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

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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 Similar unpublished prevalence figures have been found for the Haida and Pima Indians.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.

We would like to thank Drs. B. E. Miles and J. Wood for permission to report these cases.

—We are, etc.,

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Conization and the Minipill

SIR,—The incorporation of a cervical cancer screening laboratory in a family planning clinic has led to a realization regarding the (progesterone-only) minipill which I have not previously seen recorded.

Some 300 postconization cervical smears screened have been characterized by the scanty nature or even complete absence of endocervical cells and mucus despite the smears having been taken in the usual manner from the region of the cervical os. As the chief mode of action of the minipill depends on its effect on endocervical mucus it would seem apparent that this type of oral contraception would lose its efficacy if a large proportion of the gland-bearing, mucus-producing epithelium of the endocervix were removed by conization.

The abortion law in South Africa does not permit therapeutic termination of pregnancy in cases of contraceptive failure and it is therefore unjustifiable to embark on a clinical trial of this theoretical consideration. It has therefore been decided in this family planning programme to regard previous conization quite empirically as a contraindication to the use of the minipill.

It would be interesting to know whether any of your readers have had experience of minipill failures in patients who have undergone cervical conization.—I am, etc.,

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Risks of Total Hip Replacement

SIR,—We should like to discuss your leading article (10 May, p. 296) on hip replacement and also reply to Professor J. Charnley's letter (31 May, p. 498) in which he states: "I think I am right in saying that all experimental investigations have now exonerated the methylmethacrylate monomer in the concentrations likely to be encountered in the blood stream during a surgical operation."

We agree that neurogenic impulses are unlikely to cause arterial hypotension. The pressure in the medullary cavity depends on the integrity of the cortex that is destroyed during operations such as total hip replacement. The cardiovascular reaction to neurogenic stimuli is practically instantaneous, whereas the reaction to the monomer is delayed by 1 to 4 minutes.¹ Pulmonary embolism of one kind or another may cause intraoperative collapse but cannot be regarded as a satisfactory explanation of all the hypotensive episodes.

A study of the cardiovascular effects of an intravenous dose of 0.25 ml of the liquid monomer in anaesthetized dogs has shown that the monomer causes a brief arterial hypotension that is rapidly counteracted by increases in the cardiac rate and output.² The cause of the hypotension appears to be

peripheral vasodilatation. Vasodilator substances such as amyl nitrite or oxytocin may precipitate profound hypotension when given to subjects lying in the horizontal or slightly head-up position.³ In healthy conscious subjects the hypotension is immediately counteracted by the baroreceptor system that autonomically increases heart rate and output. Anaesthesia may block baroreceptor activity, especially in elderly or debilitated subjects.⁴ The addition of a vasodilator substance in the latter circumstances may cause an acute failure of the venous return with its obvious consequences. It is not unreasonable to expect that some of the monomer must inevitably be absorbed into the blood stream, especially when it is applied to highly vascular areas such as the medullary cavity of the femur.

We observed the hypotensive syndrome several years ago and modified it by placing the patients in a moderate head-down tilt during the operations. The degree and the duration of the hypotension are much reduced by this procedure when it is used with the other measures designed to maintain venous return and blood volume in anaesthetized patients. Non-rebreathing ventilatory systems are also advisable because of the possibility that absorbed monomer is excreted by the lungs.⁵

We fully support Professor Charnley's recommendation that the cement should not be applied until it is of a firm and doughy consistency because this allows the evaporation of excess monomer and diminishes the amount available for absorption into the blood stream. We are also conscious of the Report of the Working Party on Acrylic Cement in Orthopaedic Surgery,⁶ advising that the use of the cement in anaesthetized patients demands the careful maintenance of their cardiovascular and other functions during the operations.—We are, etc.,

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incident involved few casualties and occurred in close proximity to the designated hospital. In incidents involving large numbers of casualties some sort of initial assessment must be made by the site medical officer to ensure that seriously injured persons who have a chance of survival are taken to hospital first rather than the "walking wounded"—and hospitals have no treatment for the dead. We would venture to suggest that the figures available from the 1200 or so doctors all over Great Britain who feel strongly enough about initial resuscitation to have formed themselves into voluntary "accident units" bears out the premise that almost every seriously injured person will travel better and stand a greater chance of survival if given some form of initial resuscitation. This is not to say that the doctor attending a serious accident should in any way delay the transport of the injured to hospital unless he feels that the patient is not fit to start his journey without initial resuscitation.

Accident units such as that to which we belong are being formed, mostly by general practitioners but also by hospital doctors in their off-duty time, in increasing numbers. This in itself is proof of the need for such schemes, and their great advantage is that medical aid can be rendered to the patient without delaying his transport to hospital in most cases because the doctor is immediately mobile in his own transport, which permanently contains his equipment. Often the doctor's job can be done en route to the hospital in the ambulance. We have found that fire, police, and indeed ambulance personnel welcome the existence of these units, and the need is increasing all the time. They are manned entirely on a voluntary basis, and we are convinced that doctors would not spend their time going out, often in very adverse weather conditions and on their nights off, if they did not feel that their services were badly needed.—We are, etc.,

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Deaths from Non-accidental Injuries in Childhood

SIR,—Dr. K. T. Farn (9 August, p. 370) has admirably outlined the notion of the statistical machinery which records those elements apposite to estimating the number of deaths by child battering. Any error in this machinery, he states, is not possible. Alas, he has not taken account of the human factor that can make statistical assessment greatly erroneous. In your issue of 26 July (p. 238) your legal correspondent explains the discrepancy between the suicide rate in England and Wales (8.0 deaths per 100 000) and in Denmark (20.8 per 100 000) by stating that "the difference in prescribed official procedures and consequent attitudes could well be a considerable part of the explanation for the very different suicide rates in the two countries." The formal English coroner system is regarded as less accurate than the informal Danish *kredsloeger* system, the latter being better able to take account of the human factor.

Accurate figures of death from child battering are likely to come only from studies small enough to take into account elements, impossible to record in a large statistical

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Value of Accident Units

SIR,—With reference to the article by Mr. K. Tucker and Mr. A. Lettin on the Tower of London bomb explosion (2 August, p. 287), we could not agree more that mobile hospital teams are required only rarely at major incidents and would emphasize that waiting for such a team will often delay transport of the injured to hospital, as the team has to be assembled, transported to the scene by ambulance or police vehicle, and then deployed before anything is done for the patient.

However, we would strongly disagree that evacuation of severely injured casualties without initial resuscitation is most desirable, unless one is thinking entirely within the context of the mobile hospital team. Furthermore, this would be feasible only if the