

the age of 61, she still has neither symptom nor sign, although the serum iron is raised.

Until recent years there was no effective treatment for haemochromatosis. The various therapeutic regimes, such as a low-iron diet, or a diet rich in phosphorus to delay the absorption of iron, met with little or no success; this was not surprising, as large quantities of iron had accumulated in the body by the time that the disease was productive of symptoms. The only rational method of effecting improvement is to remove iron from the tissues, and this can readily be achieved by repeated venesection, each pint (570 ml.) of blood containing about 250 mg. of iron. After venesection, mobilization of body iron is rapid, and 20 to 40 pints (11.4 to 22.7 litres) of blood can be removed in as many weeks without the development of a hypochromic anaemia. The good results of this treatment were first reported by Finch (1949) and have been confirmed by other workers (Davis and Arrowsmith, 1952; Finch and Finch, 1955; McAllen, Coghill, and Lubran, 1957). The recognition of a familial incidence of the disease will enable the diagnosis to be made in the relatives of such patients at a stage before the development of symptoms. If a raised serum iron is accepted as evidence that haemochromatosis exists in a subclinical form, treatment by controlled venesection may prevent the occurrence of clinical disease. It is therefore important to examine the relatives of these patients and to make periodic estimations of their serum iron.

During the past six years, as part of a study of portal cirrhosis, I have been interested in eight patients with haemochromatosis. Three of these patients had duodenal ulceration of some severity. One man presented with a perforated ulcer; a second man died from haemorrhage when a large chronic ulcer eroded an artery; a third man had a 20-year history of chronic dyspepsia, and cirrhosis was first observed when a gastrojejunostomy was performed. This association has not previously been commented on, although four of the seven male patients with haemochromatosis reported by McAllen, Coghill, and Lubran (1957) also had duodenal ulceration. Sheldon (1935) cited only one instance of this in his review of 311 cases. It is possible that this observation is but a reflection of an increasing incidence of duodenal ulceration in men during the twentieth century, but the occurrence is reported here as it may have some relevance, particularly as the duodenum is believed to be the principal site of iron absorption.

Summary

The cases of two brothers with haemochromatosis are reported. Their sister, aged 61, has a raised serum iron but is at present asymptomatic. As repeated venesection may halt the progress of this disease, it is suggested that the relatives of patients with haemochromatosis should be examined and serum iron estimations made.

The cases of two women with classical haemochromatosis are reported. In both instances the diagnosis was made after the menopause.

The occurrence of duodenal ulceration in three out of eight patients with haemochromatosis is commented on.

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"LIPOSTABIL": A PILOT STUDY

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A number of preparations have been introduced recently for the treatment of diseases associated with abnormal lipid metabolism. Their purpose is to reduce abnormally high cholesterol levels and in other respects to restore a more normal blood lipid pattern. These preparations are mainly intended for the treatment of patients with ischaemic heart disease, and this report gives the results of a pilot trial with one of them ("lipostabil"). Each capsule contains: alpha- and beta-lecithins of soya bean, 175 mg.; 3-4-5 polyoxyethylene-sorbitolmono-oleate, 100 mg.; potassium theophyllinate potassium thiocyanate, 50 mg.; (addition compound).

Material and Methods

Ten patients with ischaemic heart disease were studied, and in most of them the disease was severe. One died, and a second developed severe congestive failure, so that our results relate only to the remaining eight patients. Details of these are given in Table I. Four had an abnormally high serum cholesterol (more than 340 mg./100 ml.), while the other four had wide pre-beta-lipoprotein bands (Besterman, 1957). The width of these bands has been expressed arbitrarily as 0-3 (Smith, 1957). In addition, two of these patients had xanthomatosis tendinosum and a third had xanthelasma.

TABLE I.—Details of Cases

Case No.	Age and Sex	Condition Present	Initial Cholesterol (mg./100 ml.)	Width of Pre-beta Band
1	M 59	Myocardial infarction and angina	263	2
2	M 46	" " "	267	2
3	M 55	" " "	264	2
4	M 50	Angina	278	1
5	F 53	Angina; xanthelasma	500	1
6	M 44	Myocardial infarction; xanthomatosis tendinosum	385	‡
7	M 56	Angina; xanthomatosis tendinosum	485	‡
8	M 66	Angina	368	0

Blood samples were taken in the morning between one and two hours after a light fat-free breakfast.

Serum cholesterol was estimated by Abell's method (Abell *et al.*, 1952); but instead of slow centrifuging to separate the ethereal and aqueous layers the tubes were left to stand at room temperature for 20 to 30 minutes.

Paper electrophoresis was carried out by the method described by Flynn and de Mayo (1951). 0.15 ml. of serum was applied to a 3-in. (7.5-cm.) strip of Whatman No. 3 filter-paper. Strips were run for 17 hours (overnight) at $\frac{1}{2}$ mA/in. Each strip was unequally divided, the narrower part being stained for protein with light-green dye and the broader for lipids with Sudan black.

Results

Most of the patients were already taking a diet restricted in fat, and no changes were made over the period of observation. Several patients showed minor fluctuations in weight, but in none was there any consistent or progressive change.

The initial dose of lipostabil was 4 or 5 capsules a day, one being taken after a small uncooked meal, and two after a larger cooked meal. For the second month the dose was increased, and for the third month it was again increased up to the limit of tolerance (usually 8 to 11 capsules a day).

Cholesterol.—Four cholesterol values were obtained at weekly intervals before starting treatment, and the later results are expressed as a monthly average (Table II). As will be seen, there was a slight

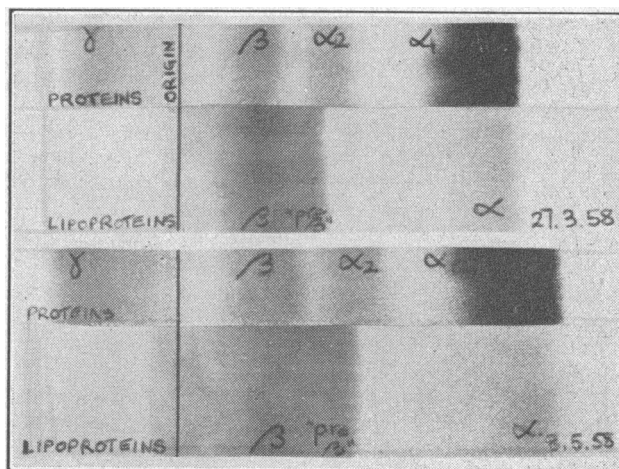
TABLE II.—Serum Cholesterol (mg./100 ml.)

Weekly Cholesterol During Control Period	First Month	Second Month	Third Month	After Stopping Treatment
351-340-344-345	335	328	312	317

progressive fall over the three-months period. However, the average value one month after stopping treatment was also lower than the control figures. There is no evidence that the effect of lipostabil can persist for some weeks after stopping treatment, and it is possible that this change might be part of a seasonal variation in diet or activity. But, in any case, the reduction was less than would be required of an effective therapeutic agent. The capsules contain linoleic acid, which is known to be of value in reducing serum cholesterol levels in man, and such reduction is related to the amount of linoleic acid given. However, the dose of lipostabil is limited by side-effects, particularly gastric upset, probably due to the theophylline, so that in practice an effective fall in cholesterol could not be achieved. Another common side-effect was constipation, but this was not as troublesome as the gastric symptoms.

Pre-beta-lipoprotein.—There is at present no satisfactory way of expressing the size and density of this band as an exact mathematical measurement, but the width has been recorded according to the grades proposed by Smith (1957). Any improvement, therefore, had to be assessed visually, but, though there were minor changes in several patients, none showed any progressive or consistent change (see Fig.).

Clinical Assessment.—The lesions in the patients with xanthomatosis and xanthelasma were photographed during the control period and comparison between these photographs and the lesions at the end of the period of



Electrophoretograms of the serum of a man age 55 before and after treatment with lipostabil for six weeks. The control strip shows a heavy pre- β band, and the pattern in the second strip is identical.

treatment showed no change. In two of the eight patients who completed three months' treatment the angina became more severe, in one it improved, and in the other five there was no change.

Summary

Ten patients with ischaemic heart disease and well-marked lipid disturbances were treated with lipostabil. Although the dosage was increased to the limits of tolerance no satisfactory fall in blood cholesterol was obtained. The lipoprotein pattern, studied by electrophoresis, and in particular the pre-beta band, was unchanged.

The clinical course of these patients was what could be expected from the natural history of this disease.

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Medical Memoranda

Unusual Case of Congenital Pyloric Stenosis

The case described presented some unusual and interesting features which make it worth recording.

CASE REPORT

A male first-born infant was delivered by caesarean section because of cephalo-pelvic disproportion. His birth weight was 7 lb. (3,175 g.) and he gained weight slowly but steadily till 14 weeks, when he weighed 11 lb. 5 oz. (5,130 g.) and appeared a normal baby.

He was admitted to hospital on March 9, 1956, at the age of 15 weeks with a history of vomiting for 10 days. The vomiting followed every feed, contained "coffee-grounds" material, and was non-projectile. Melaena stools had been passed on two occasions; at other times the stools had appeared normal.