as a 95% confidence interval so that the reader can deduce for himself how much reliance to put on what was found. In the absence of one or both of these approaches the value of their negative finding cannot be estimated by the reader.

The use of bias controlling methods may not be necessary in a preliminary assessment of the effects of a new agent as long as any positive finding is not regarded as showing a causal relation between the treatment and the "response." The value of a negative finding is not enhanced by the presence of a control group; it is still necessary to quote power or confidence intervals, or both.

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Infectious diseases physicians and microbiologists

SIR,—We were grateful that the article by Dr M E Ellis (15 November, p 1303) appeared as a Personal View, since we hope his view is not widely shared.

We would not disagree that misuse of antimicrobials occurs in many UK hospitals. Dr Ellis's suggestion of antibiotic "cover" for the child with watery diarrhoea is surely one situation in which this can occur.

Nowadays serious infection in hospitals in the UK occurs as an aspect of illness in patients suffering from other conditions. Diseases due entirely to infection still occur but are not the main problem with which we have to contend. As clinical microbiologists we spend much of every normal day on the wards seeing patients. For instance, in this regional cardiothoracic centre we treat 25-30 cases of infective endocarditis each year. We have been known to auscultate the occasional heart, but in general we find echocardiograms and the expert opinion of our cardiological colleagues to be more use. Apart from looking at the urine for evidence of nephritis we too are at a loss to find much use for a microscope in this condition. In any case the microscope is in the laboratory and the patient is not.

The implication that all our clinical skills have atrophied because we do not perform operations or conduct an outpatient clinic is one which we find insulting. In many hospitals in the UK good diagnostic medicine is practised by doctors who may have their offices near a laboratory but who also attend and treat patients. Clinical haematologists seem to have combined the two elements which Dr Ellis finds so disparate. We have yet to meet the two masters referred to by Dr Ellis.

Dr Ellis does have the grace to suggest that there may be an element of paranoia about his view. May we tactfully suggest that the self confessed isolation which he endures is delaying the cure? If he emerges into the rest of the hospital service we clinical microbiologists would be pleased to see him. We would probably learn something from him. He would certainly learn something from us.

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Paradoxical gas embolism in a scuba diver with an atrial septal defect

SIR,—One aspect of the management of the scuba diver who developed paradoxical gas embolism (15 November, p 1277) was puzzling. Dr P T Wilmshurst and others inform us that the diver was advised not to dive again after surgical correction of his atrial septal defect. Why was this? Was the surgical repair inadequate? Was the patient permanently disabled neurologically by the gas embolism? Or were the diver's medical advisers just being overcautious?

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AUTHOR'S REPLY—I am grateful to Dr Konarzewski for the opportunity to clarify why the patient was advised not to dive again. There was no suggestion that his surgical repair was inadequate.

The patient described had a paraparesis which resolved only slowly during the year after therapeutic recompression. Even in those individuals who make a rapid and good functional recovery from spinal decompression sickness, there is evidence that large areas of spinal damage can be shown histologically.[1] There is also concern that those who recover from neurological decompression sickness after prolonged treatment might be predisposed to future decompression sickness.[2] Certainly, some caisson workers appear to have a physical predisposition to decompression sickness.[3] The data available to the Medical Research Council decompression sickness panel suggest that among compressed air workers 5% of those who have decompression sickness are responsible for 40% of the bends (V Hempleman, personal communication). Among amateur divers a similar trend is observed in the incident statistics of the British SubAqua Club, with repeated serious bends occurring in a few individuals who are responsible for a significant proportion of the therapeutic recompressions performed (S Shaw, personal communication).

Given that successive bends generally prove more difficult to treat and leave greater residual neurological damage, I would advise an individual against resuming diving after neurological decompression sickness unless rapid and complete recovery had followed recompression. I believe that similar advice not to dive would have been given to this diver by most authorities concerned with safe diving practices.

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Carcinoma in situ of the contralateral testis

SIR,—Both Dr von der Maase and his colleagues (29 November, p 1398) and Mr T B Hargreave (p 1389) suggest that the efficacy of radiation in controlling carcinoma in situ of the testis is unknown and that "low dose radiation . . . is an exciting study which needs further confirmation."

However, it has been known for some time that radiation does prevent the development of second tumours. At the Christie Hospital the field used for prophylactic irradiation in early seminoma (and previously teratoma) always included the contralateral testis.[1] Although the need for its inclusion may be questioned, its effectiveness in preventing second tumours has never been in doubt. In over 1000 patients irradiated from 1960 to 1980 and followed to 15 years no case of a second testicular tumour was observed when one might have expected 50 cases if the incidence of carcinoma in situ is 5%. The dose of radiation to the testis in this series was 30 Gy in 20 fractions over 28 days from a 4 or 8 MV linear accelerator, which is probably not dissimilar in biological effect from the quoted dose of 20 Gy delivered over 10 days.

Further assessment of Leydig cell function is important. In a Manchester study of 30 men treated by orchidectomy and radiotherapy for seminoma the mean basal follicle stimulating hormone and luteinising hormone values three years after irradiation were significantly greater and the mean basal testosterone concentration significantly lower than those in a group of 14 men treated by orchidectomy only for teratoma.[2]

It is also interesting to note that of 130 patients with stage 1 teratoma of the testis under surveillance from 1979[3] only one patient has so far developed a contralateral tumour. He had previously required chemotherapy for para-aortic relapse (cisplatin, vinblastine, etoposide, and bleomycin) and subsequently died of metastases from his second tumour.

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Acquired cystic disease of the kidney

SIR,—We read with interest Mr C J Rudge's leading article (8 November, p 1186) and wish to add some comments illustrated by the following case report.

A 51 year old man who had been receiving continuous ambulatory peritoneal dialysis for six months was admitted in severe congestive cardiac failure and died shortly afterwards. He had originally been found to have renal impairment (serum creatinine concentration 250 μmol/l (2·8 mg/100 ml)) in 1971 during investigation of hypertension and angina. Renal biopsy showed hypertensive nephrosclerosis. Despite poor compliance with various antihypertensive regimens, his serum creatinine concentration remained below 500 μmol/l (5·7 mg/100 ml) until 1985, and he did not require continuous ambulatory peritoneal dialysis until April 1986. In June 1986 he reported an episode of frank, painless haematuria. Subsequent cystoscopy and retrograde ureterograms were negative and a computed tomogram was considered to show only the changes of acquired cystic disease of the kidney.

At necropsy the kidneys, each 80 g, were shrunken to 8 cm long and contained numerous cortical cysts, up to 0·4 cm in diameter, containing clear fluid. A single solid dark brown tumour, 1·5 cm in diameter, projected from the upper surface of one kidney, which on histological examination proved to be an invasive adenocarcinoma, of mixed papillary and clear cell type. No other tumours or metastases were found.

Although acquired cystic disease of the kidney is usually considered in relation to patients on dialysis, it also occurs in patients with end stage renal disease who have not received dialysis.[1] Since our patient had been on continuous ambulatory peritoneal dialysis for only six months, the acquired cystic disease and renal adenocarcinoma probably predated this treatment; another case report supports this proposal.[2] We therefore suggest that screening for renal cysts should not be delayed in patients with chronic renal failure until they reach end stage renal disease. Secondly, while we agree with the screening strategy outlined by Mr Rudge, particularly as 16-20% of patients with acquired cystic disease may develop tumours,[3-5] it is noteworthy that the tumour was not diagnosed

by computed tomography in our patient. Although the lesion was discernible in retrospect, it was not possible to make a confident diagnosis from the images obtained at the time. Finally, these tumours in patients with acquired cystic disease of the kidney have a metastatic potential of 5%, but the current consensus is that lesions under 3 cm diameter should be treated conservatively.[3-5] Although there was no evidence of metastatic spread in our patient, the tumour had invaded deeply into the renal cortex, and we would therefore suggest that this policy is kept under critical review.

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Raised concentrations of plasma atrial natriuretic peptides in cardiac transplant recipients

SIR,—We read with interest the report by Dr Donald R J Singer and others (29 November, p 1391). We have measured plasma immunoreactive atrial natriuretic peptide (ANP) concentrations in five cardiac transplant recipients after one hour at rest (sitting) and during a period of lower body positive pressure. The latter is a complex stimulus but we have shown that it results in an increase in right and left atrial dimension, systemic blood pressure, and plasma immunoreactive ANP concentrations in healthy volunteers.[1]

The five cardiac transplant recipients were all men, aged 28 to 53 years (mean 38 years), who had had their transplants 15 to 80 months (mean 38·6 (SD 11) months) earlier. All were well and showed no signs of rejection or cardiac failure. Mean (SEM) blood pressure was 123/78 (4·8/3·9) mm Hg and serum creatinine 149·5 (16·4) μmol/l. They were taking the following medication: cyclosporin (4), azathioprine (3), prednisolone (3), nifedipine retard (2), diuretics (3), methyldopa (1), and hydralazine (1).

These patients followed the same protocol as our healthy volunteers.[1] They attended a hospital sideroom on two mornings. After one hour sitting at rest they wore a medical antishock trouser (MAST) suit for one hour. On one occasion for each volunteer this was inflated to 40 mm Hg pressure. After 60 minutes the suit was removed and the patients remained sitting for a further hour. Blood was taken before inflating the suit (time 0) and at 5, 20, and 60 minutes of suit inflation and at 90 minutes—that is, 30 minutes after the suit had been removed. Plasma immunoreactive ANP concentration was measured by radioimmunoassay.[2]

The cardiac transplant recipients had a higher mean basal plasma immunoreactive ANP concentration than our healthy volunteers (n=6; aged 20 to 28 years) by a factor of 9 (table). This is greater than that reported by Dr Singer and colleagues, but our two study groups were not matched. Our healthy volunteers were younger, had lower blood pressures, and had normal renal function, all of which may have enhanced but would not have accounted for the difference in ANP values between the two groups. Plasma immunoreactive ANP concentration was raised in our one patient (aged 30 years) with normal blood pressure and renal function 80 months after transplantation. There was a tendency within the group for ANP values to fall with time since transplantation.

Mean (SEM) basal plasma immunoreactive ANP concentration and response to lower body positive pressure in healthy volunteers (n=6) and cardiac transplant recipients (n=5)

Time (mins)	Plasma immunoreactive ANP (pmol/l)	
	Healthy volunteers*	Transplant recipients
0	5·7 (1·1)	58·7 (12·6)
Inflation		
5	5·3 (0·7)	58·2 (10·5)
20	8·9 (1·8)†	69·2 (11·3)
60	9·8 (1·3)†	94·0 (15·1)†
90	5·7 (0·8)	59·0 (9·6)

*Values for healthy volunteers reproduced by kind permission of the editor, *Journal of Hypertension*.
†p<0·05 compared with time 0.

Plasma immunoreactive ANP values increased in all five patients during lower body positive pressure. The response seemed to be more delayed in the transplant recipients than in the healthy volunteers. The percentage rise at 20 minutes (mean (SEM) 128·8 (15·1)%) was less than that for our healthy volunteers (157·8 (9·7)%) but at 60 minutes the difference was less pronounced (171·2 (13·4) *v* 189 (28·6)%).

There was no significant change in mean plasma immunoreactive ANP concentration in either group on the non-inflation day. The blunted rise in ANP concentrations in response to lower body positive pressure compared with that in healthy controls is in keeping with the observations of Tomlanovitch *et al*, who (using urinary cyclic guanosine monophosphate as a measure of ANP activity) found an attenuated response to water immersion in a group of cardiac transplant recipients.[3] The explanation for this blunting effect in these patients is unclear but may in part be due to increased atrial size, which might dilute the expected increase in atrial dimension after lower body positive pressure.

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Heat inactivation of specimens—AIDS

SIR,—Our attention has been drawn to some apparent misunderstanding of the wording of paragraph 61 of the revised guidelines on AIDS issued by the Advisory Committee on Dangerous Pathogens in July of this year (*LAV/HTLV III—The Causative Agent of AIDS and Related Conditions*. HN(86)20).

The impression in some quarters is that this paragraph implies that the AIDS virus is not susceptible to heat treatment. This is not the message which it was intended to convey. Spire *et al* reported on the successful inactivation of viral enzyme by what might be regarded as the standard heat treatment regimen—namely, 56°C for 30 minutes.[1] But a later paper by Resnick *et al* cast some doubt on the efficacy of inactivation of the virus over this period.[2]

Although Resnick *et al* showed that the high titred virus they used was inactivated by tenfold in 20 minutes, there is to our knowledge no reliable estimate of the range of infectious virus titres or the rate of inactivation of virus in the serum of naturally infected subjects. Little could therefore be said about what combination of time and temperature would give a reasonable margin of safety. Also, there appears to be little or no information on the effects of longer heating times on serum analytes. Most published work refers only to periods of 30 to 60 minutes.

The committee was therefore unable, without further supporting evidence, to recommend any particular heat treatment regimen. Thus in paragraph 61 of the revised guidelines the use of the phrase "practical heat treatment procedure" was intended to convey both uncertainty about the duration of heating required to achieve inactivation of the virus and the lack of information on the reliability of results obtained from subsequent tests.

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Primary pulmonary hypertension

SIR,—We would like to clarify one or two matters which seem to have been obscured in Dr Tim Higenbottam's leading article (6 December, p 1456).

It is fundamental to understand that gas transfer for carbon monoxide is *always* low in primary pulmonary hypertension because of a greatly reduced pulmonary capillary volume secondary to constriction or obliteration of pulmonary arterioles. Primary pulmonary hypertension due to this cause has to be distinguished from pulmonary veno-occlusive disease and also from thromboembolic pulmonary hypertension, in neither of which is there benefit from vasodilator drugs. The clinical and radiological signs, incidentally, are of the pulmonary hypertension and not of the raised pulmonary vascular resistance which causes this hypertension.

Treatment is aimed both towards raising the low cardiac output and to reducing the pulmonary artery pressure in the hope of retarding progression of hypertensive damage to the lung bed.[1,2]

A good response to a vasodilator is most likely in patients who are discovered at an earlier stage of the disease. These have lower pulmonary artery pressures and higher cardiac outputs. We found that the acute response to prostacyclin was no better at predicting the degree of reversible vasoconstriction than the response to nifedipine but had the virtue of being immediately reversible in the event of an unfavourable response with a fall in systemic blood pressure. Since oral nifedipine was