stability for the articulation. The unique design of the Fenlin prosthesis appears to satisfy all of the complex requirements of a rotator cuff replacement.

It will be recalled that the anatomical musculocutaneous cuff functions not only to stabilize the glenohumeral joint, while allowing it great freedom of motion, but also to fix the fulcrum against which the deltoid can contract and elevate the humerus with power.² The hemiplegic's paralysis of the rotator cuff provokes not only painful subluxation of the joint but also loss of the ability to fix the glenohumeral fulcrum. The deltoid, then, is unable to elevate the humerus and merely shrugs the shoulder. In the hemiplegic who gradually regains muscle strength in the upper extremity the elongated rotator cuff does not decrease to its normal size. Hence shoulder pain continues and is usually accompanied by weakness in elevation of the humerus.

In the Fenlin design a large ball is attached to the scapula, while the socket is secured to the humerus. The geometry of the large ball diminishes the magnitude of mechanical force necessary for the deltoid to initiate elevation. Also, the implant is designed with an inherently stable fulcrum so that the deltoid can elevate the humerus without assistance from the rotator cuff. The positions of the ball and socket are reversed from their normal anatomical location to diminish the potential for dislocation. The other novel feature of this implant is a robust scapular anchor that greatly reduces the likelihood of loosening of the component. Early clinical experience with the Fenlin prosthesis is encouraging. Further trials in hemiplegics appear to be indicated.—I am, etc.,

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¹ Fenlin, J. M. jun., *Orthopedic Clinics of North America*, 1975, **6**, 565.

² Inman, V. T., Saunders, J. B., and Abbott, L. C., *Journal of Bone and Joint Surgery*, 1944, **26**, 1.

Corticosteroids in Treatment of Anaphylaxis

SIR,—The excellent paper by Dr. P. Davies and others (24 May, p. 434) on the value and complications of intravenous pyelography raises an important point in suggesting that patients who are thought to be at risk for anaphylaxis due to possible iodine sensitivity should be given steroid cover. In the absence of a controlled clinical trial of the effect of steroids in acute anaphylaxis it would seem that the commonly held belief that they are the mainstay of the treatment of anaphylaxis is ill-founded. Prophylactic steroid treatment is unlikely to offer a significant degree of protection against acute anaphylaxis mediated by IgE in man. If there is any effect it is likely to be delayed, as in the rat, necessitating pretreatment with a single large dose 12-24 h ahead of the risky procedure. If the patient has type III hypersensitivity steroids could be expected to give complete protection, but this mechanism by itself is unlikely to produce the sudden dramatic emergency with which we are concerned. In patients with dual sensitivity the initial reaction will be no less dangerous, but subsequent management will be easier if steroids have been given.

Though glucocorticoids are unlikely to modify the anaphylactic reaction itself, a very high dose directly reduces capillary permeability and may help to sustain the blood pressure. Here one is seeking the effect which, for instance, is also useful in the treatment of cerebral oedema. For this role a water-soluble phosphate should be activated in the tissues more readily than the hemisuccinate of hydrocortisone, and, since they penetrate tissues much faster than other preparations, dexamethasone or betamethasone phosphates are the best choices. A reasonable dose of either would be 80 mg intravenously. An equivalent dose of hydrocortisone hemisuccinate would be 2.5 g.

Adrenaline, with its blend of α and β sympathetic effects, will help to antagonize the initial catastrophic loss of blood pressure while at the same time antagonizing the intracellular consequences of anaphylaxis. Whatever the risk to the heart, when faced with profound anaphylactic collapse most doctors give adrenaline intravenously, using 0.5 ml of 1/1000 solution, diluted if possible, given slowly. Their choice is almost certainly correct, since in profound shock a peripheral injection would never reach the rest of the body. Perhaps in the future intravenous salbutamol will be judged superior. For the second injection it is logical to give intravenous aminophylline, which potentiates the intracellular β sympathetic effect. Only the third injection should be steroid.—I am, etc.,

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Perforation of Small Intestine and Slow-K

SIR,—While not discounting the possibility that Slow-K may cause small-intestinal ulceration and perforation, I feel that this preparation should not be incriminated on the evidence presented by Dr. M. A. Farquharson-Roberts and his colleagues (26 July, p. 206) and that other aetiological factors should be considered—namely, cardiovascular disease.

Of the large number of causes of small-intestinal ulceration, cardiovascular disease (arteriosclerosis and hypertension) appears to be the commonest, probably producing the damage by localized gut ischaemia.^{1,4} Thus the long history of hypertension and multiple strokes in the 57-year-old patient reported may have been of greater significance than the administration of Slow-K.

I know of no specific histological features associated with iatrogenic ulceration, and histological differentiation of ulceration due to potassium chloride medication from ulceration due to other causes has been found impossible.³ Therefore further details of the "almost certainly iatrogenic" histological picture would be required before the conclusions reached could be accepted.—I am, etc.,

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¹ Teicher, I., et al., *Surgery, Gynecology and Obstetrics*, 1963, **116**, 196.

² Alexander, H. C., and Schwartz, G. F., *Gastroenterology*, 1966, **50**, 224.

³ Wayne, D. M., and Helwig, E. B., *American Journal of Clinical Pathology*, 1968, **49**, 26.

⁴ Carlson, H. C., *Radiologic Clinics of North America*, 1969, **7**, 97.

Pyridoxine and Oestrogen-induced Glucose Intolerance

SIR,—It has been suggested that women using contraceptives should take a pyridoxine supplement to prevent oestrogen-induced changes in tryptophan metabolism.¹ These changes include the production of increased amounts of an intermediate, xanthurenic acid, after a tryptophan load. This compound has been claimed to produce diabetes due to the formation of an inactive complex with insulin.²

The possibility that xanthurenic acid is responsible for oral contraceptive-induced glucose intolerance and gestational diabetes has been examined clinically. The reduction by pyridoxine of excessive xanthurenic acid excretion after a tryptophan load has been associated with an improvement in glucose tolerance.^{3,5} However, we do not believe that the two are causally related, as has been suggested, but rather that the beneficial effects of pyridoxine are possibly due to normalization of other tryptophan metabolites. Some women suffer from oestrogen-induced glucose intolerance independent of any abnormalities in xanthurenic acid excretion. Furthermore, we have found that the administration of xanthurenic acid (Sigma, Grade A, 99% pure) 120 mg/kg intraperitoneally in ammoniated saline failed to alter blood glucose levels in male Sprague Dawley or Wistar rats. We repeated the experiments using the special high fat diet which had been used in the original studies on the diabetogenic effects of xanthurenic acid.⁶ Once again xanthurenic acid was found to be inactive (see fig.) In further experiments it was found that xanthurenic acid did not impair glucose tolerance when given one hour before an oral glucose load (3 g/kg given as a 50% w/v solution). In a single experiment in a male albino rabbit xanthurenic acid 100 mg/kg given intravenously did not alter blood glucose concentrations over a period of three hours.

Effect of intraperitoneal injection of xanthurenic acid on blood glucose concentrations in male Wistar rats. Blood samples (0.1 ml) were obtained by heart puncture under pentobarbitone anaesthesia. Results reported by Kotake⁶ are also indicated.

Our failure to demonstrate any diabetogenic effect of xanthurenic acid could not be due to contamination with the 8-methyl ether of xanthurenic acid, which has been reported to be antidiabetogenic,⁷ since the sample of xanthurenic acid used was found

to be virtually free from this contaminant when examined by mass spectrometry.—We are, etc.,

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- 1 Lubbey, A. L., *et al.*, *Lancet*, 1970, 2, 1083.
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HL-A Antigens and Ankylosing Spondylitis

SIR,—Your leading article "HL-A Antigens and Rheumatic Diseases" (3 May, p. 238) states that "only some 5% of individuals with HL-A W27 develop ankylosing spondylitis." Recent data from several sources suggest that the figure is nearer 20%.

A controlled study¹ of "healthy" blood donors at Stanford University Medical Center revealed a prevalence of symptomatic, definite ankylosing spondylitis (A.S.), satisfying the New York criteria,² in 20% of males and 17% of females carrying the W27 antigen. There were no cases among W27-negative controls. These findings have been confirmed by Cohen *et al.*³ at Northwestern University, Chicago, for male blood donors. Similar unpublished prevalence figures have been found for the Haida and Pima Indians. Some 10% of the Haida Indians develop A.S.,⁴ and Gofton, in Vancouver, has now shown that HL-A W27 is present in 50% of the Haida. Comparable studies by Bennett in Arizona have revealed W27 in about 20% of Pima Indians, a population known to have a 4% prevalence of A.S.; thus these studies also demonstrate that 20% of individuals with HL-A W27 develop disease. A review of earlier Caucasian family studies indicate that this 20% figure is to be expected; Emery and Lawrence⁵ stated that A.S. was present in 10% of first-degree relatives of patients with A.S. It has been shown that some 50% of these first-degree relatives are W27 positive.⁶

Investigations in progress include large-scale population studies with screening by questionnaires, radiographs, and HL-A typing. It will thus become apparent whether extrapolation from a 20% risk of developing the disease in an individual with W27 to a total population prevalence of 1-1.5% is justified. The clinical implication of this higher figure is evident. Ankylosing spondylitis may no longer be considered a rare disease.—We are, etc.,

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α_2 H-globulin and Ferritin

SIR,—Your leading article on "Plasma Proteins in Cancer Surveillance" (24 May, p. 407) has again raised the subject of α_2 H-globulin and once again we have noted the close similarities between the studies on this protein by Buffe and his colleagues¹ and our own investigations into "serum ferritin."²

α_2 H-globulin appears to share many properties with the iron-containing protein ferritin. It has a molecular weight of about 600 000, normally contains 15-25% iron, but can occur without iron.³ It is heat-stable and polymerizes to form dimers, trimers, etc. Indeed Buffe *et al.* have demonstrated its immunochemical identity with ferritin.³ α_2 H-globulin is found in the circulation (at concentrations of greater than 200 μ g/l) at birth and disappears from the circulation during the first few weeks of life. In many patients with malignant disease the protein is again found in high concentrations in the plasma. Studies of serum ferritin concentration in malignancy have not been extensive, as most investigations have been related to iron metabolism, but nevertheless serum ferritin concentrations follow the same pattern both during the neonatal period and in cancer patients.²

On cellulose acetate electrophoresis in barbitone buffer at pH 8.6 purified human liver ferritin moves similarly to the α_2 component of serum proteins (see figure). There are a number of other similarities. α_2 H-globulin extracted from tumour or from fetal liver appears to differ from that extracted from normal liver in carbohydrate content, iron content, and state of polymerization.¹ Similarly, differences occur between ferritin preparations from normal and malignant or fetal tissue.⁴ Furthermore, serum ferritin appears to differ from normal liver or spleen ferritin in a number of ways, including its iron content.⁶ Both serum ferritin and α_2 H-globulin concentrations are increased in patients with hepatoma or acute lymphoblastic leukaemia. A rise in α_2 H-globulin concentration precedes relapse in children with hepatoma who have undergone chemotherapy,¹ and serum ferritin concentrations may give a similar warning in children with acute lymphoblastic leukaemia.⁶

Comparison of the concentrations of α_2 H-globulin and circulating ferritin in various disease states is difficult because of the different starting materials and methods of assay employed. None the less, it seems likely that both names describe members of what now seems to be an extensive family of iron-containing proteins generally called ferritins. Further examination of the properties of circulating α_2 H-globulin and ferritin may give much information about the nature of ferritin in malignant tissue, about its release into the circulation, and about im-

munological relationships between the various proteins.

It seems likely that research in this area has been hindered by the use of different names for the same protein. The appearance of a further report⁷ identifying β -fetoprotein as ferritin emphasizes the importance of specific characterization of the protein rather than reliance on its electrophoretic mobility in order to avoid confusion.—We are, etc.,

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Unsuccessful Immunosuppressant Treatment of Paraquat Poisoning

SIR,—The successful use of immunosuppressant therapy in a case of paraquat poisoning has been described by Dr. J. A. Laithwaite (1 February, p. 266). The patient in question was treated with prednisolone 100 mg daily from admission, seven days after poisoning with about a quarter of a cupful of paraquat. Azathioprine 50 mg and potassium aminobenzoate one sachet (3 g) four times daily were started five days after admission because of deteriorating respiratory function. We report two further cases treated with immunosuppressants, one within 48 hours of poisoning and the other when breathlessness started, in spite of which both patients died.

A 38-year-old man took one mouthful of paraquat concentrate and was brought to hospital 24 hours later. Paraquat was detected in his urine. Treatment with oral bentonite was started immediately in an attempt to prevent intestinal absorption (7 December 1974, p. 569) and was continued for three days. Twenty-four hours after admission immunosuppressive treatment was started with azathioprine 50 mg and prednisone 10 mg four times daily. On the eighth day after admission he began to feel short of breath on mild exertion and on the 15th day he died in respiratory failure. Necropsy showed extensive pulmonary fibrosis.

Another man, aged 20, took four mouthfuls of paraquat concentrate, and treatment with oral bentonite, 200 ml of suspension hourly, was started within an hour and continued for two days. Paraquat was detected in his urine for the first three days after admission. On the 15th day he became short of breath and chest x-ray showed bilateral pulmonary shadowing. He was then treated with azathioprine 50 mg, prednisone 10 mg, and potassium aminobenzoate one sachet, each four times daily, but his breathlessness steadily worsened and he died in respiratory failure 25 days after poisoning. Necropsy again showed extensive pulmonary fibrosis.

Immunosuppressive treatment in the doses given did not obviously modify the course or outcome of the poisoning in these cases, but perhaps larger doses started earlier might have done so.