with my medical occupations to be able to cultivate their company. I should certainly be unable to satisfy Minerva's curiosity about their physical ills. I never met Bertie Russell or Carrington; Lytton Strachey I knew only slightly, though he was kind to me. My closest involvement was with Virginia Stephen. I was living from October 1913 to July 1914 in a room at the top of the Stephen's house in Brunswick Square and came back one night to be told that Virginia had just been found unconscious in her room apparently suffering from a deliberate overdose of drugs. The story is well known from Leonard Woolf's autobiography—the headlong rush back to Barts to get a stomach tube and funnel and the time spent that night washing out her stomach with Sir Henry Head kneeling by my side. We were in time and she recovered. This took place before she had written any of her novels and I am pleased to think that I had a hand in making possible the production of this brilliant literary achievement.

GEOFFREY KEYNES

Brinkley, Cambs

Burst abdomen—a preventable condition?

SIR,—Your leading article on burst abdomen (26 February, p 534) will make all abdominal surgeons question their technique and choice of suture material. Many gynaecologists still use plain or chromic catgut to close the peritoneum and rectus sheath. This view is supported by standard texts, even though the disadvantages of both are listed in detail.¹⁻³

More than 35 000 caesarean sections were performed in England and Wales in 1972⁴ and the number may be increasing in the drive to reduce perinatal mortality and morbidity. Many of these operations are performed by resident doctors of varying experience. Fortunately partial or complete wound dehiscence is not common. But careless suturing with plain or chromic catgut and an ill-maintained Bonney-Reverdin needle is courting disaster, especially if there are other predisposing factors such as obesity, diabetes, and prolonged labour with its risk of peritonitis. If a non-absorbable monofilament suture is used to close the rectus muscle and sheath with big loose bites⁵ then it is virtually unknown for the abdomen to burst after section or hysterectomy, however radical. The Nesta technique³ obviates any chance of a chronic sinus down to an infected knot or a slim patient feeling a lump formed by the casts used to anchor the suture. Since 1962 I have used continuous nylon sutures to close peritoneum, rectus sheath, and skin. There have been no complete abdominal bursts after caesarean section. Recently, on the advice of Mr W G Mills, I have changed to polyethylene because of its better handling.

Not all caesarean sections should be performed through one of the fashionable transverse incisions. Acute fetal distress and placenta praevia are, I submit, indications for speedy delivery and for a vertical abdominal incision. Should a haematoma form it will soon discharge through a midline incision, while if it develops in a transverse wound pain, fever, and swelling persist unduly until reabsorption or evacuation occur. Suction drainage in fat women is not always satisfactory because of infection.

Repeat sections through transverse scars are not particularly troublesome, but the rectus

muscle may have to be divided and the interior epigastric artery formally ligated. Repeat sections are easier if monofilament sutures are used because there is less fibrosis. Single-layer closure deep to the skin has its advocates,⁶ although the skin can dehiscence more readily after a two-layer rather than a one-layer suture, with morbidity and ugly scarring. Most of us would use through-and-through sutures to repair a burst abdomen. On occasion, therefore, a primary single-layer closure may be justified—for example, when a patient has had a large number of abdominal deliveries. After all, Spencer Wells⁷ practised this technique successfully over a century ago.

A M SMITH

New Cross Hospital,
Wolverhampton

¹ Howkins, J, Stallworthy, J. *Bonney's Gynaecological Surgery*, 8th ed, pp 270 and 279. Baillière Tindall, London, 1974.

² Jeffcoate, T N A, *Principles of Gynaecology*, 4th ed, p 721. Butterworth, London, 1975.

³ Cohen, J S, *Abdominal and Vaginal Hysterectomy*, p 2. Heinemann, London, 1972.

⁴ Arthure, H, et al, *Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1970-1972*, p 58. HMSO, London, 1975.

⁵ Jenkins, T P N, *British Journal of Surgery*, 1976, **63**, 873.

⁶ Dudley, H, *Lancet*, 1977, **1**, 305.

⁷ Shepherd, J A, *Spencer Wells*, p 66. Edinburgh, E S Livingstone Ltd, 1966.

Digoxin after heart failure

SIR,—The placebo-controlled trial which Dr Sylvia M Dobbs and others carried out (19 March, p 749) suggests that digoxin is useful in the long-term treatment of some patients after an attack of heart failure. The witch doctors knew of the efficacy of digitalis even before Sydenham discovered it in the seventeenth century and Withering re-discovered it in the eighteenth century.

Sir James Mackenzie proved at the start of the present century that cardiac glycosides are therapeutically effective only in patients with atrial fibrillation. This trial gives us no extra knowledge of the efficacy (or the reverse) of digoxin because 13 of the patients in the trial had fibrillation and the authors themselves claim that only 16 patients out of 48 may have benefited from the digoxin. Indeed, it would appear that the other 32 patients did not benefit.

B J O'DRISCOLL

Dublin

Hypercalcaemia after surgical treatment of Cushing's disease

SIR,—As illustrated by the very interesting case reported by Dr W W Downie and others (15 January, p 145) hypercalcaemia can be due to adrenal insufficiency. It may also occur after adrenalectomy for Cushing's disease,¹ in spite of substitution therapy, as we have observed in one patient.

A 43-year-old woman was admitted to a psychiatric institute because of a depressive syndrome. She also complained of asthenia, nausea, and diffuse pain for some weeks and had lost 10 kg during the last months. Cushing's disease had been treated by total adrenalectomy 2½ months before; replacement therapy consisted of oral cortisone acetate 25 mg daily and of intramuscular dexamethasone 25 mg every three weeks.

Blood measurements revealed hypercalcaemia of 3.54 mmol/l (14.2 mg/100 ml) and a slight

increase in plasma creatinine concentration to 0.16 mmol/l (1.8 mg/dl); plasma phosphate was 1.42 mmol/l (4.4 mg/dl), sodium 138 mmol/l, potassium 4.5 mmol/l, and bicarbonate 23 mmol/l.

Administration of isotonic sodium chloride and glucose, one litre of each intravenously daily, and hydrocortisone 125 mg intramuscularly daily corrected the clinical and biological abnormalities within five days. From this moment the dose of cortisone was gradually reduced to the initial level, at which it was maintained. No recurrence of hypercalcaemia has so far been observed over a seven-year follow-up period.

This case indicates that adrenalectomy for Cushing's disease, by the acute reduction of very high corticosteroid levels to the more physiological levels expected from the usual substitutive therapy, can lead to hypercalcaemia as well as spontaneous adrenal insufficiency.

M FUSS
J CORVILAIN

Department of Internal Medicine,

F GREGOIRE

Institute of Psychiatry,
Hôpital Universitaire Brugmann,
Brussels

¹ Sprague, R G, Kvale, W F, and Priestley, J T, *Journal of the American Medical Association*, 1953, **151**, 629.

Rubella vaccination

SIR,—The article by Dr Catherine S Peckham and others (19 March, p 760) on the low uptake of selective rubella vaccination by older schoolgirls recommends an increased effort to implement the programme. We suggest that such an effort is likely to be unproductive and that the policy of selective vaccination is wrong.

Krugman¹ has shown that the routine immunisation of all boys and girls in the USA since 1969 has reduced the incidence of rubella and congenital rubella to "all-time lows." Congenital rubella is preventable and we are failing to prevent it by operating the wrong policy. Rather than trying to make a bad policy work better, it should be changed forthwith.

CHARLES BROOK
EUAN ROSS

Central Middlesex Hospital,
London NW10

¹ Krugman, S, *Journal of Pediatrics*, 1977, **90**, 1.

Fibrinolytic activity in health and vascular disease

SIR,—We thank Dr T W Meade and his colleagues (26 March, p 837) for their comments on our paper (19 February, p 478) concerning fibrinolytic activity in health and vascular disease and were interested to see their own data. We were as concerned as they about the effect of age and sex on the "normal" values and looked at all of our data, separately and collectively, for evidence of the effect of these factors. Although we were able to find a relationship between age and plasma fibrinogen in all groups, none showed a relationship between age and fibrinolysis.

We chose to compare the patients with the normal ambulant subjects for two reasons. Firstly, and contrary to the unjustified statement in the penultimate paragraph of Dr Meade and colleagues' letter, all the patients except those with carcinoma, were active, working, ambulant outpatients and in no way

comparable to the inpatients. This point is clearly made in the article. Secondly, we were unable to find subjects over the age of 40 whom we could call "normal." A large proportion of the middle-aged population have extensive but occult vascular disease. It could be argued that the changes claimed by Dr Meade to be related to age are just as likely to be caused by occult atherosclerosis, especially as they are not seen in the women, who are known to be much less afflicted by atheroma. The fact that the fibrinolytic activity falls and then rises may also indicate the prevalence of occult disease in the population being surveyed, particularly as the fibrinogen does not fluctuate but shows a steady rise in both sexes.

The above comments are presented to show how difficult it is to study a disease which is common in what we thought to be normal subjects as well as those with clinical manifestations. Large numbers are unlikely to solve this problem. Exact quantification of the disease, occult and overt, will but is not yet possible.

N L BROWSE
P E M JARRETT

Department of Surgery,
St Thomas's Hospital,
London SE1

Effects of adrenaline during treatment with propranolol and metoprolol

SIR—Adrenaline causes vasodilatation in muscle by activation of β_2 -adrenergic receptors. After a single intravenous dose of the non-selective beta-blocking agent propranolol this vasodilating action is lost: adrenaline induces a vasoconstriction with a resulting increase of the peripheral vascular resistance and a rise in blood pressure, presumably by stimulation of α -receptors. After a single intravenous dose of the selective β_1 -blocking agent metoprolol, however, the vasodilating action of adrenaline is largely preserved.¹

These observations could be of interest in the choice of a beta-blocking drug in the treatment of hypertension if the difference between the effects of the two drugs were still present after a longer therapeutic use in hypertensive patients. Therefore, we compared the effects of propranolol (80 mg thrice daily) and metoprolol (100 mg thrice daily) in eight patients with essential hypertension (diastolic blood pressure between 100 and 120 mm Hg) in a double-blind crossover trial. There were four periods of four weeks' duration each: placebo—drug—placebo—drug. The active drugs were given in randomised order. At the end of each period we studied the effects of an infusion of adrenaline (8 μ g/min for 6 min) on the blood pressure and the blood flow in the forearm by means of mercury strain-gauge plethysmography.

The results, as changes arising during

adrenaline infusion, are shown in the accompanying table. Apparently the vasodilating action of adrenaline is still present after treatment with the β_1 -selective blocker for four weeks. It should be noted that on metoprolol this effect is not entirely normal: the decrease in vascular resistance is smaller than during placebo treatment. There is, however, no significant rise in mean arterial pressure. During propranolol treatment on the other hand the rise in blood pressure induced by adrenaline is considerable and significant. At the same time there is an important decrease in the blood flow in the forearm and a clear increase in the vascular resistance.

These results may be of clinical significance. During emotional stress endogenous adrenaline release increases,² while the blood flow through muscle rises.³ It is conceivable that adrenaline release caused by such stresses as emotion, anginal attacks, or hypoglycaemia is comparable with these adrenaline infusions. Then, during treatment with propranolol, considerable rises in blood pressure would result. This would not be the case during metoprolol treatment. Our results therefore seem to favour a selective β_1 -blocker over a non-selective one in the treatment of hypertension.

C L A VAN HERWAARDEN
R A BINKHORST
J F M FENNIS
A VAN 'T LAAR

Departments of Internal Medicine,
and Physiology,
St Radboud Hospital,
University of Nijmegen,
Nijmegen, Netherlands

¹ Johnsson, G, *Acta Pharmacologica et Toxicologica*, 1975, **36**, suppl 5, p 59.

² Levi, L, *Stress and Distress in Response to Psychosocial Stimuli*. Oxford, Pergamon Press, 1972.

³ Brod, J, et al, *Australian and New Zealand Journal of Medicine*, 1976, **6**, suppl 2, p 19.

Dangers of dextropropoxyphene

SIR—I read with interest your leading article on the "Dangers of dextropropoxyphene" (12 March, p 668) and would like to make the following observations.

(1) I think it is true to say that any pharmaceutical preparation of any clinical use is bound to have one side effect or another, and if side effects are not present it is highly likely that the preparation does not have any great effect.

(2) You discuss the problem of drug dependency and addiction but quote only one case where any possibility of addiction is present, and this due to evidence of the drug being found in the cord blood of a baby shortly after birth; this surely is not statistically significant. I also note with interest that there are no English references on the problem of drug dependency.

(3) The problem most interesting to me is that of self-poisoning. The accident and emergency department of the Hull Royal Infirmary uses dextropropoxyphene-containing compounds in considerable quantity, and there is evidence (you quote 2.5 million NHS prescriptions in England

in 1970) to suggest that such compounds are perhaps the most commonly prescribed analgesic in the North Humberside area. I cannot, however, recollect having seen in the last year one overdose except in those cases where the overdose consisted of polypharmacy.

You conclude by asking the question, "How good is the case for using the drug at all?" The major problem stressed in your article is that of self-poisoning, and I think it would be fair to say that paracetamol, the preparation which causes us most concern, can be bought without restriction from any chemist in the country, and that any drug if taken in sufficient quantity will have overdosage side effects. I think we must also keep the problem of overdosage in perspective and note that, despite the massive usage of dextropropoxyphene over the past 12 years, it in no way compares with other preparations as far as the problem of overdose is concerned.

I suppose we must now look forward to a period where the drug firms will go into competition over the usage or non-usage of dextropropoxyphene, and will receive daily circulars extolling the virtues of their simpler, "less dangerous," but also less effective, products.

J K GOSNOLD

Hull Royal Infirmary,
Hull

Vitamin C and drug metabolism

SIR—Your leading article (19 March, p 735) on vitamin C deficiency in liver disease rightly points out the lack of information in man on the effect of such deficiency on drug metabolism by the liver. In guinea-pigs vitamin C deficiency results in decreased antipyrine metabolism¹ and reduced liver cytochrome P-450 levels.² Both these abnormalities are reversed by correcting the deficiency; indeed, there is some evidence that vitamin C supplementation in non-deficient animals might stimulate metabolism.³

However, in man administration of vitamin C to non-deficient volunteers does not appear to enhance the metabolism of antipyrine.⁴ In liver disease low concentrations of leucocyte ascorbic acid do seem to be associated with impaired antipyrine metabolism,⁵ although it is possible that both are reflecting the severity of the disease.

We have studied the effect of vitamin C deficiency on antipyrine metabolism in old age. The metabolic clearance rate (MCR) in 10 deficient people was 25.3 ± 8.8 ml/h/kg, compared with 33.5 ± 11.5 in 27 non-deficient old people. This difference is significant ($P < 0.05$). When eight of the deficient group were given vitamin C for two weeks the MCR improved from 26.1 ± 9.6 ml/h/kg to 36.5 ± 12.9 ml/h/kg. The difference was again significant ($P < 0.025$). No such improvement could be demonstrated in the non-deficient group.

It seems clear that vitamin C deficiency in man causes a small but demonstrable impairment in drug metabolism that can be reversed by correction of the deficiency. As vitamin C deficiency is known to occur in about half of the old people admitted to geriatric wards⁶ it could account for at least part of the reduction in drug metabolising ability found in the elderly.⁷

As vitamin supplementation in people with no demonstrable deficiencies does not alter drug metabolism, it can be concluded that no

Effects of adrenaline on mean arterial pressure (MAP), blood flow, and vascular resistance (MAP/flow) in forearm in eight hypertensive patients (mean $\pm$ SEM) and results of Student's *t* test for paired observations

	MAP		Blood flow		Vascular resistance	
	mm Hg	P	ml/100 ml tissue/min	P	MAP/flow	P
Placebo	0 $\pm$ 2		+ 2.6 $\pm$ 0.5	<0.001	- 22 $\pm$ 4	<0.01
Propranolol	+ 21 $\pm$ 3	<0.01	- 0.7 $\pm$ 0.4	>0.10	+ 21 $\pm$ 7	<0.01
Metoprolol	+ 5 $\pm$ 3	>0.10	+ 0.7 $\pm$ 0.3	<0.05	- 5 $\pm$ 2	<0.05
Placebo v propranolol	P < 0.001		P < 0.01		P < 0.01	
Placebo v metoprolol	P > 0.10		0.05 < P < 0.10		P < 0.05	
Propranolol v metoprolol	P < 0.01		P < 0.05		P < 0.01	