Antidepressants and Barbiturates

SIR,—We were interested to read the paper by Dr. Marie Åsberg and others on the relationship between plasma level and therapeutic effect of nortriptyline (7 August, p. 331). However, the same authors in a previous paper¹ excluded patients receiving barbiturates from their study, yet failed to do so in this later paper. Some of their depressed patients received night sedation with pentobarbitone. As the authors of these papers have shown,² barbiturates lower plasma tricyclic levels. The Figure (from one of our patients studied over some months) shows the effects of 200 mg amylobarbitone nocte for 5 days (B) on the plasma level of nortriptyline. It can be seen that a marked lowering of this level occurred during this time. This effect is apparently due to the effect of barbiturates on stimulating liver microsomal activity.

As the evidence is that plasma tricyclic levels are related to clinical response, barbiturate hypnotics should not be prescribed for patients receiving tricyclic antidepressants.

Since Dr. Åsberg and others used pentobarbitone as the usual hypnotic, we wonder whether this accounts for some of the low plasma levels reported in their study compared with our own,³ and would recommend that no other drugs at all be given in studies of this kind. This is clinically possible if most of the daily tricyclic dose is given at night with advantage taken of the sedative action. We are studying the effects of other hypnotics and tranquillizers on plasma tricyclic levels.—We are, etc.,

GRAHAM D. BURROWS
BRIAN DAVIES

Department of Psychiatry,
University of Melbourne,
Royal Melbourne Hospital,
Victoria, Australia

- 1 Åsberg, M., Price Evans, D. A., and Sjöqvist, F., *Journal of Medical Genetics*, 1971, 8, 129.
- 2 Sjöqvist, F., et al., *Proceedings of the European Society for the Study of Drug Toxicity, Excerpta Medica, International Congress Series*, 1967, 9, No. 145, 246.
- 3 Burrows, G. D., in press.

An Antidysrhythmic Agent

SIR,—The management of paroxysmal supraventricular tachycardia can be of great concern to the physician when treatment both by drugs and D.C. reversion has failed.

In 1969, during a series of animal experiments, we noted as a chance observation that capture of the dog's heart to allow atrial pacing was facilitated following intravenous verapamil (Cordilox). This had not been recorded previously and led us to consider whether this drug would be of value in the management of patients with resistant supraventricular tachycardia.

Our first really intractable patient did not appear for two years. She was a woman aged 45 years, who had experienced for many years symptoms due to a pre-excitation syndrome of the Wolff-Parkinson-White type. Three years previously a paroxysm had preceded an attack of acute myocardial infarction. Subsequently, she received treatment for paroxysms of tachycardia with drugs, including digoxin, quinidine, procainamide, propranolol, practolol, and sodium hydantoinate without long term benefit. On 26 March 1971 she had a further paroxysm

with a heart rate of 180 persisting for 12 hours. This did not revert to sinus rhythm after several attempts at D.C. reversion under diazepam sedation. She was then given verapamil 5 mg intravenously at a rate of 1 mg/minute and immediately reverted to sinus rhythm. Five days later she had a further acute episode of tachycardia with a heart rate of 180 which lasted for more than ten hours. Following further intravenous injection of 5 mg verapamil she reverted immediately to sinus rhythm. Subsequently, she was maintained on verapamil, 160 mg q.d.s. We have since found that her tachycardia is controlled by verapamil 40 mg q.d.s. and if this dosage is reduced further her paroxysms return. When seen on 9 September 1971 she was extremely well and had had no attacks for five months, whereas previously the attacks were recurring daily.

We have since treated another five patients who have had supraventricular tachycardia and each has reverted to sinus rhythm following a maximum of verapamil 10 mg intravenously. One of these patients had previously been treated unsuccessfully with

digoxin, quinidine, procainamide, and sodium hydantoinate over prolonged periods. Two patients with atrial fibrillation due to ischaemic heart disease had a considerable reduction in heart rate following intravenous verapamil, one with a rate of 180 which fell to 84, and the other fell from 140 to 80.

The exact mode of action of verapamil is unknown. It has been suggested¹ that the mechanism of action of this drug on the S.A.- and A.V.-nodes involves a direct cardiac effect as well as antagonism of vagal mechanism. However, in the dog we have shown (unpublished) that verapamil can not only reverse an isoprenaline-induced tachycardia but also reverse an atropine-induced tachycardia. Our experience in man indicates that its effects appear to be most beneficial in those patients whose heart rate can be temporarily slowed by vagal stimulation.

Verapamil appears to be a drug of promise in the management of obstinate supraventricular tachycardia, and may certainly succeed when attempted D.C. reversion has failed.—We are, etc.,

S. ORAM
P. F. CATLEY
B. LIVESLEY
P. H. KIDNER

King's College Hospital,
London S.E.5

- 1 Garvey, H. L., *European Journal of Pharmacology*, 1969, 8, 159.

Transient Deafness from High Doses of Frusemide

SIR,—I should like to report a case of transient deafness during intravenous frusemide therapy in chronic renal failure. Reports of this complication of frusemide are few,^{1,2} although it is better known with ethacrynic acid.

A 49-year-old woman was admitted with oedema and chronic renal failure associated with pelvic malignant disease. In addition to peripheral oedema pericarditis and pulmonary oedema were noted.

There being no diuretic response to the oral administration, she was given frusemide intravenously, 500 mg as a single dose. The injection took approximately three minutes. Soon after completion she complained of an inability to hear anything spoken at her bedside. No deafness had been evident during routine neurological examination at the time of admission. About an hour later the hearing improved and was clinically normal within four hours. The next morning the same dose was repeated. The time taken for the injection was again about three minutes. Very soon after, the patient became distressed, saying she could hear nothing. No abnormality, apart from a profound loss of hearing, was noted during neurological examination. Loud speech was heard about an hour later and she had normal hearing by about four hours. Subsequently she was given 240 mg of frusemide intravenously very slowly, taking about five minutes for the injection. No deafness occurred then or over the next six hours of careful patient observation. The only other drug, nalidixic acid, the patient had been having for three days prior to the first dose of intravenous frusemide.

The use of large doses of frusemide in renal failure is now an established method of treatment. The dose of intravenous frusemide used in this department has ranged up to 1 g