# Excessive Oral Iron Therapy Causing Haemochromatosis

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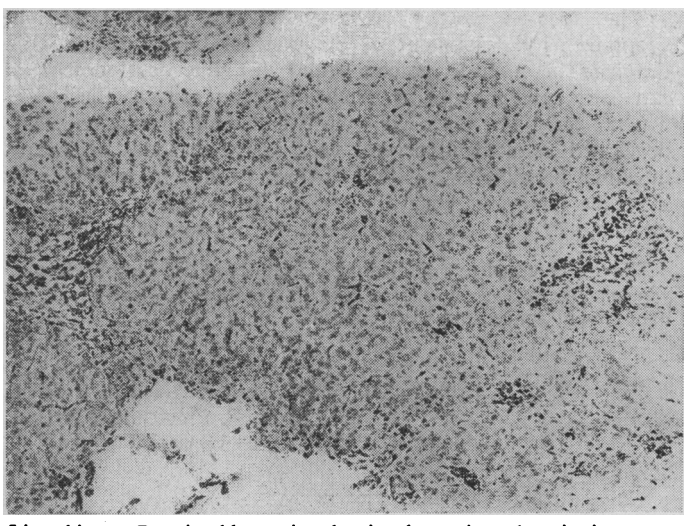
There are many similarities between primary haemochromatosis and the iron-overload state induced in some patients by multiple blood transfusions (Aufderheide, Horns, and Goldish, 1953) or excessive iron intake (Wallerstein and Robbins, 1953 ; Goldish and Aufderheide, 1953). However, it is uncertain whether the end state in the two disorders is the same. Only a few patients given excess iron develop pathological changes, while the majority merely show increased iron deposition without cell damage. There is doubt, therefore, whether the tissue changes result from the presence of the iron alone or from some other factor, possibly related to the illness for which the transfusion or iron has been given (Bothwell and Finch, 1962). The occurrence of a patient with features of haemochromatosis apparently induced by excessive oral intake of iron and who is otherwise normal is therefore of interest. The following case is believed to be only the second one to be described (Castleman and Towne, 1958).

## Case Report

A 60-year-old woman attended the out-patient clinic at University College Hospital on 6 May 1964 complaining of general lassitude of some six months' duration, with increasing difficulty in performing housework. She also complained of flatulent dyspepsia, although her appetite was good and she had not lost weight. She had noted some pigmented spots on her arms and face for about 12 months. There were no symptoms related to her cardio-respiratory or nervous system. Twenty-seven years ago she was noted to be anaemic and given oral iron. The symptoms relevant to her anaemia disappeared within a few weeks and had not returned until her recent ill-health. She continued taking iron tablets, however, in a dose of 20 Blaud pills (ferrous carbonate, 12 g.) a day until 18 months previously, when she changed to 10 ferrous gluconate tablets (2 g.) a day.

She had a cholecystectomy for gall-stones in 1942. There were no complications after this and the liver was thought to be normal at operation. She received no blood transfusions.

There was no relevant family history. Examination revealed an intelligent woman with a sallow pigmented complexion. There were many small, more deeply pigmented spots on her arms and face. The palmar creases were pigmented but there was no oral pigmentation. No abnormalities were detected in the heart, lungs, or C.N.S. The liver was hard and enlarged, reaching the umbilicus. The spleen was not palpable and there was no glycosuria.



Liver biopsy, Prussian-blue stain, showing heavy iron deposits in parenchymal cells and portal tracts, with patchy fibrosis.

*Investigations.*—Hb 14.3 g./100 ml. ; W.C.C. 8,200/c.mm., normal differential count ; E.S.R. 11 mm. in 1 hour (Westergren) ; Blood group B+. Serum iron, 246 µg./100 ml., with 100% saturation of siderophyllin. Colloidal red, cephalin cholesterol, and thymol turbidity, normal. Serum proteins 6.8 g./100 ml. ; electrophoretic strip showed a slight decrease in β-globulin. Serum alkaline phosphatase 16.9 K.-A. units. Prothrombin time 13 secs. Bromsulphthalein retention, 5% at 45 minutes. Electrophoresis and alkali denaturation of haemoglobin, normal. Glucose-tolerance test, normal. 17-Ketosteroid excretion, 4.5 mg./24 hours, 17-ketogenic steroids 10 mg./24 hours. Liver biopsy (see Fig.) showed a marked excess of iron pigment in parenchymal and Kupffer cells and patchy fibrosis with bile-duct proliferation compatible with haemochromatosis (Dr. J. Smith). Iron absorption was assessed by administering 5 µc $^{59}$Fe mixed with a standard meal containing 5 mg. of elemental iron. Less than 2% of the administered dose appeared in the circulating haemoglobin in 14 days. This indicates a low normal absorption assuming iron utilization to be normal.

Serum iron levels in the patient's two sons were: 75 µg./100 ml. in the elder, aged 29, and 70 µg./100 ml in the younger, aged 27.

Treatment was started with venesection of 1 pint (570 ml.) of blood a week. She has maintained her haemoglobin at 12 g./100 ml. and at the time of writing had had 8 pints (4.5 litres) of blood removed. Her symptoms were slightly improved and her serum iron remained high.

## Comment

Anaemic patients treated with many blood transfusions or prolonged iron therapy may deposit excess iron in their tissues. Similarly the Bantu tribe develop haemosiderosis and haemochromatosis apparently from their excessive dietary intake of iron. Some of these patients have tissue damage with varying degrees of cirrhosis, pigmentation, and diabetes. However, it is not certain that the damage and fibrosis are the direct consequence of iron in the tissues. It is possible that the cirrhosis in anaemic patients results from serum hepatitis transmitted in a blood transfusion ; or a combination of excess iron and anaemia may produce the change where iron alone would not. Again, in the Bantu the cirrhosis may well be due to dietary deficiencies and alcohol.

In the case presented here the patient took approximately 12,000 g. of elemental iron in 27 years. There is no evidence that she remained anaemic for any long period, and at the time of writing she was not absorbing more iron than normal. She gave no history suggestive of hepatitis, had had no blood transfusions, and does not take alcohol. There is thus no obvious cause for her cirrhosis. Even in the absence of diabetes a diagnosis of haemochromatosis is probably acceptable in the presence of cirrhosis with excess iron deposition and skin pigmentation. It would appear therefore that, firstly, she absorbed sufficient iron from her large and continued oral dose to produce the degree of overload noted ; and, secondly, she demonstrates that iron overload can lead to tissue damage and the clinical picture of haemochromatosis in the absence of other obvious noxious factors.

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