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

patients might have received a favourable bias as they tended to have aneurysm surgery earlier, and there were no postoperative deaths or rebleeding.

The restriction of my study to patients who had survived the presenting haemorrhage in a good condition was deliberate. In the past confusion has arisen because of failure to distinguish between the many deaths from effects of the first bleed, often days or weeks after reaching hospital, and those due to recurrent haemorrhage. Obviously, antifibrinolytic treatment (or surgery) can only improve mortality in the latter group. Inclusion of obtunded patients in a trial will lead to inclusion of many deaths from the first bleed, as in the study of van Rossum *et al*, where 18 patients died from the primary bleed as against only seven from rebleeding. I have already suggested in my paper that antifibrinolytic treatment might be positively harmful in patients in poor condition.

The trial of van Rossum *et al* was small. Of 51 patients admitted, only 24 proved to have aneurysms on angiography. The discrepancy with my findings may be due partly to delay in starting treatment and partly to the fact that their patients received only 4 g of tranexamic acid a day and for only 10 days. The fibrinolytic activity induced in the nervous system after a subarachnoid haemorrhage may last for much longer than this as shown in my study.

I feel that the comments of Drs van Rossum and Wintzen on the existing literature are hardly fair. Earlier studies have had a limited follow-up as the antifibrinolytic treatment was used merely as a prelude to surgery. The study referred to in my article as a "personal communication" from Dr Fodstad has now been published.² It provides further evidence for the apparent efficacy of antifibrinolytic treatment.

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¹ van Rossum, J, *et al*, *Annals of Neurology*, 1977, 2, 242.
² Fodstad, H, *et al*, *Surgical Neurology*, 1978, 10, 9.

Cervical presentation of rectal carcinoma

SIR,—We were very interested to read the case report by Dr M J Sworn and others (8 July, p 98) on "Rectal carcinoma presenting as massive metastatic involvement of foot bones." The authors commented that this was the first report of such massive metastatic disease of the foot. We would like to present another such case with the primary tumour being in the cervix.

A 52-year-old woman presented with occasional blood-stained vaginal discharge and after a normal clinical examination underwent dilatation and curettage. Histological examination of the curettings showed fragments of moderately differentiated squamous carcinoma. A further punch biopsy of the posterior vaginal wall showed infiltration by moderately differentiated squamous carcinoma obviously derived from the cervix. Treatment consisted in radical radiotherapy using two insertions of caesium and external megavoltage x-ray treatment.

Over a year later she was referred for review on account of a two-month history of increasing pain in her right foot culminating in inability to bear weight. A radiograph (see figure) showed extensive metastatic disease affecting

Extensive metastatic disease of right foot.

the whole foot, including the calcaneum, talus, navicular, cuboid, the three cuneiform bones, the five metatarsals, and with probably further deposits in the phalanges. A bone scan showed other metastatic areas of skeletal involvement—namely, the ipsilateral tibia and upper femur, pelvis, and lumbar spine. A biopsy specimen taken from the mid-tarsus showed invasive moderately to poorly differentiated squamous carcinoma fully consistent with the original tumour of cervix. The patient has recently had palliative radiotherapy to control her symptoms.

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Thyroid extract

SIR,—My friend Dr P B S Fowler (26 August, p 636) has, I think, misunderstood the letter from Dr W van't Hoff and his colleagues (15 July, p 200). The danger to which they refer is a negative one. The potency of thyroid extract is very variable and I have on several occasions seen a hypothyroid patient successfully treated with the extract who has suddenly become myxoedematous. The onset of myxoedema is often so insidious that the risk of coronary heart disease to which Dr Fowler has so often drawn our attention must in such patients be increased.

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Whooping-cough fatality rate

SIR,—Dr Dick (19 August, p 562) suggests that the fatality rate for pertussis may have diminished. He uses as his denominator notifications.

General practitioners are rightly selective in the way they choose to respond to the notification of infectious disease, and notifications are a notoriously unreliable indicator of the incidence of common diseases. The present interest in the incidence of pertussis is likely to increase the proportion of cases notified. As fatalities are always recorded an increase

in the proportion of cases notified will diminish the case fatality rate.

Until we have reliable measures of incidence we can make no valid statements regarding case fatality.

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Paracetamol poisoning

SIR,—Dr T J Meredith and others (12 August, p 478) quote from the *Mortality Statistics*¹ that in England and Wales in 1975 there were 105 deaths due to paracetamol and a further 107 due to paracetamol in combination with other drugs. It could be inferred from this statement that all these deaths were the direct result of paracetamol overdose. In table 10 of the *Mortality Statistics* it is noted that inclusion in the list does not necessarily imply that a substance was the cause of death even where solely involved. With this in mind, we have carried out a study which indicates that the recorded number of paracetamol deaths considerably exceeds the actual number which can be directly attributed to paracetamol.

The pathology of paracetamol overdose is now clearly defined with the clinical course being consequent on the extent of any hepatic damage. Death due to paracetamol overdose is primarily caused by hepatic failure and occurs some days after ingestion of the overdose.² Our study included a consideration of additional data made available to us by courtesy of the Office of Population Censuses and Surveys. These showed that evidence of hepatic necrosis was reported in only 50 out of the 105 deaths attributed to paracetamol alone. Additional information was obtained in 50 of the remaining 55 cases by courtesy of HM Coroners under whose jurisdiction the inquests were held. From this it was found that in 12 cases there was evidence of hepatic necrosis resulting in death, and in one instance hepatic necrosis was present but was not the immediate cause of death (peritonitis from perforated peptic ulcer). In the remaining 37 cases, however, death was sudden, and at necropsy the liver was regarded as normal. Twenty-five of these individuals were known to have ingested, in addition to paracetamol, other drugs, which were mainly those with a respiratory depressant action, particularly dextropropoxyphene. There is no evidence that the paracetamol contributed in any way to these deaths. The Office of Population Censuses and Surveys also provided us with additional data on a further 112 cases where paracetamol was listed together with other substances. As 84 of these people died before being admitted to hospital we consider it unlikely that paracetamol contributed to their death. Of the 28 who died in hospital, there were only two reported cases of hepatic necrosis while 20 died from the results of overdose of respiratory depressant drugs taken with paracetamol. In the remaining six cases the possibility that paracetamol was the cause of death could not be excluded.

We therefore estimate that the total number of deaths definitely attributable to paracetamol in 1975 in England and Wales amounted to 64. In 37 cases listed as due to paracetamol alone there was no evidence of paracetamol toxicity, and in 104 cases where paracetamol was taken in combination with other drugs it is unlikely