in one patient in whom serial biopsies showed disappearance of interlobular fibrosis and lobular distortion over a six-year period. Nevertheless, an underlying macronodular cirrhosis may be difficult to exclude in the small specimens obtained by needle biopsy. Of particular interest are the two patients of Weintraub, Conrad, and Crosby³ in whom the initial biopsy showed definite nodular regeneration with broad bands of fibrosis. At the end of venesection therapy the appearances were similar except that the iron had been removed, whereas eight years later, after the patients had been maintained on intermittent venesections, lobular architecture was normal with minimal fibrosis only. Pirat⁴ reported similar findings in a 47-year-old non-alcoholic patient with haemochromatosis. After removal of 48 litres of blood over a two-year period the liver was free of iron though fibrosis remained. Three years later a further biopsy showed disappearance of the fibrosis."

In interpreting Williams's own experience it is important to bear in mind his opinion that "a prolonged period may be necessary for repair of the initial damage to the liver after the iron has been removed and further accumulation prevented." Only 24 of his 40 patients had been under treatment for more than four years. That these patients, with two exceptions, had not shown increasing severity of cirrhosis indicates that they have not deteriorated in the manner of untreated haemochromatosis.

I respectfully submit that the authority of the *British Medical Journal* should not appear to encourage a passive attitude in a disease where patients can be salvaged by a therapy of demonstrated effectiveness.—I am, etc.,

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** It was not our intention to deny that venesection therapy can be of value in the treatment of haemochromatosis, but other publications by Williams and his group¹ have shown that arthropathy can develop even after venesection therapy has been completed, and symptoms of it, if it has appeared earlier, are not relieved like those of the other manifestations of the disease. As Professor Crosby points out, there is good evidence now that venesection therapy can prolong life and relieve many of the symptoms of the disease.—Ed., *B.M.J.*

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Adhesions and Fibrosis

SIR,—I am glad that Mr. F. T. Crossling (6 September, p. 593) accepts in principle my suggestion of a fibrotic diathesis (9 August, p. 350). Unfortunately he appears to have wrongly concluded that I was attributing all thick scars to such a diathesis.

Many scars without the marked surface elevation or irregular contour commonly associated with keloids remain palpably

thickened permanently. Most of the thickened scars in my series of (European) patients with a history of adhesion obstruction were of this type. Preliminary studies had shown a significantly higher incidence of thickening greater than an arbitrary 3 mm. in mature vertical central abdominal scars in these patients (18 out of 23) compared with a control series (13 out of 52). Scars so situated were chosen because all the adhesion patients had at least one, and controls with similar scars were readily available.

These results do, I believe, lend support to the concept of a fibrotic diathesis, but they do not lead to the conclusion that all thickened scars arise from this cause. Mainly because certain areas of the body are more prone to gross scarring, as Mr. Crossling pointed out, I am sure that many if not most thick scars are due mainly to dermal factors. Similar remarks would apply in the case of peptic ulceration.—I am, etc.,

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Immunoglobulins and the X-chromosome

SIR,—We are interested in the paper by Dr. K. Rhodes and his colleagues (23 August, p. 439) in which they compared the levels of IgM globulin in women with an additional X-chromosome (XXX) with those in normal women (XX) and normal men (XY). The mean IgM level was found to be highest in the XXX group, intermediate in normal women, and lowest in men; these differences were statistically significant.

We have determined the levels of IgM and IgG globulins in 27 women with Turner's syndrome (XO), and in two groups of normal women (XX) and normal men (XY) matched for age. Estimation of the levels of these proteins was carried out using the simple radial diffusion technique.^{1,2} Antibodies against *Esch. coli* WF 96 and *Listeria monocytogenes* were tested using the indirect haemagglutination method.³ The individual levels of IgM in the three groups are shown in Fig. 1. Statistical analysis of the data revealed a significantly higher mean IgM

level in the XX group than in the XY and XO groups ($P < 0.01$). No difference was observed between the XY and XO groups ($P > 0.5$). The mean levels of IgG globulins were similar in the three groups. Fig. 2

FIG. 2.—Levels of antibodies against *Listeria monocytogenes* and mean values in XO, XX, and XY subjects. Titres expressed as "score."

shows the individual titre of antibodies against *Listeria monocytogenes* in the three groups. Previous studies have shown that these antibodies are associated with IgM globulins in subjects not experiencing an acute infection.³

The statistical analysis of results was carried out using the antibody titre expressed as score.^{3,4} The mean level of antibodies against *Listeria monocytogenes* was higher in the XX group than in the other two groups ($P < 0.01$); once again there were no differences between XY and XO ($P > 0.5$). Similar results were observed testing the antibodies against *Esch. coli* WF 96.

These data support the suggestion expressed by Dr. Rhodes and his colleagues that genetic factors control the levels of IgM globulins in man. These studies will be published in detail elsewhere.

This work was supported by the Spastics Society and the Medical Research Council.

—We are, etc.,

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Sugar and Ischaemic Heart Disease

SIR,—Since atherosclerosis leading to occlusive arterial disease such as ischaemic heart disease is generally supposed to be a process that extends over many years, Dr. J. M. McGarry (30 August, p. 530) is right to point out that one needs to assess the

FIG. 1.—Individual values and mean levels of IgM globulin in XO, XX, and XY subjects.

magnitude of possible causative agents over a long period. It is for this reason that the first studies suggesting dietary sugar is such an agent deliberately excluded information from subjects who admitted to changing their intake of sugar.¹ It is, of course, not possible to measure precise sugar consumption over a lifetime, but since habitual intakes of sugar differ widely between individuals we believe it can be adequately measured by a careful dietary questionnaire. We feel too that this assumption was supported by the findings, in two separate surveys, of considerable differences between individuals with and without occlusive arterial disease, and by the fact that the values were very similar in the three groups of controls that we studied, and in the three groups of patients.

Although Mr. R. W. Howell and Dr. D. G. Wilson (19 July, p. 145) include separate data for subjects who claim not to have changed their intake of sugar, they do so almost as an afterthought. Similarly, having given the figures for all their subjects, they match for age only at the end of their presentation, although in early studies^{1,2} it was pointed out that sugar intake varies with age. These factors of age and of reasonable constancy of sugar intake were thus made essential features of the design of the investigations by my co-workers and myself, whereas Mr. Howell and Dr. Wilson refer to the introduction of these features as "considerable manipulations." This is almost as if one were reporting on the incidence of myocardial infarction in two groups of people, and only at the end of the report took into account the sex and age of the people comprising the groups.

When these essential features are taken into account, then there is indeed a higher intake of sugar in those subjects of Mr. Howell and Dr. Wilson with confirmed disease, though not of the same magnitude as that found in the earlier work. Moreover, Mr. Howell and Dr. Wilson were then left with a total of 29 subjects and 29 controls; the studies of ours which they refer to as having small numbers had in fact twice as many.² Both sugar intake and the chances of developing ischaemic heart disease are also affected by class and occupation. In each of the studies reported,^{1,2} there was—to some extent fortuitously—an almost exactly similar distribution according to these criteria. It would be interesting to know the precise occupations of the subjects with ischaemic heart disease and of the control subjects in the study of Mr. Howell and Dr. Wilson.

There is one conclusion of these authors that we find impossible to understand. They write: "These results suggest that considerably more confirmation is required before acceptance of Yudkin's hypothesis that high sugar intake is the chief dietary factor causing ischaemic heart disease." Where in their paper is there evidence that there is some other, more important, dietary factor? And if the chief dietary factor is not sucrose, are we supposed to believe that it is fat, which is the dietary factor most actively canvassed as being implicated in causing ischaemic heart disease? But Mr. Howell and Dr. Wilson would obviously reject this for the same reasons they reject sucrose. For, as far as we know, properly conducted and controlled investigations of the sort we have discussed here have never revealed differences in the intake of fat between individuals that

developed ischaemic heart disease and individuals that did not.—We are, etc.,

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Hazard of Self-inflating Resuscitation Bags

SIR,—We would like to draw attention to a hazard of the use of resuscitation bags of the self-inflating type, such as the Ambu bag, which depend on a sponge foam insert for their self-inflation properties.

In this hospital Ambu bags are used regularly, not only as a simple device for providing intermittent positive pressure ventilation in an emergency, but also to achieve forced expansion of the lungs to aid chest physiotherapy in patients treated by mechanical ventilation, or in those whose vital capacity is severely diminished.

Recently a patient suffering from tetanus was curarized and ventilated for two weeks. Chest physiotherapy aided by inflation with an Ambu bag was performed three times each day. On the tenth day some small pieces of sponge foam were aspirated from the tracheostomy. Fig. 1. The Ambu bag was at once examined, and it was found that further identical pieces of sponge foam could be expelled from it on forcible compression. We cut the outer rubber bag open and exposed the interior to find that the sponge

FIG. 1

FIG. 2

foam insert had torn across at one point and small fragments were breaking away from the torn edge and falling into the lumen of the bag. Fig. 2.

All the Ambu bags in this hospital were originally supplied with Ambu non-return valves. These had been changed for Ruben valves as a matter of personal preference. Examination of the original Ambu valves showed that they were fitted with wire mesh filters which would prevent any but the minutest of sponge foam particles from passing from the bag into the patient. The Ruben valves had no such filter, and thus could readily transmit relatively large particles from the disintegrating insert of the bag. The Ambu bag in question had been in use for about one year, had never been autoclaved or subjected to any sterilizing technique, and had not been stored near a radiator, so the deterioration of the insert is, we presume, due to normal wear and tear in normal usage.

We believe that there may well be others who, like us, have been using alternative non-return valves on these commonly used bags without realizing the importance of a wire mesh filter, and may thus be exposing their patients to accidental insufflation of foreign matter into the airways. Fortunately our patient suffered no irreparable harm from this unfortunate accident.—We are, etc.,

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Azathioprine for the Nephrotic Syndrome

SIR,—We have read with great interest the report by Dr. M. W. Moncrieff and others (15 March, p. 666) on the use of cyclophosphamide in the treatment of the nephrotic syndrome.

We present here results achieved with the exclusive use of azathioprine in 12 adult subjects with an age range from 15 to 55 years, all with the nephrotic syndrome. On the basis of light microscope examination they were subdivided as follows: glomerulonephritis with minimal changes (1 case); membranous nephritis (6 cases); membranous-proliferative nephritis (5 cases). The glomerular filtration rate was, in all patients, within normal limits. Azathioprine was administered daily for at least one year at a dosage of 100 mg./day. Evaluating the efficacy of the drug by proteinuria (as did Dr. Moncrieff and colleagues) we have obtained complete remission in one case; partial remission in nine cases (decrease of at least 50% of proteinuria); and in two cases there was no effect. In 11 of our patients the administration of azathioprine, mostly at half-dosage, has been continued without interruption up to the present time (in three cases for more than three years, in four cases for more than two years); a complete remission was achieved in another two patients, while the situation in the other patients remains unchanged, except for one who has deteriorated. Leucopenia (less than 2,000 leucocytes/cu. mm.) occurred in three patients, of whom, however, only one had to stop treatment for a prolonged period.

Nine of our patients had had steroids without any beneficial effect before starting