disease was reported by Aisenberg.² A modification of this test is described here.

The skin of the deltoid region is cleansed with acetone, and a circle 2 cm in diameter is drawn on the skin with a ball-point pen. Wearing plastic gloves, a micropipette (Drummond 10 microlitres) is charged by unscrewing the stopper of the container and inserting the pipette into the solution of DNCB (see Fig.). Complete filling of the pipette should be verified by carefully watching

for the entry of solution into the portion of the micropipette which lies within the microcap. The point of the charged pipette is then drawn over the skin to coat evenly the demarcated area. The solvent evaporates almost immediately. The area is then covered with a vaccination pad. Two solutions have been used: a sensitizing solution containing 2 mg DNCB in 0.01 ml of acetone, and a challenging solution containing 0.2 mg DNCB in 0.01 ml acetone. They may be distinguished and rendered more visible by colouring them respectively with traces of gentian violet and scarlet red.

The skin reactions observed have been moderate and well circumscribed. Aisenberg² employed a sensitizing dose of 5 mg DNCB in 0.1 ml of acetone and he placed the solution in a 2.2-cm well and applied it to the skin. The acetone was evaporated by a warmed-air stream from a hair dryer. An objection to this method is that sensitized subjects can be affected by droplet-borne particles of DNCB carried across the room in which the test is being carried out. Pooling of solution round the wall of the well may produce more severe reactions. Also spillage is more likely in dispensing 0.1 ml of solution than in the micropipette method, which has proved simple to use. Sensitization of the skin over the deltoid is readily accomplished, minimizing the risk of self-inoculation of other skin areas. The container has been designed to restrict the evaporation of solvent, which can lead to unintentional overdose. The brass collar, cemented in place by Araldite, has an upper reservoir to catch any solution which may seep past the pipette.

Drummond "Microcaps" 10 microlitres size are sold by Shandon Scientific Company Limited, Pound Lane, Willesden, London N.E.10. Vaccination protective pads are sold by Wade Pharmaceuticals Ltd., Bishopbriggs, Glasgow. The containers were made for me by Mr. W. Hyslop, Department of Clinical

Physics and Bioengineering Workshops, Western Infirmary, Glasgow. The figure was drawn by Mr. Gabriel Donald, Department of Medical Illustration, Western Infirmary, Glasgow.—I am, etc.,

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- 1 Epstein, W. L., and Kligman, A. M., *Journal of Investigative Dermatology*, 1959, 33, 231.
- 2 Aisenberg, A. C., *Journal of Clinical Investigation*, 1962, 41, 1964.

Acute Renal Failure from Carbamazepine

SIR,—We would like to report the following case of acute renal failure in a patient treated with carbamazepine.

A man aged 59 was admitted to hospital in July 1971 with a two-year history of attacks of typical trigeminal neuralgia, more severe in the past month. Carbamazepine 200 mg four times a day for 14 days before admission had failed to control the pain. He was unable to eat, drink, or shave for fear of precipitating an attack. He had not taken any drugs other than carbamazepine. His general health was good. He had no past history of renal disease. Routine blood examination and liver function tests were normal. The symptoms were controlled by increasing the dose of carbamazepine to 400 mg four times a day and he was discharged.

The patient was readmitted in September 1971, eight weeks after starting on carbamazepine and five weeks after increasing the dose. Two weeks before readmission he developed dry throat and later felt ill, with fever and sweating. He had been passing small amounts of dark urine, and, in the belief that he was suffering from a urinary tract infection, he was treated at home with ampicillin 250 mg four times daily. Three days before admission his eyes and face became swollen and he began to pass large volumes of pale urine. On admission he was pale and anxious. There was no periorbital oedema. His temperature was 37°C, respiration normal, pulse 110/min, and blood pressure 140/90 mm Hg. Haemoglobin was 11.0 g/100 ml; total white cell count 7,900/mm³; blood sedimentation rate 84 mm/1st hr; blood urea 285 mg/100 ml; serum creatinine 6.5 mg/100 ml; Na⁺ 131 mEq/l; K⁺ 5.1 mEq/l; Cl⁻ 93 mEq/l; HCO₃⁻ 22 mEq/l; blood sugar 100 mg/100 ml. The urine showed a trace of protein and on microscopy some hyaline casts but no red cells. The urinary output was 2,790 ml in the first 24 hours after admission.

The patient improved rapidly on conservative management of the renal failure and withdrawal of carbamazepine. Dialysis was not required. During the next two weeks blood urea fell to 60 mg/100 ml, with normal serum electrolytes. The haemoglobin was then 9.1 g/100 ml with a blood sedimentation rate of 53 mm/1st hr. There was no evidence of throat or urinary tract infection. Unfortunately the renal biopsy specimen contained only medullary tissue, which showed non-specific tubular damage, and it was thought unjustified to repeat this examination. Since discharge the patient has remained well with only a few minor attacks of facial pain. The haemoglobin has risen to 13.9 g/100 ml, the blood urea is 51 mg/100 ml, and the creatinine clearance 46 ml/min.

Carbamazepine has many dose-related side effects. Animal studies showed no evidence of nephrotoxicity, though a review by Arieff and Mier¹ of carbamazepine in clinical use mentioned a case of oliguria, hypertension, and vertigo. Since then Rompel and Bauermeister² noted a single case of dysuria in an extended therapeutic trial in 48 patients with migraine. A therapeutic trial of 12 patients with trigeminal neuralgia in Poland reported one case of transient haematuria.³ Our

patient was receiving the maximum dose of carbamazepine. It seems certain that the acute renal failure was due to acute tubular necrosis resulting from the treatment, and this toxic effect of carbamazepine has not been reported before.

We are grateful to Dr. R. T. Williams for his permission to report this case and for his helpful criticism, and also to Dr. A. W. Galbraith, of Geigy Pharmaceuticals Ltd., for his advice.—We are, etc.,

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- 1 Arieff, A. J. and Mier, M., *Neurology*, 1966, 16, 107.
- 2 Rompel, H., and Bauermeister, P. W., *South African Medical Journal*, 1970, 44, 75.
- 3 Szulc-Kuberska, J., *Neurologia i Neurochirurgia Polska*, 1967, 1, 687.

Vasectomy in the Surgery

SIR,—I read with dismay Dr. E. R. Seiler's letter (28 October, p. 232) concerning his experiences of vasectomy performed under local anaesthesia. I am a general practitioner myself, and I have been trained to perform this simple operation entirely under local anaesthesia. I am now actively engaged (via the training courses arranged by the newly-formed Vasectomy Advancement Society of Great Britain) in training my general-practitioner colleagues in this technique.

I feel that the difficulties encountered by your correspondent are greatly exaggerated. Total local anaesthesia is certainly not only possible but is also almost instantaneous if the proper technique is used. The vas must first be digitally fixed subcutaneously in the scrotum (a knack which can be learned and taught), a skin bleb raised, and then 2% lignocaine infiltrated into the sheath of the vas with a $\frac{3}{8}$ in (16 mm) subcutaneous needle. A total of 10 ml of local anaesthetic or less is all that is required.

A few patients are tense, but this can be assessed at the preoperation discussion and can be dealt with by giving diazepam 10 mg orally half an hour preoperatively or, in rare instances, by giving 7-10 mg intravenously. Even in these cases the patient is able to go home half an hour postoperatively.

Now that vasectomy is to become available on the N.H.S., and anticipating the logistic difficulties that this will raise, I feel that it is imperative that full encouragement should be given to all general practitioners who wish to be trained in an operation which is eminently suitable to be performed by them—be it in their own surgeries (if properly equipped), local authority or family planning clinics, or hospital outpatient departments (if they are offered facilities), so relieving genitourinary or other surgeons of an additional and unnecessary work load.—I am, etc.,

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Protection against Hong Kong Influenza

SIR,—The possibility that attacks of "Asian" influenza may have provided some protection against "Hong Kong" influenza was discussed in your correspondence columns last year.^{1,2}

Evidence in support of this hypothesis is

General Attack Rate in "Hong Kong" H ₃ N ₂ Influenza Epidemic	Previous "Asian" H ₃ N ₂ Virus				Previous B-type Influenza Virus			
	No. in Group	Infected with H ₃ N ₂ Virus		No. in Group	Infected with H ₃ N ₂ Virus		No. in Group	Infected with H ₃ N ₂ Virus
		Expected	Observed		Expected	Observed		
Epidemic I 5% ..	118	5.9	0	73	3.6	1	73	3.6
Epidemic II 15% ..	118	17.7	5	72	10.8	9	72	10.8
Epidemic III 4% ..	113	4.5	0	63	2.5	2	63	2.5
Total		28.1	5		16.9	12		

given in the accompanying Table, where it is shown that a group of persons known to have been infected with "Asian" H₃N₂ virus had a significantly lower attack rate with "Hong Kong" influenza virus (H₃N₂) than a group known to have been infected with influenza B during the same period. The difference was four-fold. The figures are derived from a combined field and laboratory study of respiratory disease in a general practice population of 3,600. The investigation began in October 1961 and is continuing.—I am, etc.,

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1 Gill, P. W., *British Medical Journal*, 1971, 3, 308.

2 Hope-Simpson, R. E., *British Medical Journal*, 1971, 3, 531.

Warfarin and Hydroxyethylrutosides in Deep Vein Thrombosis

SIR,—Although the exact pharmacological mechanisms involved are not yet fully understood, it is known that hydroxyethylrutosides have a beneficial effect on capillary function, reducing oedema and augmenting venous return in venous stasis.^{1,2,3} In an attempt to determine whether long-term oral anticoagulant treatment of patients with deep vein thrombosis could be improved by the addition of rutosides 12 such patients admitted consecutively were treated with a standard regimen of 4 to 5 days of continuous heparin infusion followed by oral warfarin plus troxerutin (Paroven; a preparation of hydroxyethylrutosides) given orally at the rate of 250 mg every six hours. After discharge the patients were examined regularly as outpatients, when blood samples were tested for haemoglobin concentration, haematocrit, white blood cell count, total platelet count, in vivo adhesive platelet count,⁴ plasma fibrinogen, plasma viscosity, and prothrombin ratio (P.R.). Warfarin dosage was adjusted according to the plasma activated partial thromboplastin time (A.P.T.T.)⁵ and, in addition, the heparin-retarded activated partial thromboplastin clotting time was estimated routinely.⁶

It had previously been found that the A.P.T.T. is reduced below the normal range after thrombosis, trauma, or haemorrhage,⁷ and a comparison of the A.P.T.T. with its

By the t test there is no significant difference between the mean values for any two of these three clinical groups. (P>0.05.)

Clinical Condition (Deep Vein Thrombosis)	No. of Patients	No. of Tests	Mean A.P.T.T.:P.R. ratio	S.D.
Post-operation warfarin only ..	52	372	32.09	5.59
"Spontaneous," warfarin only ..	39	883	30.93	5.19
Warfarin plus troxerutin ..	12	129	31.98	4.84

Logarithm of heparin-retarded A.P.T.T. results plotted against the corresponding A.P.T.T. results in (a) patients treated with warfarin only, and (b) patients treated with warfarin plus troxerutin, after deep vein thrombosis.

corresponding P.R. during long-term oral anticoagulant therapy appeared to show this same tendency in patients after deep vein thrombosis when compared with patients after myocardial infarction.⁸ When the present series of patients treated with

warfarin and rutosides was compared with similar patients treated with warfarin only no significant difference in the A.P.T.T.: P.R. ratios was found (see Table), nor was there any significant difference in the adhesive platelet counts.

There is an exponential relationship between the A.P.T.T. and the concentration of added heparin, and it has been reported that after thrombosis or trauma heparin has less effect in prolonging the A.P.T.T. than normal,⁹ this apparent resistance to heparin decreasing with recovery. In the present series no difference in response to heparin was found between the two clinical groups (see figure).

Haemorrhage is a well-known complication of oral anticoagulant therapy. During 1967-71 inclusive 301 patients were treated with long-term oral anticoagulants in this laboratory outpatient department for a total of 3,445 man/months, and 103 haemorrhagic episodes occurred.¹⁰ During 100 man/months of treatment of 12 patients with oral warfarin plus troxerutin four haemorrhagic episodes occurred, two of which were known to have been caused by the unwitting prescription of drugs known to potentiate the action of warfarin (imipramine hydrochloride and phenylbutazone respectively).

These findings are disappointing in that we have no clinical or laboratory evidence for more rapid improvement in recovery following deep vein thrombosis when troxerutin was given with warfarin. On the other hand these findings show that there is no potentiation of warfarin activity when troxerutin is given, and it appears that this drug can be given orally with safety during warfarin therapy.

We are grateful to our clinical colleagues at Frenchay Hospital for their encouragement, and we thank Zyma S.A. for generous supplies of Paroven.—We are, etc.,

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Pulmonary Aspiration after Fibre-endoscopy

SIR,—Drs. B. J. Prout and C. Metreweli (4 November, p. 269) stress the contribution made by local pharyngeal anaesthesia to the hazard of pulmonary aspiration during gastrointestinal endoscopy. They conclude that the effect of local anaesthesia is unavoidable, but their results may well have been influenced by the remarkably heavy dosage used.

Pharyngeal anaesthesia is a traditional preparation for endoscopy, but it is omitted in a number of foreign centres. Controlled studies of tripelethamine (Pyrizemine)¹