wine, and oranges. Strong beer and red wine regularly produced attacks.

The assay on the isolated jejunum showed a content of 2-3 µg histamine/ml in the red wine confirmed on the chromatogram, while the white wines were free of histamine, but contained large amounts of bradykinin. Many amines other than tyramine or histamine are found in the wine precipitating migraine and in these wines tyramine was conspicuously absent. Antihistamine preparations do not relieve migrainous headache or migrainous neuralgia. The presumed kinin SRS is present in large quantity in the wines not precipitating migraine. Youdim *et al.*⁶ have shown a deficiency of conjugation of tyramine in migraine subjects. We suggest deficiency of conjugation of substances other than tyramine or histamine may account for the migrainous headache, and is probably related to a genetic deficiency since the condition is familial. Conjugation (acetylation) of the amine histamine occurs in the normal liver⁷ and very rapidly in one to two minutes

logical importance in the production of cirrhosis.—We are, etc.,

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Lignocaine Overdose and Ampoule Labelling

SIR,—I am reporting the survival of a 70-year-old man following the accidental administration of 1 g of intravenous lignocaine, given over a period of three minutes. My aim in doing so is to decry the lack of relevant labelling on some commonly prescribed drugs.

The patient was admitted in ventricular fibrillation which was immediately converted electrically to sinus rhythm. One hundred mEq of sodium bicarbonate were given. Ventricular tachycardia supervened, and lignocaine as a 1% solution was given with an immediate return of sinus rhythm. A dose of 100 mg had been asked for and unfortunately 1% was interpreted as 1 mg/ml so that 10 times the dose was given.

Blood pressure remained stable and pulse rate was steady at 82 per minute. Respiratory arrest occurred immediately but spontaneous respiration returned after five minutes artificial ventilation. Grand mal convulsions lasted 30 minutes and generalized rigidity one hour. Initial treatment consisted of 250 mg thiopentone intravenously, positive pressure ventilation for five minutes via an endotracheal tube, and intermittent doses of intravenous diazepam to control the convulsions and following restlessness. The patient remained stuporose and restless for 12 hours and he remained disorientated for three days. After this till discharge he was intermittently depressed and euphoric and was amnesic for the 24 hours following his cardiac arrest.

The electrocardiograph showed an antero-septal myocardial infarction. The only other abnormality which developed was a rise in blood urea from 38 mg 15 hours after admission to 134 mg/100 ml on the 15th day. When see two months later it was 28 mg/100 ml. Urine output remained above 800 ml in 24 hours after the first day.

The pharmacology and the toxic effects of lignocaine have been well described since the first report of its use in ventricular fibrillation in 1950.¹ Binnion *et al.*² have reported myocardial failure in dogs following 400 mg of lignocaine. Crampton and Oriscello³ describe a fatal toxic reaction following an infusion of 4.56 g of lignocaine over 24 hours terminating in respiratory and cardiac arrest.

Thiopentone is a controversial drug to use

in treatment. Steinhaus *et al.*⁴ suggested barbiturates have an additive effect on medullary depression. Possibly paralysing the patient and maintaining him by artificial ventilation may be more effective.

Although reporting the above misadventure is embarrassing I feel that it underlines the need for all drugs to be labelled clearly with the units usually needed in clinical practice. Astra have overcome this problem for lignocaine with disposable syringes containing a fixed amount of lignocaine, but other drugs such as calcium and potassium are still often dispensed in inadequately labelled ampoules.—I am, etc.,

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Malignant Lymphoma and Acute S.L.E.

SIR,—A number of reports of acute systemic lupus erythematosus (S.L.E.) and reticulosis have been recorded, mainly by authors in the U.S.A.¹ We should like to report a further case.

The patient, a 79-year-old spinster, was admitted with a short history of increasing lethargy, weakness, febrile symptoms, diarrhoea, abdominal pains, and a generalized rash. Her previous health had been unremarkable and she denied being on any medication. On examination she exhibited a generalized maculopapular rash, lymphadenopathy, hepatomegaly (spleen not palpable), and pitting oedema of both feet.

The abnormal investigations were as follows: Hb. 6.9 g/100 ml; W.B.C. 10,400/mm³ (eosinophils 8%); E.S.R. 83 mm/hr; serum bilirubin 1.6 mg/100 ml; direct Coombs test positive; latex L.E. and R.A. slide test strongly positive; L.E. cells in peripheral blood; plasma proteins albumin 2.8 g/100 ml, globulin 4.9 g/100 ml (gamma globulin 2.9 g/100 ml). Chest radiograph—bilateral pleural effusions. The patient refused a lymph node biopsy but a skin biopsy showed changes compatible with lupus erythematosus. Treatment with prednisolone produced a dramatic improvement in her general well being, disappearance of the rash and lymphadenopathy, and suppression of the autoimmune haemolytic phenomenon. A few weeks later she exhibited return of the lymphadenopathy, now very gross and extensive, enlargement of the spleen and palpable abdominal masses. She rapidly deteriorated and died. A necropsy confirmed widespread lymphoma (Hodgkin's type).

The concurrence of malignancy with dermatomyositis,² the occurrence of lymphoma in Sjögren's syndrome,³ and a similar case report of S.L.E. with lymphoma associated with a high titre of IgM antinuclear antibody⁴ suggest a potential relationship between the autoimmune connective tissue diseases and neoplasia, in particular reticulosis. This type of association is possibly more common than suspected and a careful look for underlying lymphoma is worthwhile in patients presenting with S.L.E. or other connective tissue disease states, particularly

FIG.—Chromatogram run for one hour (a) and for four hours (b) in butanol acetic-water. Stained with ninhydrin. At W white wine spot, R red wine spot, T tyramine, H histamine, CR concentrated red. Note tyramine is absent in red wine, but histamine and a particular amine spot with 2½ times mobility of histamine present.

for the amount present in wine. This principle will explain the long duration of migraine headaches and the fact that the substance or substances precipitating migraine do not produce migraine in "normal" subjects.

A further point of interest is that the histamine content of the red wine is comparable to the output of histamine from dog liver by alcohol.⁸ It has already been pointed out that thioacetamide intoxication in rats no longer produces cirrhosis of the liver in the presence of antihistamine and histamine stimulates fibroblasts to activity. It is not inconceivable, remembering the relatively low histamine content in human liver, that the histamine content of the red wine (and also strong beer) might be of aetio-

when occurring in atypical age groups.—We are, etc.,

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- ¹ Miller, D. G., *Annals of Internal Medicine*, 1967, **66**, 507.
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Monitoring of Carbon Dioxide in Anaesthesia

SIR,—I read with great interest Dr. B. James's letter on "Monitoring of Carbon Dioxide in Anaesthesia" (24 June, p. 770). May I mention the use of yet another apparatus which is quite different in principle from that of Dr. James. Based on the property of CO₂ to absorb infra-red light of a particular wavelength, Godart's capnograph measures and records the concentration of CO₂ rapidly and continuously. For more than a decade this apparatus has been in routine use in Academisch Ziekenhuis (University Hospital), Utrecht.—I am, etc.,

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- ¹ Smalhout, B., *Opuscula Medica*, 1970, **15**, 129.

Febrile Convulsions in Early Childhood

SIR,—Having pointed out (10 June, p. 631) that mesial temporal (Ammon's horn) sclerosis and the epilepsy to which it commonly gives rise are a common sequel to a severe febrile convulsion in infancy, may I be permitted to make some comments on the leading article on "Febrile Convulsions in Early Childhood" (p. 608). You stress the benign characteristics of febrile convulsions in childhood, whereas my purpose was to indicate that these are not always present.

It would appear that the incidence of febrile convulsion may be as high as 50 to 70 infants per thousand.¹ They are therefore common. However, to divide them arbitrarily into two groups: simple febrile convulsions, and epileptic seizures precipitated by fever, as Livingstone does^{2,3} is fallacious, because both are epileptic phenomena, both occur in the same age periods in infancy, both have a similar incidence of epilepsy in the family history, and both probably have the same aetiology.¹ The chief difference is the severity of the attack, and as one is milder it carries a better prognosis. However, even the milder seizures are frequently followed by later recurrences.³⁻⁵

A febrile convulsion is an epileptic seizure occurring in the context of a febrile illness which is not primarily of cerebral origin, and thus is not meningitis or encephalitis. Authorities are not agreed on the duration of a febrile convulsion before it should be placed in the second group rather than the first. Your leading article stated an upper limit of ten minutes, but others allow periods as long as thirty minutes.⁴ It is not surprising that the convulsions of longer duration should sometimes have features of a focal nature (for example, hemiparesis) or be more

likely to show E.E.G. abnormalities. However, in my experience, even after the more severe febrile seizures, the E.E.G.s may appear normal.

It is the contention of my colleagues and myself (10 June, p. 631) that a prolonged febrile convulsion in infancy (of the order of half an hour or more) may lead to hypoxic changes in such structures as the hippocampus, amygdala, and parahippocampal gyrus, which result in the lesion formerly called Ammon's horn (hippocampal) sclerosis, but which we prefer to term mesial temporal sclerosis. This lesion in its turn becomes a frequent cause of habitual temporal lobe epilepsy in children (and in adults), and it is commonly unilateral.

The proportion of infants who have severe as compared with mild febrile convulsions is high. Ounsted¹ reported that in a personally observed series of 438 infants with febrile convulsions 33 (8%) convulsed to death, while 120 of the 405 survivors (30%) developed drug-resistant habitual seizures. Livingston, whom your leading article quotes, stated in a later report³ that, of 622 infants seen at the Johns Hopkins Hospital with their first febrile convulsive seizure and subsequently followed up for at least 15 years, 256 came within the category of simple febrile convulsions, and only seven of these (3%) subsequently developed recurring febrile seizures. However, of the remaining 366 infants, 355 (97%) subsequently developed various types of seizure unassociated with fever.

The sequelae of a febrile convulsion are thus related to its severity (as measured by its duration) rather than to any apparent differences in aetiology. A mild convulsion may be the precursor of a more severe one. In reviewing the histories of patients with epilepsy due to mesial temporal sclerosis, I have been struck by the long and inexplicable delays that at times occurred before treatment to cut short the convulsion had been started. That is why I wrote "No doctor called to see a convulsing infant should leave that infant until the attack is over." (10 June, p. 631). Only by taking prompt measures to cut short a continuing convulsion will the subsequent incidence of epilepsy caused by mesial temporal sclerosis be reduced.—I am, etc.,

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Urinary Calculi and Ulcerative Colitis

SIR,—I read with interest the article by Professor R. C. Bennett and Mr. E. S. R. Hughes (27 May, p. 494). In earlier reports of renal stone formation occurring with greater frequency in patients with chronic ulcerative colitis¹⁻³ and particularly in those patients who have undergone ileostomy, although it has usually been stated that these patients form uric acid stones scrutiny of

the published data reveals that as many formed calcium-containing stones as formed uric acid stones. I have previously postulated a mechanism which explains the increased liability to either type of stone in these patients.⁴

There is a considerable amount of evidence that a relationship exists between the level of urinary sodium and the occurrence of renal stones.^{4,5} My previously reported studies suggest that it is the urinary sodium/calcium or the urinary sodium/uric acid ratio respectively which is the key-relation, and that an inverse relationship exists between the ratio and the liability to stone formation. It has been shown^{6,7} that patients who have undergone ileostomy for chronic ulcerative colitis generally have a very low urinary output of sodium, in some instances as low as 10 mEq a day (the average output of urinary sodium in my normal controls is 210 mEq a day). There is no evidence that the urinary excretion of calcium, or uric acid, is altered. The urinary sodium/calcium or urinary sodium/uric acid ratio could be expected to parallel this reduction in urinary sodium and thereby increase the liability to stone formation.—I am, etc.,

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Treating Incontinence Electrically

SIR,—It is encouraging to see that the *B.M.J.* is maintaining interest in newer methods for treating these unfortunate patients. However, I wish to correct some impressions created by your leading article (17 June, p. 670). Although it was stated that Hopkinson is the only author to claim cures for electrical treatment, I have reported similar results.¹⁻⁴ Further, experience in the last three years has led me to offer the implant electrode to patients requiring long-term stimulation. Why change to an implant electrode? It is more accurately positioned and more powerful. It is more acceptable socially than either a vaginal or anal electrode, and causes less discomfort. The external electrode stimulators currently available may be difficult to retain during strenuous activities.

When considering success rates it should be remembered that many patients treated in the specialist centres have had not one but several unsuccessful conventional operations before stimulation was attempted. If patients were referred earlier for the less drastic treatment by stimulation there would be more muscle and less scar tissue, with a resultant improvement in performance. In this context, it is not generally realized that the implant operation is a relatively minor procedure with few complications. For example, using basically the suprapubic approach demonstrated to me by Mr. K. P. S.