Control programme referred to in Dr. Payne's letter the performance of the U.C.H. laboratory was equally satisfactory—that is, calcium, mean bias 0.00 and precision (S.D.) 0.08 mg/100 ml; albumin, mean bias 0.15 and precision (S.D.) 0.12 g/100 ml.

In our opinion an important reason for the discrepancy lies in the manner in which the reference albumin level has been selected. Dr. Payne and his colleagues, while stating that their normal range for serum albumin is 3.7–4.7 g/100 ml, chose to use 4.0 g/100 ml as their reference point because it gave a mean adjusted calcium level of 9.7 mg/100 ml. At U.C.H. 4.6 g/100 ml was chosen as the reference level because it approximated to the mean concentration found in a balanced population of 1,000 healthy blood donors, with equal numbers of males and females in 10 age groups between 18 and 65 years.

Whatever albumin level is chosen as the point of reference is arbitrary because there are significant differences in the levels between the sexes, and very appreciable changes occur with ageing and alteration of posture. Thus while our normal range for plasma albumin in male outpatients of 18–25 years is 4.4–5.3 g/100 ml the 95% limits applicable to female inpatients of 56–65 years is 3.6–4.5 g/100 ml. Fortunately the regression coefficients of total plasma calcium on albumin arrived at by Dr. Payne's team and at U.C.H. are very close to one another and therefore there is no reason why Mr. Sanderson should not derive his own formula for the adjustment of serum calcium levels based upon an arbitrary serum albumin level appropriate to the type of population he normally deals with.—We are, etc.,

E. M. BERRY
C. E. DENT
F. V. FLYNN
M. M. GUPTA
S. TURNER

Department of Clinical Pathology,
University College Hospital,
London W.C.1

Sickling Pain and Season

SIR,—Attacks of painful crisis in sickle-cell anaemia seem to be more frequent in winter than in summer in our experience. Edington¹ has referred to the common presentation of sickle-cell disease with cold weather rheumatism in Ghana and Konotey-Ahulu² has discussed this in a paper entitled "Sicklaemic Human Hygrometers," pointing out that the recrudescence of joint pains in such patients tends to occur in the period just before the rains. It is Isaacs-Sodeye's impression that in Nigeria the rainy season (May–August) and the cold harmattan months (late December–mid-February) are associated with an increase in painful episodes.³ Other references to possible effects of cold are mentioned below. Few systematic observations have been recorded, though very recently Seeler⁴ reported an apparent lack of seasonal variation in sickle-cell crisis in children in Chicago. Since the city of Buffalo in upstate New York endures wide seasonal fluctuations in temperature and humidity, it was decided to examine the monthly incidence of episodes of severe pain requiring admission to hospital in

patients with sickle-cell anaemia and sickle-cell disease.

The records of all patient with these disorders admitted to three Buffalo hospitals, the Buffalo General Hospital, the Children's Hospital of Buffalo, and the E. J. Meyer Memorial Hospital, during 1967–71 were examined. There were 230 admissions for 78 patients; 51 had sickle-cell anaemia and 27 had haemoglobin S-C disease. Episodes in which acute pain was the sole or main reason for admission accounted for 134, or more than half the total admissions, and only these are discussed further. Episodes in which evident infection was detected on admission were excluded, but there were relatively few of these, even though infection was searched for diligently.

The total numbers of painful episodes requiring admission for each month over the five-year period are shown in the upper part of the accompanying figure. The monthly totals show significant deviation from expected values if we assume a uniform admission rate and composition throughout the year and a uniform incidence of sickle crises ($\chi^2=28.3$; D.F.=11; $P<0.01$). Weather is difficult to summarize and in the lower part of the figure only the temperature and humidity are shown, averaged for each month of the same five-year period. The averaging tends to obscure some of the extremes of temperature experienced and cannot show rapid changes of weather which may have important biological effects.⁵ However, there is a tendency for more episodes of pain to be associated with lower temperature and higher humidity.

A variety of factors are known or suspected to precipitate painful crisis.^{6,7} Infection is perhaps the most important single factor, particularly in Africa.⁷ Though many of our patients experienced episodes of overt infection, including pneumonia and urinary infections, these were not included in the episodes scored in the figure. Absence of

subclinical degrees of bacterial or, more especially, viral infection is difficult to prove, and in a retrospective study it cannot be claimed that such infection could not on occasion have been overlooked. However, the supposed role of infection in precipitating crisis is well known and throat, sputum, and urine cultures were carried out on most patients. It is unlikely that infection alone can account for the winter excess of painful episodes and it seems likely that cold

or humidity or both may have an important effect. Alternatively, it might be argued that warm and dry weather in summer has a beneficial effect in preventing crisis. Several of our patients regarded cold as a precipitating factor for pain. Rubenstein⁸ has mentioned similar subjective effects and demonstrated in vitro that cool temperatures increase blood viscosity and could thereby contribute to local vascular obstruction in sickle-cell anaemia patients. Other possible mechanisms to be considered include combined effects of diuresis and lowered temperature⁹ and the presence of cold agglutinins.¹⁰

The present retrospective study was of small numbers but suggests that there is an effect of season which deserves more detailed, prospective investigation. It may have practical implications in the prognosis and management of patients with severe sickling syndromes. As a first step it would be useful to examine hospital admissions for sickling pain in relation to season in a number of different places with different climatic variation, including other parts of the United States, the United Kingdom, Africa, and the Caribbean.

We are indebted to the Record Room staffs and Committees at the three hospitals for their co-operation.

—We are, etc.,

HASSAN AMJAD
R. M. BANNERMAN
JANIFER M. JUDISCH

Departments of Medicine and Pediatrics,
State University of New York at Buffalo,
Buffalo, New York

- 1 Edington, G. M., *British Medical Journal*, 1953, 2, 957.
- 2 Konotey-Ahulu, F. I. D., *Lancet*, 1965, 1, 1003.
- 3 Isaacs-Sodeye, W. A., personal communication.
- 4 Seeler, R. A., *Lancet*, 1973, 2, 743.
- 5 Tromp, S. W., *Medical Biometeorology*. Amsterdam, London, and New York, Elsevier, 1963.
- 6 Diggs, L. W., *American Journal of Clinical Pathology*, 1965, 44, 1.
- 7 Konotey-Ahulu, F. I. D., *Lancet*, 1971, 2, 1255.
- 8 Rubenstein, E., *American Journal of Medicine*, 1961, 30, 95.
- 9 Addae, S., *Lancet*, 1971, 2, 1256.
- 10 Charmot, G., Reynaud, R., and Bergot, J., *Lancet*, 1963, 2, 540.

Laparoscopic Tubal Ligation

SIR,—Laparoscopic sterilization by electro-coagulation has two well-recognized disadvantages—the danger of burns to other structures¹ and the poorer chances of reversibility as compared with tubal division and ligation. Indeed, many gynaecologists are electing to sterilize their younger patients by tubal division at laparotomy since tubotubo anastomosis after ligation is reported to have a pregnancy rate as high as 70%.² Clarke³ has successfully devised instruments to be used through an operating laparoscope to perform tubal ligation, but this undoubtedly requires considerable skill and patience. There is also much research into the development of various forms of clip, which it is hoped will provide a simple and perhaps easily reversible sterilization procedure, though reports to date have shown a discouragingly high failure rate.^{4,5}

We have evolved a simple method of tubal division and ligation using the laparoscope which we have not heard of or seen described before. Routine laparoscopic instrumentation is undertaken under general anaesthesia, after the method of Steptoe.⁶ The biopsy (or coagulation) forceps is introduced via its trocar in the midline or

through two separate lower-quadrant incisions 2 cm above the symphysis. A fallopian tube is grasped in its middle third and drawn to the surface by withdrawing forceps and trocar. This manoeuvre is aided by an assistant lifting the uterine cornu to the incision and occasionally made easier by deflating the abdomen. Simple tubal division and ligation with excision of a small portion for histological examination is then performed and the tube returned to the peritoneal cavity (where it is inspected) by allowing the uterus to fall away. The procedure is repeated on the opposite side after reintroducing trocar and forceps.

To date, we have performed this procedure on 20 successive patients of varying abdominal wall thickness (the obese would obviously not be suitable, however) and have experienced no operative difficulty, neither haemostasis nor tearing of the tube being a problem. Operative time is about 20 minutes and the patients have all been discharged home the following day with no postoperative complication. The procedure should have the same known minimal failure rate and potential reversibility rate as open tubal division and ligation, with the advantages of patient acceptability, low bed occupancy, and no diathermy hazards. A larger series will be reported in due course.—We are, etc.,

K. R. GREENE
D. I. WISE
H. A. H. MELVILLE

Royal Sussex County Hospital,
Brighton, Sussex

- 1 *Medical Defence Union Annual Report* 1972, p. 16. London, M.D.U., 1973.
- 2 Williams, E. A., personal communication, December 1973, and *Oxford Medical School Gazette*, 1972, 24, 34.
- 3 Clarke, H., *Fertility and Sterility*, 1972, 23, 274.
- 4 Davidson, A. C., and Donald, I., *Scottish Medical Journal*, 1972, 17, 210.
- 5 Palmer, R., in *International Conference on Contraception, Sterilisation and Abortion*, Paris, 1973. In press.
- 6 Steptoe, P. C., *Laparoscopy in Gynaecology*. London, Livingstone, 1967.

Coping with Minor Casualties

SIR,—Your leading article (2 March, p. 339) draws attention to the problems which minor accident cases pose for overworked hospital casualty departments. The alternative, the treatment of minor cases by general practitioners, is, as you point out, not particularly satisfactory. An additional possibility which you do not discuss is that minor industrial accidents which are at present treated in casualty departments could be treated by an occupationally based health service.

With Dr. D. M. Richardson of the Mid Sussex Area Health Department I have recently carried out a survey of the treatment of industrial accident cases in the accident and emergency department of the Royal Sussex Hospital in Brighton. This study was carried out by kind permission of Mr. N. Laurence. We found that of a sample of 2,000 cases seen by the emergency department between 9 a.m. and 9 p.m. Monday to Friday in June 1973, 45% were non-workplace minor injuries which could have been treated elsewhere; a further 18% were minor injuries to children, mostly occurring at school; 17% were workplace injuries mostly of a minor nature; 17% were genuine emergencies requiring immediate hospital treatment; and the remain-

ing 4% were overdoses, self-injury, or psychological complaints.

Two hundred industrial accident cases were investigated in detail. We judged that 32 of these cases were severe enough to need treatment in a hospital emergency department; but the remaining 168 cases could have been treated by an occupationally based health service with minimal loss of working time. Such services—which are not part of the National Health Service—have been established on a fee-paying basis in some half-dozen centres in Britain.

We sent a postal questionnaire to the 168 persons who had suffered "minor" industrial accidents and 107 of these were returned. Five days after the accident 13% of those followed up had lost two or more working days, in addition to time lost through travel to the emergency department and waiting to be treated. A further 13% of the sample returned to the emergency department for the removal of dressings etc., while 42% consulted their G.P. for this purpose. All of these services could have been provided by an occupationally based health service such as that set up in Harlow.¹ Such a service would not of course confine itself to treatment but would also concern itself with basic preventive work and safety education.

Generalizing from our sample, 8,500 of the 50,000 cases seen each year in the emergency department of the Royal Sussex Hospital are industrial accident cases; approximately 84% (about 7,140) of these cases could have been dealt with by an industrial health service. Accidents and illness at work cost the nation approximately £2,000m a year.² If the capital costs of a nationwide voluntary health service could be publicly provided, at a cost of approximately £200m, the cost would be recovered in a year if only 11% of working days lost through industrial accident and illness could be prevented. In addition, the proportion of minor accident cases making demands on casualty departments should also be reduced.—I am, etc.,

CHRISTOPHER BAGLEY

Department of Sociology,
University of Surrey,
Guildford

- 1 Taylor, Lord, *Lancet*, 1959, 1, 875 and 933.
- 2 *Off Sick*, London, Office of Health Economics, 1971.

SIR,—Most of the evidence and recommendations in the recent report from the House of Commons Expenditure Committee on accident and emergency services¹ fall into line with the thinking of members of the Casualty Surgeons Association, who actually do the work of seeing emergencies. There is, however, one important omission. The main reason for attendance at a hospital casualty department for a minor emergency as opposed to a health centre (even if it were open 24 hours a day) is that the patient can ring 999 free for an ambulance to take him to hospital and not to a health centre. How this situation can be remedied is debatable, but is nevertheless a factor which should be taken into consideration.—I am, etc.,

M. ELLIS
Hon. Life President, C.S.A.
Morecambe, Lancs.

- 1 *Fourth Report from the Expenditure Committee, Session 1973-74, Accident and Emergency Services*. London, H.M.S.O., 1974.

Therapeutic Non-equivalence of Digoxin Tablets

SIR,—The letter from Dr. A. H. Dewar (2 February, p. 197) helps to perpetuate two misunderstandings.

When Burroughs Wellcome reverted to their original manufacturing process in 1972 it was noticed that the "new" tablets produced higher plasma digoxin levels than previously. Their warning letter emphasized the importance of reviewing the dosage of all patients receiving Lanoxin tablets: "In these patients it may be advisable to consider reducing the dose of Lanoxin by half." Since the circularization of this letter the belief has grown among doctors and pharmacists that "new" Lanoxin is twice the strength of other digoxin tablets, a belief which is as potentially dangerous. A study of the data in the article by Dr. T. R. D. Shaw and others (29 December 1973, p. 763) quoted by Dr. Dewar shows that there is no significant difference between the plasma levels obtained with "new" Lanoxin tablets and Nativelle digoxin tablets. The bioavailability of these two products is the same and the consequence of doubling the dosage for a patient changing from "new" Lanoxin to Nativelle digoxin would be just as serious for the patient receiving a product of lower bioavailability.

The other misunderstanding is that "effectiveness," "bioavailability," and "dissolution rate" mean the same thing. Our research has shown quite clearly that a tablet can be produced which has an excellent dissolution rate but a poor therapeutic effect, or, conversely, a tablet with an excellent therapeutic effect (mean plasma levels of 1.3 ng/ml) but with a relatively poor result from a dissolution rate test. The standard dissolution rate test favours certain tablets with slower disintegration characteristics. I have personally observed tablets with the fastest disintegration time (and giving optimal plasma levels) burst into small particles in the test, the particles falling through the rotating perforated basket into a non-agitated part of the apparatus where they remained undissolved when the test samples were taken. We do not believe that the current dissolution rate test indicates the bioavailability of a product without correlation with plasma level studies.—I am, etc.,

P. T. HAIRSNAPPE
General Manager,
Willcox Laboratories
London, S.W.9

Smoking in Pregnancy

SIR,—Many B.M.A. members will have received a letter from the Health Education Council inviting them to co-operate in our campaign to deter pregnant women from smoking. Among the enclosures were a scientific memorandum blessed by the senior bodies in your profession, including the B.M.A. Board of Science, and a leaflet telling its readers how to give up smoking and illustrated with a photograph of a naked pregnant woman.

The leaflet seems to be doing its job. We received orders in the first fortnight of the campaign for half the 500,000 copies that would normally last 18 months. A few doctors, however, have complained that the naked woman's photograph is in poor taste,