placebo to the diet of 22 obese, poorly controlled diabetic outpatients. Over a three-month period, there was no significant reduction in body weight or of fasting or postprandial blood glucose concentration. The type of patient studied differed, as Jenkins *et al* had only two patients significantly above the desired body weight; but obese, poorly controlled patients would have been expected to benefit from any long-term effect of fibre additive. We would suggest that optimistic reports of the use of fibre supplementation in the therapy of diabetes mellitus should be confirmed by careful long-term studies.

M COHEN
F I R MARTIN

Department of Endocrinology,
Royal Melbourne Hospital,
Melbourne, Australia

Conservation surgery for laryngeal cancer

SIR,—Although I fully agree with your leading article (11 November, p 1318) that early vocal cord tumours are best treated with radiotherapy, I disagree with your statement that with conservative surgery the cure rate for small supraglottic tumours (presumably T1 and early T2 N0 lesions) is higher than with radiotherapy. Regrettably, you have failed to mention one of the largest series of supraglottic cancer treated by irradiation. This is the series from the Fondation Curie in Paris. It is an unfortunate omission, since this is one of the most prestigious radiotherapy centres in the world, where treatment of laryngeal cancer was pioneered several decades ago. In its recent studies^{1,2} (its series is one of the largest in the world), which have been published in English, the absolute and determinate survivals at three years were 80% and 87% respectively for these early stages. The preservation of the voice was excellent in over 90% of the patients. It should be pointed out that conservative surgery can be performed only on a very select and favourable group of early cancers, whereas such a selection does not apply for patients referred to the radiotherapist. Furthermore, because of the high incidence of occult nodal metastases in supraglottic cancers, the neck nodes bilaterally have to be treated electively with radiotherapy, even if conservative surgery has been performed.^{3,4}

You have quoted the results from centres in New York, Texas, St Louis, etc, but not from Paris, which is a stone's throw from London—or is it? I hope that you will be able to correct this unfortunate omission in your editorial.

N A GHOSSEIN

Department of Radiology,
Albert Einstein College of Medicine,
New York

¹ Bataini, J P, *et al*, *Cancer*, 1974, **33**, 1253.

² Ghossein, N A, *et al*, *Radiology*, 1974, **112**, 187.

³ Agazzi, C, *Matinées Carcinologiques ORL de l'Institut Gustave Roussy*, 1-5, October 1970.

⁴ Leroux-Robert, J, *Annals of Otolaryngology*, 1965, **82**, 305.

Typhoid fever

SIR,—Your leading article on typhoid fever (27 January, p 213) comments on isolation of *Salmonella typhi* from the blood stream for up to 10 days after the start of treatment and that there is no apparent explanation for this. In fact, the presence of *S typhi* in blood clot

of patients on treatment with chloramphenicol can be demonstrated much later than this. We have seen it in patients after 17 days' treatment and it is probable that such isolation may be obtained at any stage of illness in spite of therapy.¹

The reason almost certainly relates to the intracellular location of the organism in reticuloendothelial cells and to their ability to survive there and reinvade the blood stream periodically. We have shown that such intravascular shedding occurs in typhoid carriers and indeed may be the only manifestation of the carrier state.² Such isolations may also be made from patients with no previous history of clinical typhoid fever.² Both in this group and in patients with clinical relapse during the acute disease release of intracellular organisms will result in positive blood cultures. In the latter group sufficient organisms are released to provoke clinical signs and symptoms. The nature of the host-parasite relationship in typhoid fever is such that phagocytic uptake and release of organisms probably occurs continuously during the acute disease. Blood sampling will then detect those organisms that have just recently been released and which have not yet been destroyed or inhibited by antibiotic. Once removed by antibiotic or by antibody and complement mechanisms they are replaced from the reticuloendothelial sites. It has also been shown that both penicillin and streptomycin are capable of stimulating phagocytic uptake of bacteria¹ and it is possible that antibiotic treatment may increase the potential reservoir of organisms in reticuloendothelial sites capable of reinvading the blood stream.

K C WATSON

Central Microbiological Laboratories,
Western General Hospital,
Edinburgh

¹ Watson, K C, *American Journal of Tropical Medicine and Hygiene*, 1957, **6**, 72.

² Watson, K C, *Lancet*, 1967, **2**, 332.

³ Linz, R, *Annales de l'Institut Pasteur*, 1953, **85**, 295.

Beta-blockers, blood sugar control, and renal function

SIR,—I was interested to read the paper from Dr A D Wright and his colleagues comparing metoprolol and propranolol in diabetics (20 January, p 159). I would agree that on their evidence there is no strong reason for choosing a cardioselective beta-blocker from the point of view of the minor differences in hyperglycaemia associated with their use. However, I think that they should have emphasised more the benefits of cardioselectivity in the recovery from insulin-induced hypoglycaemia, the evidence for which they review in their introduction.

My main purpose in writing is to confirm their observation of a greater deterioration in renal function during treatment with a non-selective compared with a cardioselective beta-blocking drug. We have recently completed a study comparing propranolol and atenolol in the treatment of 15 patients with essential hypertension in an open crossover trial. In doses producing equal reduction in blood pressure the creatinine clearance fell from 162 ± 9.4 (SE) l/24 h in the untreated state to 132 ± 8.5 l/24 h during propranolol treatment ($P < 0.01$), but only to 152 ± 13.9 l/24 h during atenolol treatment ($P = 0.05$). The reduction in function during propranolol

treatment was significantly greater than that during atenolol treatment ($P < 0.0125$). It is well known that non-selective beta-blocking drugs reduce creatinine clearance,¹⁻³ and it is of interest that there is now evidence that both of the most cardioselective drugs available cause less reduction in renal function. These differences in effect on renal function are, of course, of little importance in essential hypertension, but may be important in patients with renal disease.

R WILKINSON

Department of Medicine and Nephrology,
Freeman Hospital,
Newcastle upon Tyne

¹ Nayler, W G, *et al*, *American Heart Journal*, 1967, **73**, 207.

² Schirmeister, J, *et al*, *Arzneimittel Forschung*, 1966, **16**, 847.

³ Ibsen, H, and Sederberg-Olsen, P, *Clinical Science*, 1972, **44**, 129.

Mechanisms of sudden death

SIR,—Your leading article (23-30 December, p 1734) suggested that platelet embolism could be the precipitating factor for sudden death. I think this must be rarely so. Roberts has shown that, with few exceptions, neither sudden death nor myocardial infarction occur until two of the three main coronary arteries are narrowed by 75%.¹ It seems unlikely that platelet embolism would be delayed until this critical stage had been reached. Moreover, if platelet embolism were to blame, sudden death would occur more often during exertion or stress rather than at rest. An explanation more directly related to the degree of coronary narrowing is required.

Roberts argues that blood stasis from reduced perfusion is the initiating mechanism for ischaemia leading to heart attack. For ventricular fibrillation then to occur, the work of Lubbe *et al*² suggests that critical metabolic gradients must develop between well and poorly perfused myocardium. If fibrillation does not occur and ischaemia should persist, myocardial infarction could develop with or without thrombosis, depending on duration of survival.¹

The question now arises: what causes the reduced perfusion? Given the prerequisite of 75% coronary narrowing of two vessels, which are presumably rigid and virtually incapable of dilatation in response to demand, elementary principles of physics should apply. Quite small falls in blood pressure could reduce coronary perfusion critically and predispose to a heart attack if collateral circulation is stretched. It may be relevant that the following circumstances are associated with a poor prognosis: (a) when blood pressure falls as a result of exercise in patients with known ischaemic heart disease^{3,4}; (b) After recovery from myocardial infarction, if the blood pressure remains more than a few mm Hg lower than its preinfarction level^{5,6}; (c) When the blood pressure falls over the months or years following recovery from myocardial infarction.⁷

It may also be relevant that smokers have a lower blood pressure than non-smokers,⁸⁻¹⁰ which in the practolol trial persisted for about a year after giving up smoking.¹⁰ An increased mortality also persists for some time after giving up smoking. Finally, heart attacks often occur during sleep when oxygen requirements are minimal but when blood pressure is at its lowest.

Blood pressure reduction may, of course, be an expression of existing cardiac damage, as in the first three studies cited above.¹⁻³ But