3,850,000	-
4.	71	Aortic and Mitral V.D.H.	82	4,060,000	35
5.	35	Mitral incompetence	88	3,090,000	38
6.	41	Aortic and Mitral V.D.H.	80	3,580,000	39
7.	40	Mitral incompetence	76	4,320,000	40
8.	35	Aortic V.D.H.	80	3,100,000	36
9.	25	Mitral stenosis	88	5,430,000	39
MALE:					
10.	18	Mitral stenosis	70	4,280,000	38

Cases 1, 3 and 4 were females past the menopause and the anaemia detected in them is difficult to explain but arteriosclerosis, diet lacking in iron, or impaired absorption of iron from the bowel may have contributed to anaemia in these cases. Cases 1 and 3 died of acute oedema of the lungs and Case 4 died of cerebral haemorrhage due to associated

hypertension (B.P. - 280/130).

In the remaining females, menstruation was the most likely source of the anaemia. A definite history of menorrhagia was obtained from Cases 2, 7 and 8.

The occurrence of anaemia in a young adult male, was a surprise finding. In childhood he had suffered from rheumatic fever, and in this condition the anaemia is believed to be only temporary, being caused by haemodilution during the recovery phase after the acute attack (Cochrane, British Medical Journal, 15.9.51, p.637). Thus it is probable that his anaemia was due to a recent flare-up of endocarditis in an already grossly damaged heart.

The administration of oral iron to these patients produced a considerable degree of clinical improvement in all cases. Case 6, who had a failing heart with oedema of the ankles, had a particularly gratifying response for such a mild degree of anaemia.

Case 10, the young man, who had felt very tired and unable to work, gained strength rapidly on iron therapy and has remained well and at work as a labourer for the past 7 years.

The conclusion from this short series of cases, none of whom had severe anaemia, is that it is worth while to do a blood examination in all patients with valvular disease of the heart. The detection and correction of even a very mild hypochromic anaemia produces a most welcome improvement in these patients.

MISCELLANEOUS DISEASES.

Secondary anaemia occurred in the following diseases not previously mentioned:-

(1) Chronic Nephritis:- Anaemia was detected in two elderly females with this condition. Both died shortly after the blood examination and there was therefore no opportunity to note how the anaemia responds to iron therapy. Example: Mrs. M., aged 65 years, an extremely pale woman, was confined to bed on 9.10.44 with congestive cardiac failure. Her B.P. = 240/100 mm.Hg. and she had polyuria and slight albuminuria. Her Hb. = 58%, R.B.C. = 3,300,000, W.B.C. = 3,400, Colour index = .87 and Film normocytic.

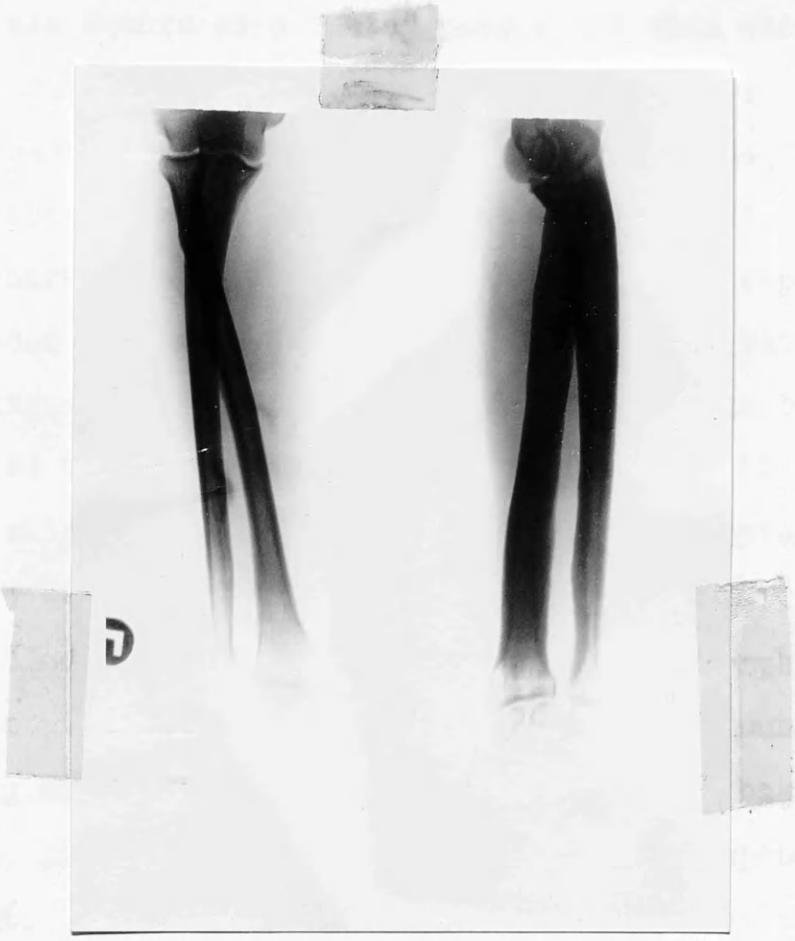
(2) Acute Rheumatism:- Slight anaemia was seen in two young women suffering from clinically mild acute rheumatism with joint pains. Example: C.M., aged 18 years in 1946. Her E.S.R. was 7 mm. in 1 hour and her P.C.V. = 39, Hb. = 82%, R.B.C. = 3,750,000 and W.B.C. = 2,800. Both patients recovered quickly on salicylates.

(3) Pyloric Stenosis:- Anaemia occurred in two elderly females with this condition. One of the patients resembled malignant disease closely, both clinically and at operation. Example: Mrs. D.,

aged 60 years, seen in March, 1951, was then extremely emaciated. She complained of epigastric pain and vomiting, and had a large epigastric mass. Her Hb. = 88%, R.B.C. = 3,220,000 and W.B.C. = 7,600. The Colour index = 1.3, yet the film showed a microcytic anaemia. Gastro-enterostomy was performed at the Western Infirmary, Glasgow in April, 1951. A large mass was seen on the lesser curvature and pylorus, but no glands or hepatic enlargement discovered. A soft ulcer was found on opening the stomach. By April, 1952 this patient had gained 2 stones 7 lbs. and Hb. = 90%. She felt very fit and had no dyspepsia.

(4) Osteosclerosis:- Anaemia was associated with osteosclerosis in two patients - Case 1, Mrs. V., aged 74 years, had no bone pain but was deformed with marked kyphosis and slight bowing and thickening of the right humerus and right femur. These deformities, judging from family photographs, had not been present in her youth. Paget's disease of bone was therefore suspected. On 9.2.47 she had a normocytic anaemia, Hb. = 80%, R.B.C. = 3,120,000, W.B.C. = 3,000. Her B.P. = 150/65 mm.Hg. and her urine was normal. She was diagnosed at the Western Infirmary, Glasgow, as a case of idiopathic senile osteosclerosis in 1947.

She survived approximately 18 months after this diagnosis and developed epigastric pain and vomiting. The faeces were positive for occult blood to guaiacum and benzidine. A mass was palpable in the epigastrium and, in addition, she had a uterine haemorrhage. Vaginal examination was normal. Thus she had two possible sources of malignant disease, namely, stomach and uterus. The anaemia did not respond to iron and was finally microcytic, being in July, 1948, Hb. = 45%, R.B.C. = 2,960,000, W.B.C. = 8,600 and P.C.V. = 25. By contrast, Case 2 was a young woman, Mrs. P. aged 21 years in 1944. She had no deformity but very severe bone pains. These responded slightly to salicylates at first and she was regarded as a case of rheumatism. In October, 1949, however, she looked ill and felt very tired. She had lost weight and was anaemic - Hb. = 82%, R.B.C. = 3,770,000, W.B.C. 6,600 and P.C.V. = 38. Colour index = 1. The anaemia was normocytic. An x-ray of her chest was carried out at the Russell Institute, Paisley. This showed no lung disease but revealed markedly increased density of ribs. Further x-rays showed a generalised osteosclerosis of entire skeleton resembling marble-bone disease of Albers-Schonberg. In this condition, leuco-erythroblastic



Osteosclerosis (Mrs. P.). X-ray appearances of right forearm and right leg (lateral views). Note - (1) widening of long bones, (2) increased density of bone due to centripetal thickening of cortex, and (3) reduction of marrow cavity.

anaemia occurs as a "late" phenomenon when the bone marrow has been replaced by progressive increase of cortical bone (Price, F.W., 1944, "Textbook of the Practice of Medicine, p.784). A remarkable feature of this case was the complete freedom from bone pain experienced by this patient during each of her three pregnancies, presumably due to decalcification of bones. On 14.4.52 she was still anaemic but had a definite leucocytosis, Hb. = 82%, R.B.C. = 4,010,000, W.B.C. = 10,000. The blood film was normocytic with a polymorph leucocytosis, the differential white cell count being neutrophils = 74%, eosinophils = 4%, basophils = 2%, large lymphocytes = 10% and small lymphocytes = 10%. The spleen was not enlarged. The serum calcium, phosphorus and alkaline phosphatase were estimated at the Pathology Department of the Paisley Royal Alexandria Infirmary in October, 1953 and were all normal.

(5) Rosacea:- One patient, Mrs. S. aged 45 years, had rosacea and keratitis. Her anaemia was due to a haematemesis on 11.4.48 when her blood was Hb. = 58%, R.B.C. = 2,470,000, This responded rapidly to iron as in four weeks on 9.5.48, the Hb. = 88%, and R.B.C.

= 3,230,000. She made an uneventful recovery.

(6) Malaria:- A soldier, J.A., returned from Burma in 1945. He had taken suppressive "mepacrine" and had escaped malaria whilst abroad. In January, 1946 he developed a typical benign tertian malaria and the parasites were obvious in my blood film. As a result of this, he obtained a small War Pension. On the 8th day of his illness, Hb. = 100%, R.B.C. = 3,600,000, W.B.C. = 4,400 and P.C.V. = 42. The serum was strongly icteric.

(7) Vaginal Ulceration:- Mrs. M., aged 74 years, had a huge vaginal haemorrhage in 1946. This was due to ulceration caused by a pessary which had been inserted for prolapse ten years previously and had never been changed. In spite of arteriosclerosis and B.P. = 260/120 mm.Hg. the anaemia responded to iron, e.g.

Year	Hb.%	R.B.C. per c.mm.	P.C.V.
1946 (April)	43	2,670,000	
1947 (July)	92	4,010,000	39.5

(8) Epistaxis:- This can be severe when associated with hypertension, e.g. a male, P.F. aged 53 years, had epistaxis due to hypertension on 1.1.48. On 31.1.48, Hb. = 64%, R.B.C. 3,600,000, P.C.V. = 35. He showed a rapid response to iron, as on 13.3.48,

his Hb. = 100% and the R.B.C. = 5,788,000. He died of a cerebral haemorrhage on 23.4.51.

(9) Ulcerative Colitis:- Mrs. E.McC. aged 26 years, had ulcerative colitis in 1949. In the early stage of the illness the patient was fevered, and there was anaemia and leucocytosis, Hb. = 88%, R.B.C. = 4,590,000, W.B.C. = 13,200. Three years later in 1952 the Hb. was 100% and the patient was clinically much improved.

(10) Thrombophlebitis:- In December, 1944 a village postman, J.W. aged 50 years, developed a bilateral femoral thrombosis with gross oedema of both lower limbs. At the Western Infirmary, Glasgow, no cause for this was found. He recovered after being off work for one year. At the onset his Hb. = 82%, R.B.C. = 3,900,000, W.B.C. = 11,000. This anaemia was associated with fever.

(11) Meningitis:- In 1945 an unusual case of meningitis occurred which, even after autopsy, remained undiagnosed. There was an unexplained anaemia. The patient was Mrs. S., aged 56 years, who developed a mild fever with bronchitis in December, 1945. This responded to sulphonamides. In addition, she seemed slightly jaundiced and blood examination showed Hb. = 65%, R.B.C. = 3,890,000, W.B.C. = 3,000,

P.C.V. = 34. The serum was icteric but the cells were normocytic. She was given liver and iron but after five weeks the anaemia had not responded very well and her fever had returned, Hb. = 70%, R.B.C. = 4,310,000, W.B.C. = 5,400, P.C.V. = 37. The serum was more strongly icteric. On 5.1.46, the patient suddenly became comatose and was admitted to the Western Infirmary, Glasgow, where a non-purulent meningitis was discovered but no causal organism. At autopsy no lesion to explain the anaemia was found (8.1.46).

HEREDITY and ANAEMIA.

An inherently weak gastric mucosa with impaired secretion of gastric juice and achlorhydria, has been responsible for the occurrence of cases of idiopathic hypochromic anaemia and of pernicious anaemia in members of the same family (Whitby & Britton, 1950, "Disorders of the Blood", p.198).

A familial tendency to idiopathic hypochromic anaemia was seen in only two (unrelated) families in my practice. The diagnosis of this condition is assumed in the four females concerned as each was suffering from iron deficiency anaemia and menorrhagia. Vaginal examination was normal in each case, e.g.

1st Family:	Hb.%	R.B.C. per c.mm.	P.C.V.	Treatment
Mrs. B. 46 yrs.	69	4,470,000	34	X-ray induction of menopause.
Mrs. S. 39 yrs.	88	3,840,000	41	Iron
2nd Family:				
Mrs. K. 39 yrs.	43	3,210,000	22	Iron
Mrs. G. 45 yrs.	47	3,780,000	-	X-ray induction of menopause.

It is reasonable to assume that a large scale survey would reveal many similar examples of familial idiopathic hypochromic anaemia.

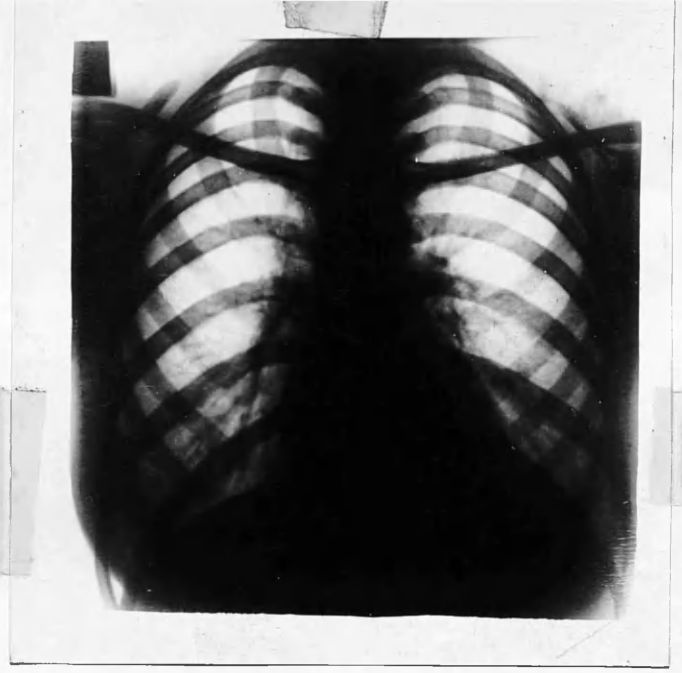
With regard to pernicious anaemia no familial incidence of this disease was seen. On 25.6.44,

hypochromic anaemia (Hb. = 64%) was detected in Mrs. J.C. aged 46 years, whose mother (Mrs. C.) has pernicious anaemia and who has already been described in detail in this paper. After the menopause Mrs. J.C. completely recovered from her anaemia.

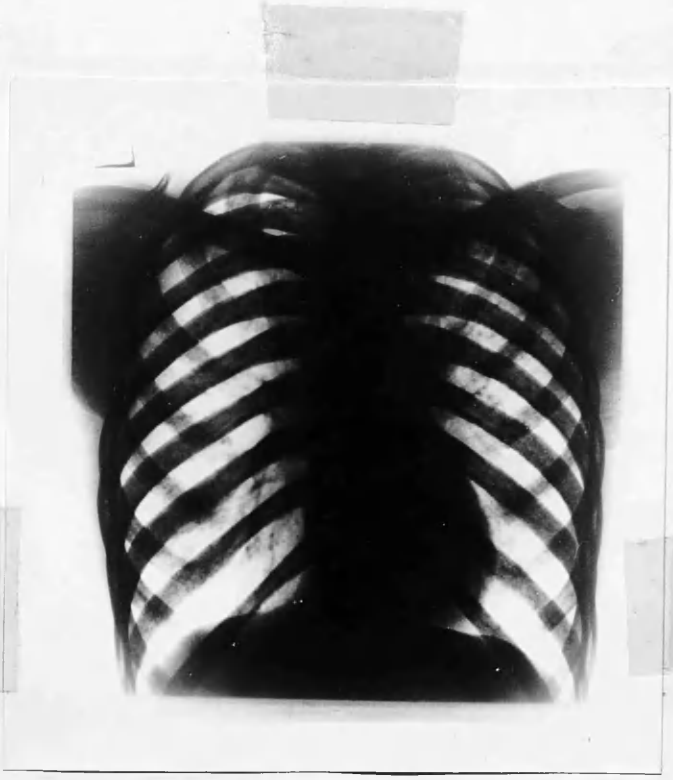
An unusual coincidence was the occurrence in two members of the same family of pernicious anaemia (Alan F.) and chronic lymphatic leukemia (Alex F.). Both those patients have been described previously. Another patient with pernicious anaemia, M.K., also described previously, developed cancer of the stomach and it seems, again, an unusual coincidence that this patient's mother died of cancer of the rectum in 1943, a few months before M.K. developed pernicious anaemia.

An investigation carried out on the relatives of the patient with marble-bone disease (Mrs. P.) showed that an apparently identical condition had caused the death, at the age of 45 years, of an uncle (her mother's brother). This man was x-rayed at the Russell Institute, Paisley, and his ribs showed greatly increased density and broadening, almost obliterating the intercostal space. His tibiae were also greatly

thickened and bowed. (I am indebted to Dr. J.R.R. Holms, Snr., of Paisley, for this information). Severe osteosclerosis was also found in a daughter (M.G.) of this man. In 1953 this young woman, at the age of 26 years, developed pulmonary tuberculosis. I have recently (1953) had the opportunity of studying this case. Her x-rays show generalised osteosclerosis of skull, and long bones throughout the entire skeleton. Blood examination showed a normal blood count, Hb. - 92%, R.B.C. = 4,290,000, W.B.C. - 9,400 and P.C.V. = 43. The blood film was normal. The Wassermann reaction was negative (Bacteriological Dept. for Renfrewshire and Bute) and the serum calcium, phosphorus and alkaline phosphatase have been normal on two occasions (Pathology Department, Royal Alexandra Infirmary, Paisley). On a third occasion the serum calcium was 16 mgm.% which may be significant in view of the theory that osteopetrosis is due to a mild sustained hyper-parathyroidism (Dible & Davie's Pathology, 1947, p.836). A mild form of osteo-sclerosis has also been discovered in Mrs. P's mother and also in a daughter of Mrs. P. aged 5 years. Thus the condition of osteosclerosis has been demonstrated in three generations of one family

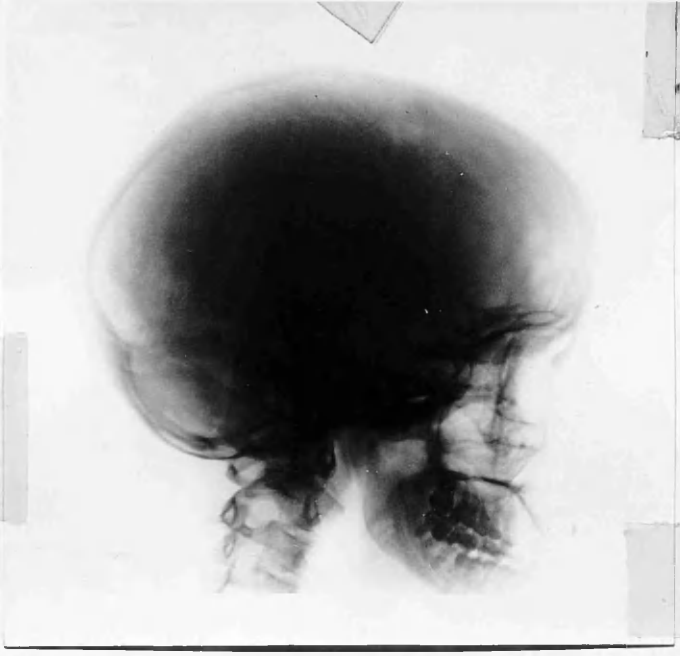


X-ray appearance of Normal Chest
(B.M. aged 26 yrs. Radiographer,
Paisley Chest Clinic).

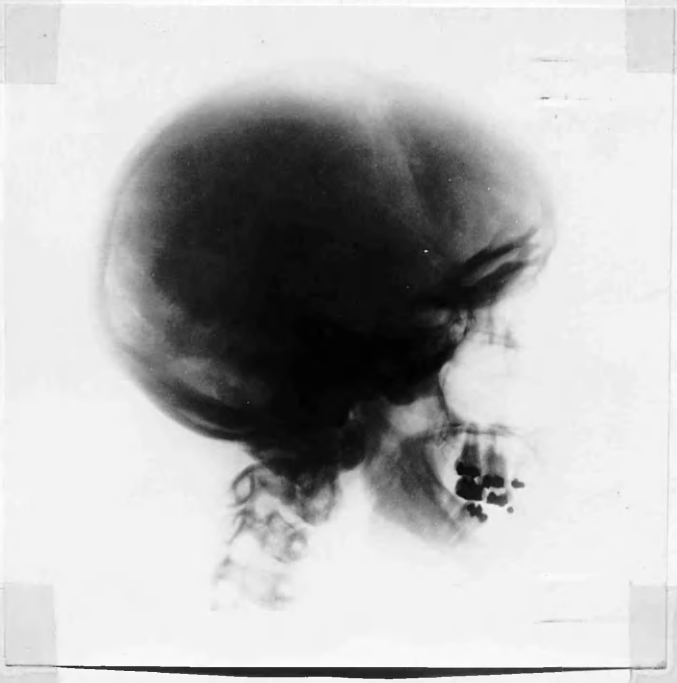


Chest in osteosclerosis (M.G. 26).

N.B. (i) Broadening and increased density of ribs. (ii) Narrowing of intercostal spaces. (iii) Some tuberculous infiltration at left upper lobe.



X-ray appearance of Normal Skull.
(Nurse E.M. aged 26 years,
Paisley I.D.H.).



Skull in osteosclerosis (M.G. 26).

N.B. (i) increased density of bone over entire base of skull, and (ii) narrowing of sella turcica.

and in two generations of a related family and in no patient has there been severe anaemia (I am grateful to Dr. H.W.O. Frew, Consultant Chest Physician for Renfrewshire and Bute, who carried out the radiological studies of Mrs. P. and her family. The enclosed photographs were taken for me by Miss Campbell, radiographer to the Chest Department, Paisley, to whom my thanks are due).

A case of haemophilia was encountered in a boy, aged 8 years, with a bleeding tooth socket. His haemophilia had been previously diagnosed at the Royal Hospital for Sick Children, Glasgow, before the patient came to live in my area in 1947. In this instance the disease could be traced back for several generations in the mother's family, and showed the classical tendency of haemophilia to be transmitted by unaffected females to their male offspring. The unfortunate patient developed ankylosis of a knee joint following a simple trauma which caused haemorrhage into the joint.

SUMMARY.

My experiences in the diagnosis and treatment of anaemia in general practice have been described.

During the eight year period, 1944-52, I encountered 157 cases of iron deficiency anaemia and 13 cases of macrocytic anaemia.

The macrocytic anaemias consisted of 9 patients with pernicious anaemia, 2 with myxoedema, 1 with a leuco-erythroblastic anaemia which was probably due to malignant disease, and 1 whose anaemia was associated with pemphigus foliaceus.

Because of the varying degrees of macrocytosis seen in blood films, I occasionally experienced difficulty in deciding whether or not there was sufficient evidence to justify the label of "macrocytic anaemia". Only when macrocytosis was pronounced, could this diagnosis be made with confidence. This uncertainty would not have arisen if the state of bone marrow erythropoiesis had been known.

One of the 9 patients with pernicious anaemia developed cancer of the stomach after 10 year's treatment with liver. The relationship between pernicious anaemia and cancer of the stomach should

always be kept in mind.

In the treatment of pernicious anaemia, considerable difficulty was experienced in achieving and maintaining a red cell count of over 4 million per c.mm.

In the 157 iron deficiency anaemias, there occurred only 2 cases of Plummer-Vinson Syndrome.

The "idiopathic" hypochromic anaemia of menstruating women was the most common type of anaemia encountered during the eight year period. No case of "idiopathic" hypochromic anaemia was seen in 27 men with anaemia.

Anaemia of pregnancy was comparatively rare, there being only 7 cases detected showing obvious anaemia, in approximately 296 pregnancies. This was probably due to prophylactic administration of iron to every pregnant woman. No case of macrocytic anaemia of pregnancy was seen.

In a number of anaemic women who had passed the menopause, there was no obvious explanation of the anaemia. A diet lacking in iron, and impaired absorption of iron from the bowel were possible etiological factors in these cases.

In the treatment of iron deficiency anaemias,

it was important to observe the response of the haemoglobin. A sluggish response of the haemoglobin level to iron therapy was sometimes the first indication of the presence of serious latent disease. This was of particular importance in the early diagnosis of cancer of the stomach.

Cancer and tuberculosis were the most common causes of secondary anaemia.

Gastro-intestinal haemorrhage was also a frequent source of anaemia, and the detection of occult bleeding in the faeces was of great assistance on several occasions in explaining a severe anaemia.

Anaemia was detected in a number of patients with valvular disease of the heart. The administration of iron to correct anaemia helped these patients considerably and justifies a routine blood count in all patients with heart disease.

Three patients with leukemia and one with splenic anaemia were seen in the eight year period.

A number of miscellaneous diseases associated with anaemia were encountered and have been included in this report. Among them were two unusual cases of osteosclerosis. The diagnosis of "marble-bone" disease has been made in one of these patients and

a follow-up investigation of her family has shown the condition to be present in three generations of that family and in two generations of a related family.

What appeared to be a hereditary tendency to idiopathic hypochromic anaemia and menopausal haemorrhage was seen in two separate families, and one example occurred of pernicious anaemia and idiopathic hypochromic anaemia in members of the same family.

Conclusion:-

As most anaemias encountered in general practice are of the idiopathic hypochromic type, occurring in menstruating women, they can be adequately investigated and treated at home. Hospital investigation should not be delayed if this type of anaemia fails to respond to treatment with iron.

Early admission to hospital is indicated in all cases of post-menopausal iron deficiency anaemia as these are often secondary to serious disease, the detection of which is only needlessly delayed by experimental treatment at home.

The detection of macrocytic anaemia is, again, an indication for referring the patient to hospital where diagnosis should be confirmed and subsequent treatment outlined and supervised.

Although these concluding remarks would suggest that the role of the general practitioner in the diagnosis and treatment of anaemias is strictly limited, nevertheless it is still his responsibility to detect anaemia.

A haemoglobin estimation and examination of a stained blood film will reveal the degree of iron deficiency present and also the type of anaemia.

The general practitioner who performs those simple investigations will be doing a great service to his patients as the information thus obtained is of the greatest value, both to the family doctor and his specialist colleagues, in obtaining a correct diagnosis at an early stage of the illness.

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