At present there is no published evidence demonstrating higher plasma or cerebrospinal fluid Se levels in those using a SeS₂ shampoo. However, future investigations attempting to assess the role of Se in motor neurone disease will need to take into account this iatrogenic source.

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¹ Schwartz, K, *Medical Clinics of North America*, 1976, **60**, 745.

² Kilness, A W, and Hochberg, F H, *Journal of the American Medical Association*, 1977, **237**, 2843.

³ Kilness, A W, personal communication.

⁴ Griffiths, N M, and Thomson, C D, *New Zealand Medical Journal*, 1974, **80**, 199.

⁵ Watkinson, J H, *Analytical Chemistry*, 1966, **38**, 92.

⁶ Schwartz, K, *Journal of the American Medical Association*, 1977, **238**, 2365.

⁷ Kurland, L T, *Journal of the American Medical Association*, 1977, **238**, 2305.

⁸ Association of the British Pharmaceutical Industry, *Data Sheet Compendium*, pp 26 and 1096. London, ABPI, 1978.

Cost of carrying out clinical diagnostic tests

SIR,—The cost of the NHS will always tend to outstrip the funds available and it is proper to look for ways in which money can be saved or redistributed within the service to better effect. Capital costs (buildings, plant, and equipment) and staff wages and salaries swallow up a major part of the available funds and—at least at the local level—it is by manipulation of the small but flexible “revenue” moneys that distribution anomalies can be rectified and new developments fostered.

It is against this background that we take issue with Mr D J Barnard and his colleagues (3 June, p 1463). They gave an itemised breakdown of the cost of carrying out a variety of diagnostic tests in their laboratory with particular reference to a number of radioimmunoassay (RIA) tests. Because the cost of labour, maintenance, and capital depreciation is large compared with the cost of reagents in the price of a single test they conclude that the use of expensive commercial RIA “kits” rather than inexpensive “in-house” reagents is justified. They claim that the labour cost reduction more than compensates an increased reagent cost and quote a specific case (serum B₁₂ and folate) as proof.

Maybe so, but from their own figures the 23% of their total tests which were carried out using commercial kits cost them £1386, while the 77% for which they used “in-house” methods cost only £416. Had they used commercial kits throughout the reagent costs would presumably have been close to £6000—an increase of more than £4000 in revenue expenditure. If this increased expenditure produces the labour-saving effect that they claim, then they will have saved the cost—and time—of at least one whole technician—a remarkable achievement.

Unfortunately the real implication of all this is that in money terms their whole RIA operation is inefficient. Their high cost-per-test is a consequence of the small number of tests done: as the load of tests increases the labour and fixed costs-per-test decrease. A comparison with this laboratory will demonstrate this. During the same period a little over 40 000 tests were carried out. Four technicians and one principal biochemist were involved. Although not all of their time was spent on RIA tests, for the sake of simplicity full time

is assumed (this results in an overestimate of time and costs). The tests carried out were thyroid-stimulating hormone, total thyroxine, total triiodothyronine, thyroid hormone binding index, growth hormone, follicle stimulating hormone, luteinising hormone, and prolactin. The average time for one test was 14 min and the average cost of time 57.5p. The average time and cost of time to Mr Barnard and his colleagues (from their data) were 27 min and 122p. Because our laboratory area (71.25 m²) is almost identical with theirs we may assume the same yearly discounted replacement and building maintenance costs. Our Nucleonic and other equipment (an automated system) is more expensive (£30 000). Discounting over seven years (an accountancy fiction: in the NHS equipment is used until it falls to pieces) gives £4286 per annum and maintenance (7% per annum) £2100. Our cost of collection and distribution (£2500) is rather more than four times theirs. Our total cost for radio-pharmaceuticals, reagents, and consumables, rounded up, is £5000. Adding administration costs at 3.3% to our total running costs of £39 000 (£1287) gives an average total cost per sample of nearly 101p. The average total cost per sample (radioimmunoassay) to Mr Barnard and his colleagues was 318p.

Hence it is uneconomical for laboratories to carry out small numbers of those tests, which are better handled in large numbers centrally by semi-automatic processing. These comparisons underline the fact that for every laboratory to provide a full service of available tests is very expensive. Radioimmunoassay test results in particular are rarely needed urgently and there is a strong case for handling the service load in specialised units of an appropriate size.

Specialised units are in a far better position to develop and maintain their own reagents and radiopharmaceuticals. This is important because commercial kits—if used—are the one item in the cost-per-sample which does not decrease as the scale of operation increases (apart from the marginal effects of discounts for quantity). Our reagents bill would increase by more than £25 000 per annum if we were to use commercial kits and there would be no saving in labour costs. This amounts to a very substantial saving in revenue costs which can then be deployed elsewhere.

The two conflicting views—that all laboratories providing a general service should “do everything” or that certain functions are best centralised—pose a problem which those who make the policy decisions must solve. But it is clear, in the case of radioimmunoassay at least, that small numbers of samples assayed in many laboratories are much more expensive than large numbers processed in centralised laboratories. If small operators also use commercial kits (and the temptation to do so is strong) the cost to revenue funds is needlessly high.

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The continent urostomy

SIR,—I should like to support the balanced view given in your leading article (19 August, p 520) on the various techniques for appliance-free urinary diversion. Whether an ileocaecal segment or ileal pouch is used, catheterisation

of the urinary reservoir often becomes increasingly difficult and may require later conversion to a free draining conduit. Our experience over the last five years is with an ileocaecal segment,¹ which is ready made, but the ileal pouch may be preferable and worth constructing to avoid mucus problems and bowel spasm with distension.²

The criticism of all these techniques is the absence of a sphincter. Following the encouraging reports of the Heitz Boyer-Hovelacque procedure for exstrophy of the bladder in children,³ we have had an early encouraging experience in adults with a continent urinary diversion based on similar principles. The ileocaecal segment is isolated and the ureters anastomosed to the tail of the terminal ileum. A separate isolated length of ileum is then anastomosed to the caecal urinary reservoir and sleeved submucosally for about 10 cm through the anterior wall of the intact rectum and anal canal, to open on the perineum within the anal sphincters. It is too early to say whether problems with metabolic absorption will arise, but this continent diversion within the natural sphincter seems preferable in principle to intermittent catheterisation of a urinary reservoir. We hope to develop this technique, while agreeing that urinary continence must not be achieved to the long-term detriment of renal function.

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¹ Ashken, M H, *Journal of the Royal Society of Medicine*, 1978, **71**, 357.

² Madigan, M R, *Journal of the Royal Society of Medicine*, 1978, **71**, 542.

³ Taccioli, M, Laurenti, C, and Racheli, T, *British Journal of Urology*, 1977, **49**, 385.

Legionnaires' disease and acute renal failure

SIR,—The occurrence of acute renal failure or transient impairment of renal failure in legionnaires' disease (Professor D N S Kerr and others, 19 August, p 538) would not come as a surprise to anyone familiar with the work of the late James Reilly on autonomic irritation¹ and still less to anyone who had read his monograph on the role of the autonomic nervous system in renal disease, published in Paris unfortunately in 1942, which summarises the result of six years' work on over 1000 animals.²

Among other findings, Reilly showed that the toxins of bacteria, both Gram-negative and Gram-positive, constantly produced albuminuria and haematuria in experimental animals when placed in contact with sympathetic nerves, such as the splanchnic, or if injected intravenously.² The microscopic changes, congestion, haemorrhages, exudation, and sometimes thrombosis of glomeruli were identical with those seen in a series of 80 human subjects dying in a large fever hospital from overwhelming bacterial infections of all kinds.³

Such changes are seen less often since the elimination of the common infectious illnesses with antibiotic therapy. Gram-negative infections are an exception, and Reilly showed quite decisively that damage can occur with over-enthusiastic antibiotic therapy (“frappe fort”) releasing overwhelming amounts of endotoxin. Post-mortem findings in human subjects as well as experimental

animals revealed renal changes similar to those already described for other acute infective diseases.⁴

Human subjects and higher mammals vary more in their response to bacterial toxins than smaller experimental animals. Hence gross renal changes do not always occur in acute infections or severe endotoxaemia, although albuminuria with a few red cells is surely not uncommon.

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¹ Hopkin, D A B, and Laplane, R, *Annals of the Royal College of Surgeons of England*, 1978, **60**, 108.

² Reilly, J, et al, *Le Rôle du Système Nerveux en Pathologie Rénale*. Paris, Masson, 1942.

³ Marquiez, R A, and Ladet, M, *Le syndrome malin au cours des toxi-infections. Le rôle du système neuro-vegetatif*. Report to the Congress of Paediatrics, Paris, 1938.

⁴ Reilly, J, et al, *Annales de Médecine*, 1950, **51**, 597.

Isolation to control infection

SIR,—In the admirable paper by Professor K D Bagshawe and his colleagues (2 September, p 684) there are included in the table two diseases concerning which the recommendations are misleading.

For *Taenia solium* infection it is stated that no isolation is required but precautions are necessary when dealing with dressings and discharges in the ward. The ova of *T solium* are dangerous and if swallowed cause cysticercosis, with epilepsy and other serious complications. As these ova are passed with the patient's stool and may contaminate fingers and clothing, isolation and adequate measures to dispose of infective faeces are essential.

Secondly, yellow fever is stated to require no isolation. There is evidence that it has been transmitted by blood in areas in which it is not endemic. Precautions similar to those used for serum hepatitis should therefore be taken in dealing with such patients' blood and tissues. Even in Britain it would also be advisable to ensure that the patient's room is kept free from mosquitoes and other biting insects, for mechanical transmission by these is theoretically possible. In endemic areas strict isolation of the patient from mosquitoes and other insects is an established necessity.

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Stroke after myocardial infarction

SIR,—We were interested to learn (12 August, p 457) that the experience of Drs P L Thompson and J S Robinson with strokes after myocardial infarction led them, as it did us,¹ to adopt a selective anticoagulation regimen. Our regimen, however, differs from theirs in two ways.

Firstly, we use a plasma fibrinogen level of 7.5 g/l (750 mg/dl) or more as an indicator of risk. The estimation, using nephelometry, is not difficult: we found it more predictive and it obviates the possibility of missing the creatine kinase (CK) peak. Moreover, there are patients whose fibrinogen levels, for one reason or another, are consistently higher than normal. In such patients a relatively small infarct could push the fibrinogen up to dangerous levels.

Secondly, but perhaps more important, is the timing of anticoagulation. We too found that the majority of strokes occurred in the first week after infarction and not uncommonly by the fourth day. To wait even 48 h for the CK to peak may add to the risk of thromboembolism. We therefore anticoagulate all our patients from admission and stop on the sixth day if they are not at risk.

We use subcutaneous heparin (10 000 U twice daily) for six days and give a loading dose of warfarin on the fourth day. If, on the sixth day, the plasma fibrinogen has reached 7.5 g/l we continue warfarin for six weeks. Otherwise we stop all anticoagulation.

In two groups, each of 120 patients, the first unanticoagulated and the second anticoagulated in this way, the incidence of all thromboemboli was 10 and one respectively ($P < 0.01$) and the incidence of strokes was five and one. We have continued to use this regimen for a further 18 months and have not encountered a stroke in patients so treated.

The ideal way of dealing with the problem may well lie somewhere between our two methods, but there seems little doubt that some form of selective anticoagulation after myocardial infarction can safely prevent a measurable amount of tragic morbidity.

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¹ Fulton, R M, and Duckett, K, *Lancet*, 1976, **2**, 1161.

SIR,—I read with interest the paper by Drs P L Thompson and J S Robinson (12 August, p 457) on the relation of stroke to size of myocardial infarct.

It is clear from their study that strokes, in this setting, are associated with very high levels of creatine kinase (CK). However, this may not be due entirely to the presence of a large myocardial infarct per se. Thus Dimant and Grob¹ found that 25% of stroke patients without myocardial infarction have elevated CK levels with a median level $2\frac{1}{2}$ times the upper limit of normal. The CK in such cases almost certainly arises from cardiac muscle and is probably a result of the subendocardial haemorrhages and myocytolysis seen secondary to cerebral injury.²

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¹ Dimant, J, and Grob, D, *Stroke*, 1977, **8**, 448.

² Connor, R C R, *British Medical Journal*, 1968, **3**, 29.

Carcinoma of bronchus presenting with Henoch-Schönlein purpura

SIR,—Dr S A Cairns and others (12 August, p 474) describe two cases of squamous cell carcinoma of the bronchus presenting with Henoch-Schönlein purpura. It is suggested that tumour antigen may have precipitated the attack.

On 20 July 1956 a man aged 59 consulted his general practitioner on account of pain and swelling in both knees and a purpuric rash affecting both lower legs. No treatment was offered initially, but he returned one week later, when the rash was more marked and he mentioned that on one occasion only he had coughed up a little blood. He was thought to have Henoch-Schönlein purpura, started on

oral penicillin, and advised to submit weekly urine specimens. On 10 August the urine contained frank blood and he was admitted to hospital on 13 August. At that time he still had a rash typical of Henoch-Schönlein purpura over both lower legs. His blood pressure was 180/80 mm Hg. The urine contained albumin +++ and numerous red blood cells. His haemoglobin concentration was 9.6 g/dl, and leucocyte count $10.8 \times 10^9/l$ ($10\ 800/mm^3$) with 56% polymorphs. X-ray of the chest showed some collapse of the right lower lobe.

He was treated with combined penicillin and streptomycin and the rash gradually faded and the urine cleared except for some persistent red blood cells. However, the collapse became rather more complete, although the right hilar shadow was normal. He was transferred to Oxford on 29 September 1956. There a specimen of sputum was obtained containing typical squamous carcinoma cells and bronchoscopy showed "right stem bronchus blocked by cauliflower mass." On 22 October the middle and right lower lobes were resected. The pathologist reported: "This is one of the earliest carcinomata of the bronchus seen here." Lymph nodes were clear.

There has been no recurrence of rash, nephritis, or tumour. At the age of 81 he is in fair health and caring for his invalid wife.

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SIR,—I was interested to read the paper by Dr S A Cairns and others (12 August, p 474) concerning two patients with squamous cell carcinoma of the bronchus who presented with Henoch-Schönlein purpura.

Last year we showed at the clinical section of the Royal Society of Medicine a man who presented in October 1973 with an acute Henoch-Schönlein syndrome including haemoptysis.¹ In contrast with Dr Cairns's cases he subsequently had recurrent episodes of purpura which only cleared after pneumonectomy for squamous cell carcinoma of the bronchus in November 1975. He remains well; it is of particular interest that the patient gave a history of Henoch-Schönlein purpura as a child.

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¹ Mitchell, D M, and Hoffbrand, B I, *Journal of the Royal Society of Medicine*. In press.

Antifibrinolytic agents for ruptured intracranial aneurysms

SIR,—Might I be permitted to reply to the criticisms raised by Drs J van Rossum and A R Wintzen (19 August, p 568) of my study (15 April, p 945) of the effect of prolonged antifibrinolysis on ruptured intracranial aneurysms and at the same time comment on their trial,¹ which showed no benefit for antifibrinolytic treatment?

Although my study was not double-blind, it did possess randomly selected controls. As the criteria for failure of treatment (that is, death or recurrent haemorrhage confirmed by lumbar puncture or necropsy) were fairly objective occurrences, knowledge of which patients were receiving drug treatment could not be expected to bias the results in favour of the treatment group. However, the control