tremendous variability in GPs' behaviour. We feel that this should be a cause for concern and debate. Is it justifiable and what effects does it have on patients?

Finally, we are concerned that the issue of list size should not be lost among arguments about how many hours GPs work. Our paper provides strong evidence to support the case for a reduction in maximum list size to below 2500 as a means of increasing time available to patients. There is no evidence, however, that reductions in lists which are already below 2500 will have the same effect. If the aim of the DHSS and General Medical Services Committee is to increase the amount of time doctors devote to each patient they might look for more effective instruments than reducing *average* list sizes, which seems as likely to result in a shorter working week as in greater patient contact time.

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1 Butler JR. *How many patients?* London: Bedford Square Press, 1980. (Occasional Papers on Social Administration 64.)

The rules of the game

SIR,—As the original source of the "leak" of one of the findings of Dr D Wilkin and Professor D H H Metcalfe (1 December, p 1501), I would like the opportunity of adding to the comments made by Dr Richard Smith (p 1529) and in Professor Bain's leading article (p 1474).

Professor Metcalfe reported his findings before an invited audience at a meeting on performance review in general practice, held at King's Fund College in June 1984. When speaking at the annual symposium at the Wessex faculty of the Royal College of General Practitioners on 20 October about policies and possibilities for prevention, and the question of time was raised, I considered it, therefore, perfectly reasonable to quote these results (not in fact inaccurately) as part of the argument that there may be scope for the reallocation of priorities in the way general practitioners' time is used.

A reporter from *Doctor* was present at the meeting and heard the discussion, in which Professor Bain and Dr Bill Styles also took part. None of us spoke to her directly about Dr Wilkin's and Professor Metcalfe's study and we were all equally surprised to find ourselves quoted on the front page.

I appreciate the difficulties that this report and its circulation to the national press caused Dr Wilkin and Professor Metcalfe and have apologised to them personally for my part in it.

However, producing evidence and discussing its importance are the principal purposes of academic meetings. It would be extremely inhibiting if this could not take place before the results were published in learned journals. You appear to take the same view in your leading article.

If comment in the so called free press either on the original presentation or on the subsequent discussion is liable to be inaccurate and to misrepresent the findings as grossly as this report in *Doctor*, and also jeopardise their future publication, the only conclusion I can draw is that the organisers of academic meetings should now exclude reporters from medical newspapers, and speakers should abjure "free" publicity and content themselves with seeking to have their work published only in reputable journals.

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Metabolic effects of bicarbonate in the treatment of diabetic ketoacidosis

SIR,—The results section of the paper by Dr P J Hale and others (20 October, p 1035) does not mention mortality or morbidity in the bicarbonate treated and control groups. In the methods section I see that one patient died 36 hours after admission to hospital, but it is not clear whether this patient was excluded from the study or included in either the bicarbonate treated or the control group. Clearly, although there may have been extenuating circumstances contributing to this patient's death, it is important to establish whether she received bicarbonate or not.

In their introduction the authors point out that acidosis causes negative inotropism and peripheral vasodilatation, which may exacerbate hypotension and hypothermia. They also point out that the risk of ventricular arrhythmias may be increased in metabolic acidosis. In the results section, however, they make no mention of blood pressure, state of perfusion, or core temperature. I wonder if they performed 24 hour electrocardiographic monitoring to determine whether there were any differences in cardiac arrhythmias between their bicarbonate treated patients and the controls. Lastly, patients who are profoundly acidotic often have associated hyperkalaemia, and this is undoubtedly an important factor with regard to cardiac arrhythmias. Infusion of bicarbonate tends to lower the serum potassium concentration, and I wonder whether the authors have data on the changing serum potassium concentrations in the two groups.

In the absence of this information I wonder if the last sentence of their discussion should not read, "There is therefore no metabolic indication for the use of intravenous bicarbonate in the treatment of diabetic ketoacidosis with respect to intermediary metabolites, but the value in protecting against arrhythmias and improving cardiac function in the severely acidotic patient needs further investigation."

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SIR,—In their study of the metabolic effects of bicarbonate in the treatment of diabetic ketoacidosis Dr P J Hale and others found faster recovery of acid base indices (pH and bicarbonate) but slower recovery of total and individual ketone and lactate concentrations with bicarbonate, and no difference in the rate of fall of glucose concentration.

In our study there was no statistically significant difference in the hourly rate of recovery of arterial blood pH or bicarbonate between those given bicarbonate (mean 130 mmol(mEq)) and those not given bicarbonate.[1] This was also true in five patients given bicarbonate on one occasion but not on another. In addition the rate of recovery of plasma glucose was faster in those not given bicarbonate (table). The difference between our findings may reflect the fact that we studied more severely acidotic patients (pH $<7{\cdot}1$), many of whom were deeply comatose and severely dehydrated (initial systolic blood pressure <100 mm Hg, blood urea nitrogen >10 mmol/l (14 mg/100 ml)). We did not observe any difference in the incidence of hypokalaemia (potassium $<3{\cdot}3$ mmol(mEq)/l) or any difference in neurological improvement between the treated and untreated groups.

These data support the hypothesis that bicarbonate treatment in diabetic ketoacidosis is at best ineffective and may well be deleterious.

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1 Lever E, Jaspan JB. Sodium bicarbonate therapy in severe diabetic ketoacidosis. *Am J Med* 1983;**75**: 263-8.

**The authors reply below.—ED, *BMJ*.

SIR,—Dr K G Taylor raises a number of points regarding our article. The patient died for the reasons given in our paper. Since death occurred more than 30 hours after the study this patient's results were included in our analysis. We would not wish to draw any conclusion from a mortality of one in 38 patients, and mortalities from this centre have been reported.[1 2] In addition Marr *et al* observed no difference in mortality in children between those who received bicarbonate and those who did not.[3]

We did not choose to study blood pressure, peripheral perfusion, or core temperature but isolated one specific effect of bicarbonate—on metabolism. Patients are routinely monitored for cardiac arrhythmias, and none were observed. Systematic analysis of potassium concentrations is not possible since the results were used in adjusting rates of potassium infusion. It is well recognised that bicarbonate infusion has a potassium lowering effect.[4] Our conclusion was drawn from the results of our metabolic study and we would not wish to extend it beyond that.

Lever and Jaspan analysed retrospectively the results of 73 episodes of diabetic ketoacidosis where patients had received bicarbonate and 23 episodes of similar severity where bicarbonate had not been used.[5] Treatment was not randomly allocated, clear guidelines for bicarbonate use were not available, and the results were averaged over the time from admission to recovery. It is perhaps not surprising that in these conditions no difference in change in pH was observed

Rate of recovery of pH, bicarbonate (HCO_3), and glucose in patients given bicarbonate and in those not given bicarbonate

	Patients given bicarbonate	Patients not given bicarbonate	p value
Change in pH (units/h)	$+0{\cdot}051 \pm 0{\cdot}06$	$+0{\cdot}053 \pm 0{\cdot}09$	$>0{\cdot}05$ NS
Change in HCO_3 (mmol/h)	$+1{\cdot}03 \pm 0{\cdot}9$	$+1{\cdot}28 \pm 0{\cdot}43$	$>0{\cdot}05$ NS
Change in glucose (mmol/h)	$-3{\cdot}5 \pm 0{\cdot}99$	$-4{\cdot}6 \pm 1{\cdot}34$	$p=0{\cdot}05$

Conversion: SI to traditional units: HCO_3: 1 mmol/l = 1 mEq/l. Glucose: 1 mmol/l ≈ 18 mg/100 ml.

between the groups. The increase in pH which we observed at two hours was small and might not be apparent in five patients.

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1 Soler NG, Bennett MA, FitzGerald MG, Malins JM. Intensive care in the management of diabetic ketoacidosis. *Lancet* 1973;i:951-4.
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3 Marr TJ, Traisman HS, Traisman ES, Typlin B, Ban S. Juvenile ketoacidosis: the use of sodium bicarbonate in the treatment of diabetic children. *J Kans Med Soc* 1981;**892**:282-4.
4 Soler NG, Bennett MA, Dixon K, FitzGerald MG, Malins JM. Potassium balance during treatment of diabetic ketoacidosis. *Lancet* 1972;ii:665-7.
5 Lever E, Jaspan JB. Sodium bicarbonate therapy in severe diabetic ketoacidosis. *Am J Med* 1983;**75**: 263-8.

SIR,—Dr P J Hale and his colleagues (20 October, p 1035) showed that giving intravenous sodium bicarbonate solution does not hasten the fall of "total ketone" (3-hydroxybutyrate plus acetoacetate) or lactate concentrations in patients with diabetic ketoacidosis. Indeed, they found that patients given bicarbonate had almost no decrease of blood ketones and lactate during the hour when they received that treatment. To explain this surprising finding they suggested, "Possibly the greater increase in pH in patients who received bicarbonate altered renal excretion of ketone bodies." There is, however, no good evidence that the urinary excretion of acetoacetate, 3-hydroxybutyrate, or lactate is pH dependent. Moreover, the excretion of organic anions such as salicylate and phenobarbital is increased by urinary alkalinisation. Therefore, unless bicarbonate administration increased lipolysis or ketogenesis, there must be another explanation for the delayed decrease of blood ketones and lactate.

One possibility, as was found with phenobarbital,[1] is that the distribution of the ketones and lactate between cell and extracellular fluids might be pH dependent. If so, alkalinisation of the plasma might increase the ratio between cell and extracellular fluid anion concentrations and so increase blood concentrations. Acetoacetic, 3-hydroxybutyric, and lactic acid have pHs of 3·56, 4·70, and 3·08 respectively. Consider the case of 3-hydroxybutyric acid, first at blood pH 7·0 and then at 7·2. Assume that "cell fluid pH" is 6·9, which is, to be sure, an oversimplification.[2] The Henderson-Hasselbalch equation gives the ratio of 3-hydroxybutyrate to 3-hydroxybutyric acid at pH 6·9 as about 160. In extracellular fluid at pH 7·0 the ratio is about 200. Thus, the concentration of the acid is very low at either pH. If we assume that the acid passes freely across cell membranes its concentration will be "the same" in cell and extracellular fluid. Then the ratio of the concentration of the anion, 3-hydroxybutyrate, in extracellular fluid to cell fluids will be 200:160, or 1·25. If the blood pH is raised to 7·2 the ratio of the concentration of 3-hydroxybutyrate in extracellular fluid to cell fluids will be 316:160, or nearly 2·0, which is about 1·6 times higher than when the blood pH was 7·0.

Similar calculations can be made for acetoacetate and lactate. Although the foregoing assumptions and calculations are oversimplified, they predict that the blood concentrations of those anions might increase during alkalinisation. Of course, that neglects other possible influences, such as altered production of ketones due to changes of lipolysis and ketogenesis and altered disposition due to changes in their metabolism or renal excretion.

Dr Hale and his colleagues stated that the mean blood pH in the patients given bicarbonate was significantly higher at 120 minutes (7·23) than in those given saline (7·12). They apparently gave bicarbonate only during the first hour, during which the mean blood ketone and lactate concentrations did not change. Subsequently, there were parallel declines of those anion concentrations in the bicarbonate and the saline treated patients. It would be interesting to know the serial blood pH values in each group. If the mean difference in pH between the two groups was about the same at both 60 and 120 minutes that would fit with my suggested explanation.

The interesting finding that blood ketones and lactate did not decrease during the first hour in the bicarbonate treated patients may have resulted from several opposing influences: a shift of those anions from cell to extracellular fluids, which would tend to increase their concentrations in blood, and continued metabolism and excretion of the anions, which would tend to lower their concentrations in blood.

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1 Waddell WJ, Butler TC. The distribution and excretion of phenobarbital. *J Clin Invest* 1957;**36**:1217-26.
2 Cohen JJ, Kassirer JP. *Acid/base*. Boston: Little, Brown, 1982.

Distribution of adipose tissue and risk of impaired glucose tolerance in pregnancy

SIR,—I was interested to read the paper by Dr Leif Lapidus and his colleagues and that by Larsson *et al*[1] from Sweden. These workers have found that central body shape, as measured by waist:hip ratio, was the best predictor of cardiovascular problems.

I have been studying obese pregnant women[2] and have found that a waist:hip girth ratio of $>0{\cdot}85$[3] helped predict more than half of the obese women with impaired glucose tolerance, as defined as an area under the curve of a three hour oral glucose tolerance test of >42 units.[4] The sensitivity of the index was 53% (10/19), the specificity 80% (37/46), and the predictive value 53% (10/19).

An extreme example of central (android) obesity occurred in a woman in the third trimester of pregnancy whose weight was 150% of ideal body weight. Her waist:hip ratio was 0·95 after we had corrected the waist girth by 22 cm to allow for pregnancy. The area under the curve in the glucose tolerance test was 73·3. The patient was treated with diet only; her HbA_{1c} was normal at 6·6%. She was induced at 37 weeks on account of fetal macrosomia. After 12 hours, because of no progress, a caesarean section was performed and a 4700 g girl was delivered in good condition. The infant had transient hypoglycaemia in the first 12 hours and hyperbilirubinaemia, which was treated with phototherapy. The mother developed a wound infection which was treated and went home with the baby on the 10th day after delivery.

It seems that body shape can predict which obese pregnant women are at risk of impaired glucose tolerance, and only those with a waist:hip ratio of $>0{\cdot}85$ should have a glucose tolerance test.

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1 Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjornsorp P, Tibblin G. Abdominal adipose tissue distribution, obesity and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *Br Med J* 1984; **288**:1401-4.
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A sensitive immunoradiometric assay for serum thyroid stimulating hormone

SIR,—We read with interest the report of Dr J Seth and others (17 November, p 1334) on the use of a sensitive immunoradiometric assay for thyroid stimulating hormone (TSH) produced by Boots-Celltech. Over four months we have used this assay routinely to assess thyroid function in 3629 patients from a variety of sources within a general hospital, including the endocrine clinic. Somewhat to our surprise we found that undetectable serum TSH values—that is, serum concentrations less than 0·1 mU/l—were relatively common, occurring in 443 (12%) of the patients studied. When these 443 patients were classified according to the information on the request form, supplemented by telephone inquiry and appropriate additional tests, the largest number (197 (44%)) were found to be receiving thyroxine replacement therapy; 120 (27%) were clinically thyrotoxic with increased thyroxine concentrations; 48 (11%) were undergoing treatment for hyperthyroidism or had recently done so; and 12 (3%) were found to have triiodothyronine (T3) toxicosis. In the remaining 66 patients there was at that stage no explanation for the undetectable TSH.

So far 27 of this unexplained group, all of whom had normal concentrations of serum thyroxine, have been recalled for clinical evaluation and laboratory reassessment, which included serum T3 measurement and thyrothropin releasing hormone (TRH) testing. Four patients recalled had detectable TSH (0·1, 0·2, 0·4, 14 mU/l). Their TRH tests showed increments of 1·0, 1·9, 0·6, and 75 mU/l respectively. Eight patients proved to be on treatment for thyroid disease—six on thyroxine replacement and two on carbimazole. Two patients were shown to have T3 toxicosis. Eight patients were in clinical remission after treatment for hyperthyroidism from five months to 14 years previously. The remaining five patients were clinically euthyroid with undetectable TSH, a flat TRH response, and normal serum T3 concentration. Two of them had atrial fibrillation.

In the course of this work we have confirmed the finding of Dr Seth and his colleagues that an undetectable basal serum TSH will predict a flat response to TRH. Moreover, we have found that this sensitive TSH assay provides a valuable pointer to patients with thyroid disease, both in excluding thyrotoxicosis and in identifying patients who need further study. Not all laboratories carry out serum T3 measurements, and this TSH assay seems to allow hyperthyroidism to be excluded whatever the cause. The frequent finding of undetectable serum TSH in other clinical conditions, such as in patients on thyroid replacement therapy or in apparent remission after antithyroid therapy, re-emphasises the need for good clinical information when test results are interpreted.