standard deviations below the mean, and the authors would need to measure the plasma potassium in more than 2000 patients taking a thiazide before they could expect to turn up a similar case.[2] An event of such rarity is hardly a sound reason for changing ordinary practice. Rather it is an indication for detailed investigation of the individual patient, and the authors should perhaps have excluded syndromes of mineralocorticoid excess other than hyperaldosteronism (for example, liquorice abuse) and other factors contributing to hypokalaemia (for example, laxative abuse). Incidentally, "closely monitored" is a phrase with little meaning to the practising doctor—does it mean measurement daily, weekly, monthly, or what?

Dr Skehan and his colleagues state that an increased incidence of ventricular arrhythmias after myocardial infarction is a "complication" of hypokalaemia, quoting a recent paper[3] in support. The study cited did *not* establish a causal relationship between hypokalaemia (or diuretic use) and arrhythmias, and one of the authors of the article concerned has in fact conceded this.[4]

At present there is no sound evidence that the mild or moderate hypokalaemia which generally accompanies thiazide treatment is harmful, nor do we know that it is harmless. The question is clearly very important, and there is considerable commercial interest in promoting the supposed risks of hypokalaemia. Reports which give undue weight to rare events, and which accept uncritically the supposed risks of hypokalaemia, are unlikely to lead to more rational management of diuretic-induced hypokalaemia.

L E RAMSAY

University Department of Therapeutics,
Royal Hallamshire Hospital,
Sheffield S10 2JF

[1] Morgan DB, Davidson C. *Br Med J* 1980;**280**:905-8.
[2] Swinscow TDV. *Br Med J* 1976;ii:33-4.
[3] Cole AG, Arkin D, Solomon R. In: *Malignant ventricular dysrhythmias in myocardial infarction: the role of hypokalaemia.* International congress and symposium series No 44. London: Royal Society of Medicine, 1981:47-53.
[4] Solomon R. In: *Malignant ventricular dysrhythmias in myocardial infarction: the role of hypokalaemia.* International congress and symposium series No 44. London: Royal Society of Medicine, 1981:63.

SIR,—I read with interest the report of Dr J D Skehan and others (9 January, p 83) in which they describe hypokalaemia induced by the beta-blocker and thiazide combination sotazide. I have recently encountered a similar problem during a study using fixed combination therapy for mild-to-moderate hypertension.

A 42-year-old white hypertensive man had been under treatment for moderate hypertension at King's College Hospital since 1980 and had been taking propranolol 80 mg daily without side effects. He was entered into a randomised double-blind, placebo-controlled hypertension study, comparing Trasidrex (oxyprenolol 160 mg, sustained release, and cyclopenthiazide 0·25 mg) and Moducren (timolol maleate 10 mg, hydrochlorothiazide 25 mg, and amiloride hydrochloride 2·5 mg). During the first placebo phase (four weeks) his blood pressure was 188/112 mm Hg lying and 174/122 standing. He had a sinus tachycardia of 105 beats/min and grade 1 hypertensive retinopathy. His serum potassium was 4·1 mmol(mEq)/l on propranolol prior to entry into the placebo phase, at the end of which time his serum potassium remained at 4·2 mmol/l. His renal function was normal. After two months' treatment with Moducren (blood pressure 148/92 mm Hg lying and 144/96 mm Hg standing) his serum potassium remained normal at 4·0 mmol/l. Following four weeks' treatment with Trasidrex, one tablet daily, he developed non-specific influenza-like symptoms—in particular proximal limb girdle muscle weakness and myalgia affecting the legs. His blood pressure was controlled, being 130/85 mm Hg lying and 138/92 standing, but the serum potassium had fallen to 2·8 mmol/l. He was then started on potassium supplementation, potassium chloride (Slow K) 1200 mg and amiloride 10 mg daily, which resulted in correction of the serum potassium concentration. After a further two weeks he discontinued his potassium replacement and the amiloride and a recurrence of symptoms was noted, the serum potassium at that time being 3·2 mmol/l. The addition of amiloride 10 mg to the Trasidrex resulted in the return of the serum potassium to 4·3 mmol/l, with disappearance of his symptoms. He has subsequently been followed up for over six months on Moducren, two tablets daily; the serum potassium has remained normal and his hypertension has remained controlled.

I would agree with the important conclusion of Skehan and his colleagues that regular monitoring of serum potassium is mandatory even in symptomless patients taking a beta-blocker and thiazide combination. A beta-blocker and thiazide combination including a potassium-sparing drug has obvious advantages for long-term treatment of hypertension.

PETER J RICHARDSON

Cardiac Department,
King's College Hospital,
London SE5 9RS

Smoking and IgE levels

SIR,—We read with interest the article by Dr O Zetterström and others (7 November, p 1215), which demonstrated that smoking can lead to increased circulating levels of IgE in non-atopic subjects and to an increased risk of sensitisation after unnatural exposure to (occupational) allergens.

It has been possible for us to correlate the smoking histories with IgE data from 489 patients referred for investigation of possible allergies. All patients were more than 20 years old, commonly had respiratory symptoms, and were classified as atopic if they had detectable serum IgE antibodies to at least one of the three most common UK allergens naturally inhaled—that is, grass pollen, house-dust mite, and cat epithelium.[1] After the atopic and non-atopic patients had been subdivided by sex and smoking history their geometric mean IgE levels were calculated. Unlike Zetterström and colleagues, we were unable to find any significantly different IgE levels (using Student's *t* test) between smokers and non-smokers, except the expected one between any atopic and non-atopic groups. However, it can be seen from the accompanying table that a significant sex difference was noted among the non-atopic subjects, and this was concentrated in the smoking group.

In UK population surveys of subjects who were aged (*a*) 20-44 years[2] and (*b*) over 70 years,[3] geometric mean IgE levels for males were higher than for females, although only in the latter group was the difference significant—38·6 U/ml versus 27·2 U/ml. These community surveys, and a similar survey in Arizona,[4] showed no significant differences in IgE levels with increasing age among non-atopic adults. However, in our patients who were non-atopic yet had symptoms IgE levels rose with increasing age, and this was more significant for men than women.

In a hospital survey of definitely non-atopic patients we recorded a geometric mean IgE value of 21 U/ml,[5] and the higher levels—rising with age—recorded in our present groups may be due to the sensitisation of apparently non-atopic patients referred for allergy investigations to unrecognised (possibly occupational) allergens. If this is so, it would be expected that IgE levels would increase with age, owing to longer exposure to smoke and allergens, and would be higher among men than women because men are more likely to be heavy smokers[6] and to be atopic.[7]

IgE concentrations in atopic and non-atopic smokers and non-smokers

Group	Males		Females		Significance of difference in means between males and females
	No	95% confidence limits of geometric mean of IgE (IU/ml)	No	95% confidence limits of geometric mean of IgE (IU/ml)	
Non-smoking and non-atopic	38	33·4–99·8	73	30·7–61·1	NS
Smoking and non-atopic	92	60·7–106·2	72	29·9–56·2	$p < 0·01$
Non-atopic	130	56·6–93·9	145	33·4–53·2	$p < 0·01$
Non-smoking and atopic	57	156·1–334·4	67	193·5–424·1	NS
Smoking and atopic	60	205·0–413·8	30	111·6–401·6	NS
Atopic	117	200·1–334·6	97	187·0–363·9	NS

C F A PANTIN
T G MERRETT

RAST Allergy and Research Unit,
Benenden Chest Hospital,
Cranbrook, Kent TN17 4AX

[1] Merrett TG, Pantin CFA, Dimond AH, Merrett J. *Allergy* 1980;**35**:491-501.
[2] Burr ML, St Leger AS, Bevan C, Merrett TG. *Thorax* 1975;**30**:663-8.
[3] Merrett TG, Burr ML, St Leger AS, Merrett J. *Clin Allergy* 1980;**10**:433-9.
[4] Burrows B, Halonen M, Barbee RA, Lebowitz MD. *Am Rev Respir Dis* 1981;**124**:523-5.
[5] Nye L, Merrett TG, Landon J, White RJ. *Clin Allergy* 1975;**5**:13-24.
[6] Lee PN, ed. *Statistics of smoking in the UK.* 7th ed. London: Tobacco Research Council, 1976:66-7. (Research Paper No 1.)
[7] Davidson AG, Baron B, Walzer M. *J Allergy* 1947; **18**:359.

Mistletoe hepatitis

SIR,—In the issue of 17 January 1981 (p 186) we reported the case of a woman who had developed a severe hepatitis when she took a herbal medication for "nervous symptoms." The challenge test confirmed the toxicity of this product for this particular patient, and from a review of the literature we concluded that mistletoe was the herb in the medication which was most likely to have been the toxic agent.

Professor N R Farnsworth and Dr W D Loub in a letter (17 October, p 1058) reported the case of a Chinese lady who had developed a hepatitic reaction to a herbal remedy, which was subsequently found to contain phenylbutazone. They suggested that there might be a known hepatotoxic drug in the herbal medication taken by our patient. The remedy contained motherwort, kelp, wild lettuce, skullcap, and mistletoe, a combination which it was not practicable to analyse completely. However, Dr Gary Thomas of the Portsmouth