have had several attacks because they have not been warned about the risk of non-steroidal drugs and other substances—for instance, tartrazine, that can trigger attacks in aspirin intolerant patients. The role of the upper airway in acute severe asthma has recently been emphasised.[5] However, doctors in intensive care units have from time to time observed patients with acute severe asthma who needed surprisingly low inspiratory pressures when they were intubated and artificially ventilated.[4]

In my opinion it is important to define the temporal course of the attack when faced with a patient with an exacerbation of his or her asthma. I propose the term "severe exacerbation of asthma" instead of "acute severe asthma." Furthermore, each severe exacerbation should be classified as acute or subacute according to the speed of the evolution of the attack.

CESAR PICADO

Hospital Clinico,
Barcelona 36,
Spain

[1] Cochrane GM, Clark TJH. A survey of asthma mortality in patients between the ages of 35 and 64 in the greater London hospitals in 1971. *Thorax* 1975;**30**:300-5.
[2] Hetzel MR, Clark TJH, Branthwaite MA. Asthma: analysis of sudden deaths and ventilatory arrests in hospitals *Br Med J* 1977;i:808-11.
[3] Picado C, Montserrat JM, Roca J, *et al.* Mechanical ventilation in severe exacerbation of asthma. Study of 26 cases with six deaths. *Eur J Respir Dis* 1983; **64**:102-7.
[4] Cohen JI, ed. Upper airway obstruction in asthma. *Johns Hopkins Med J* 1980;**147**:233-7.
[5] Lisboa C, Jardim J, Angus E, Macklem PT. Is extrathoracic airway obstruction important in asthma? *Am Rev Respir Dis* 1980;**122**:115-21.

Recovery of renal function after transplantation

SIR,—Dr T O Nunan and others (23 July, p 248) describe a phenomenon that obviously is not so rare as could be judged from the few published reports.[1-3] We should like to describe two patients in whom the function of their own kidneys recovered after transplantation.

Case 1—A man born in 1926 had had a subacute glomerulonephritis and succeeding nephrotic syndrome since 1964. Renal biopsy in 1980 showed a severe membranous glomerulonephritis. Haemodialysis was started at serum creatinine concentration of 780 μmol/l (8·8 mg/100 ml) in May 1980. He received a cadaveric renal transplant in the same month. After one rejection the function of the transplant was adequate with a creatinine level of 240 μmol/l (2·7 mg/100 ml). In May 1983, however, a transplantectomy had to be performed due to an abscess in the transplant. A renal radiography at an earlier control visit had surprisingly shown a good function in his own kidneys. This function proved to be sufficient to maintain a creatinine concentration not exceeding 250 μmol/l (2·8 mg/100 ml) since the transplantectomy. The patient has continued taking methylprednisolone 8 mg every second day.

Case 2—A man born in 1950 had had a type I diabetes since 1966. Diabetic nephropathy was proved by a biopsy, and a severe nephrotic syndrome developed. Peritoneal dialysis was started in February 1982, replaced in August by haemodialysis because of relapsing peritonitis. At that time the creatinine concentration had risen to 680 μmol/l (7·7 mg/100 ml). He received a cadaveric renal transplant in October 1982. Due to increased proteinuria after transplantation a renography was performed. It showed a non-functioning transplant but good function in his own kidneys. A control biopsy showed progression of diabetic nephropathy. The renal function has remained good with a creatinine concentration of 120 μmol/l (1·4 mg/100 ml) and proteinuria of 5 g daily. He has continued receiving antihypertensive drugs but not corticosteroids.

We conclude from these two cases that the recovery of renal function after renal transplantation is rare but possible (two patients out of 1338 transplantations to 1129 patients performed from 1964 to 1983 in Finland). However, the real incidence of this recovery might be greater as the routine clinical visits after transplantation do not include tests for own renal function. A suitable test—for example, radionuclide scanning—may indeed be necessary to evaluate fully the results of kidney transplantation, as suggested by Dr Nunan and others. It remains uncertain how those patients with recovered renal function should be treated. We have discontinued the immunosuppressive treatment with azathioprine, but a further use of corticosteroids may be useful.

RISTO SIPILÄ
BÖRJE KUHLBÄCK

Fourth Department of Medicine,
Helsinki University Central Hospital,
Helsinki, Finland

[1] Kopsa H, Schmidt P, Zazgornik J, Pils P, Balke P. Recovery of renal function following prolonged acute renal failure. *Proc Eur Dial Transplant Assoc* 1979;**15**:495-9.
[2] Brynger H, Brunner FP, Chantler C, *et al.* Combined report on regular dialysis and transplantation in Europe. X, 1979. *Proc Eur Dial Transplant Assoc* 1981;**17**:2-86.
[3] Swenson RS, Hall DA, Coplon NS. Clinical course of renal insufficiency in lupus nephritis [Abstract]. In: *Twentieth Congress of the European Dialysis and Transplant Association.* Amsterdam: Excerpta Medica, 1983:128.

Influence of ranitidine on plasma metoprolol concentrations

SIR,—We would like to reply to the letter of Dr D Jack and others (25 June, p 2064) relating to our results on the interaction of metoprolol and ranitidine.

Firstly, and most importantly, Dr Jack and his colleagues state that we interpreted the results of Hoensch and Hutzel[1] inaccurately. Dr Hoensch, who is a coauthor of this letter, confirms our opinion that his results without doubt suggest the possibility of interactions between ranitidine and other drugs that are mainly metabolised by the liver. Rendic *et al* also found that ranitidine binds to and inhibits cytochrome P450.[2] Furthermore, Speeg *et al* described an appreciable inhibition of the aminopyrine test by ranitidine.[3] Dr Jack ignored three studies[4-6] which show that ranitidine decreases liver blood flow by about 20%.

Our study is not the only one which suggests an influence of ranitidine on other drugs: interactions with warfarin (P V Desmond and others, paper presented to meeting of the Gastroenterology Society, Australia, 11-12 October 1982), fentanyl,[7] alcohol, midazolam,[8] procainamide, and nifedipine have been also reported. Furthermore, interactions of ranitidine with antacids and propranthelline have been described. Our results with metoprolol and its influence on exercise tachycardia agree with the data of Regardh *et al*,[9] who used the standard metoprolol tablet, comparing it with the slow-release form.

Finally, re-evaluation of our kinetic data showed that the difference between the period of treatment with metoprolol alone and the combined treatment phase with ranitidine is greater than indicated in our original table (14 May, p 1546), peak concentration being 177·2 (28·0) ng/ml mean (SEM), area under curve 1167 (191·6) ng/ml/h, and half life 4·4 (0·6 h) during treatment with metoprolol alone. The values for the combined treatment with ranitidine and metoprolol were: peak concentration 265 (33·0) ng/ml, area under curve 2140 (362·4) ng/ml/h ($p < 0.05$) and half life 6·5 (0·6 h) ($p < 0.05$). We apologise for this error, which does not, however, change the meaning of the data presented. Because of limitations of space, we did not mention in our original article that the monotherapy and combined treatment periods were separated by an interval of about 10 months.

H SPAHN
E MUTSCHLER

Pharmacological Institute,
University School of Pharmacy,
Frankfurt am Main 70,
West Germany

W KIRCH
H HOENSCH
E E OHNHAUS

Medical Department,
University School of Medicine,
Essen 1, West Germany

H D JANISCH

Gastroenterology Department,
Klinikum Charlottenburg,
Berlin, West Germany

[1] Hoensch H, Hutzel H. Hemmung der fremdstoffabbauenden Enzymaktivität in der menschlichen Leber durch Ranitidin und Cimetidin. *Verh Dtsch Ges Inn Med* 1982;**88**:653-7.
[2] Rendic S, Alebic-Kolbah T, Kajfez F. Interaction of ranitidine with liver microsomes. *Xenobiotica* 1982; **12**:9-17.
[3] Speeg KV, Patwardan RV, Avant GR, Mitchell MC, Schenker S. Inhibition of microsomal drug metabolism by histamine H_2 receptor antagonists studied in vivo and in vitro rodents. *Gastroenterology* 1982;**82**:89-96.
[4] Feely J, Guy E. Ranitidine also reduces liver blood flow. *Lancet* 1982;i:169.
[5] Garg AC, Weidler DJ, Jallad S, Eshelman FN. The effects of ranitidine and cimetidine on hepatic blood flow. *Clin Phrmacol Ther* 1982;**31**:228-9.
[6] Reimann IW, Klotz U, Fröhlich JC. Effects of cimetidine and ranitidine on steady-state propranolol kinetics and dynamics. *Clin Pharmacol Ther* 1982;**32**:749-58.
[7] Lee MR, Gandolfi AJ, Sipes IG, Bentley J. Effect of histamine H_2-receptors on fentanyl metabolism. *Pharmacologist 24* 1982;**145**:(A 282).
[8] Elwood AJ, Hildebrand PJ, Dundee JW, Collier PS. Ranitidine influences the uptake of oral midazolam. *Br J Clin Pharmacol* 1983;**15**:743.
[9] Regardh C-G, Johnsson G, Jordö L, Sölvell L. Comparative bioavailability and effect studies on metoprolol administered as ordinary and slow-release tablets in single and multiple doses. *Acta Pharmacol Toxicol (Copenh)* 1975;**36**:45-8.

Climacteric flushing in a man

SIR,—Dr Jean Ginsburg's leading article (23 July, p 242) and her short report with Ms Barbara O'Reilly (23 July, p 262) drew attention to the striking similarity between hot flushes in menopausal women and in men after orchidectomy. In 1941 Huggins *et al* mentioned hot flushes after orchidectomy for treatment of carcinoma of the prostate,[1] but the matter apparently fell into oblivion.

There are no published data on the incidence of hot flushes after orchidectomy. We therefore conducted a retrospective and prospective study of the incidence, frequency, and severity of hot flushes in 90 patients who had undergone orchidectomy for carcinoma of the prostate in 1980-2. A total of 66 (73%) had hot flushes, the incidence being significantly higher in the oldest patients. In most cases flushes started during the first four weeks after orchidectomy, but in six cases they appeared after three months. The number of hot flushes recorded during 24 hours was 1-3 in 29 (44%) patients, 4-10 in 31 (47%) patients, and >10 in six (9%) patients. Thirty three (50%) were not troubled by the flushes, 15 (23%) were slightly inconvenienced, and 18 (27%) were greatly distressed.