were in the larger hydroceles and I would certainly recommend that this form of treatment be reserved for hydroceles less than 500 ml unless the patient's general condition precludes surgery.

It is clearly important to have long-term follow up in this type of study and I plan to continue reviewing the patients I have treated.

J R NASH

Department of Surgery,
University of the Witwatersrand Medical
School,
Johannesburg 2001, South Africa

¹ Moloney GE. *Br Med J* 1975;iii:478-9.

² Nash JR. *Br J Surg* 1979;66:289-90.

Beta-blockade, myopathy, and thyrotoxicosis

SIR,—The report by Dr J C Forfar and others (24 November, p 1331) on proximal myopathy and myositis associated with the use of beta-blocking agents prompts us to call attention to another clinical situation leading to myopathy during beta-blockade.

We have recently treated three male patients, aged 36-57 years, who developed thyrotoxicosis during treatment with the beta-blocking drugs timolol, pindolol, and propranolol. All of them showed chronic thyrotoxic myopathy, and one was in addition suffering from chronic diarrhoea. On examination, two of them were considered clinically euthyroid. There was no nervousness, hyperkinesia, or tremor. The third patient had some thyrotoxic symptoms such as increased sweating and occasional palpitations. The pulse rate of the patients was 80-90 beats/min, and all showed regular sinus rhythm. The most prominent finding in all the patients was wasting of the proximal muscles of the extremities. The muscle power, however, was only slightly impaired.

Apparently, the diagnosis of thyrotoxicosis was delayed in two of the patients. The symptoms had lasted from one to six months, and the patients had lost 10-16 kg before their thyroid function was tested. One of the patients underwent extensive gastroenterological examinations because of chronic diarrhoea of six months' duration. In another patient the diagnosis of thyrotoxicosis first became evident when the drug treatment was interrupted because of a suspicion of an uncommon side effect of beta-blockade.

All the patients showed unequivocal biochemical hyperthyroidism, with serum total thyroxine concentrations of 296-323 nmol/l (23-25 mg/100 ml); the normal range is 60-160 nmol/l (4.7-12.4 mg/100 ml). The myopathy was corrected after the treatment of thyrotoxicosis in each patient despite continued treatment with the beta-blocking agents.

Electromyographic abnormalities of some degree have been found in 90% of thyrotoxic patients, but clinically evident myopathy is infrequent. Beta-blocking agents may improve the muscle power in thyrotoxic myopathy,² and indeed in our patients the muscle power was rather good in relation to the severe degree of muscle atrophy. However, in the report of Dr Forfar and his colleagues the myopathy and myositis were ascribed to treatment with the beta-blocking agents. It remains an assumption that there might be some additive effects of thyrotoxicosis and beta-blockade on the myopathy in our patients.

Little attention has been paid to the development of thyrotoxicosis during beta-blockade.³ This coincidence is probably rather common, because both treatment with beta-blocking agents and thyrotoxicosis are common clinical conditions. Beta-blocking

agents mask many of the most typical clinical signs of thyrotoxicosis, such as tachycardia, tremor, and nervousness, without affecting the underlying metabolic disorder, except the deiodination of thyroxine to triiodo-thyronine.^{4,5} On the other hand, the development of thyrotoxic myopathy is not prevented by beta-blockade. Thus thyrotoxicosis presenting with atypical clinical symptoms and signs is probably the most common aetiological factor to be considered in proximal myopathy developing during beta-blockade.

MATTI UUSITUPA
ANTTI ARO
TIMO KORHONEN
EERO JUKKA

University Department of Medicine,
SF-70210 Kuopio 21,
Finland

¹ Ramsay ID. *Lancet* 1966;ii:931-4.

² Pimstone N, Marine N, Pimstone B. *Lancet* 1968; ii:1219-20.

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⁵ Anonymous. *Br Med J* 1977;ii:1039-40.

Combined antidepressant treatment

SIR,—Dr J P R Young and his colleagues (24 November, p 1315) are to be congratulated on having carried out the first controlled comparison of combined antidepressant therapy. Their results show clearly that trimipramine was superior to combined antidepressants and monoamine oxidase inhibitors alone.

The authors express surprise at these results because they do not accord with their clinical experience that combined antidepressant therapy is effective in depressive disorders. This might be because the patients in the study differed from those normally treated by combined antidepressant therapy in clinical practice in that they suffered from mild and moderate depression only. Combined antidepressant drugs are normally reserved for patients who have failed to respond to other forms of treatment. While this should not be regarded as a prerequisite for starting combined antidepressant therapy, such patients usually suffer few unwanted effects while on combined therapy because of tolerance to previous and often prolonged single-antidepressant medication. Marked unwanted effects during combined antidepressant therapy was noted in Dr Young's study and this is likely to hinder drug compliance and clinical response.

The tendency for unwanted effects to be experienced more with monoamine oxidase inhibitors and combined antidepressant therapy may have been responsible for the relatively low mean dosage of monoamine oxidase inhibitors taken in the study. There is now good evidence that clinical response to phenelzine is greater in a daily dose of 60-90 mg,¹⁻³ whereas the average dosage in Dr Young's study was 44-45 mg daily.

Although combined antidepressant therapy should not be used for mild and moderate depression as first-choice treatment this does not mean that it has no place in other depressive and associated disorders.

P J TYRER

Mapperley Hospital,
Nottingham NG3 6AA

¹ Ravaris CL. *Arch Gen Psychiatry* 1976;33:347-50.

² Quitkin F, Rifkin A, Klein DF. *Arch Gen Psychiatry* 1979;36:749-60.

³ Tyrer P, et al. *Br J Psychiatry* (in press).

Aggressive patients—what is the answer?

SIR,—I read Dr A Bailey's comments (8 December, p 1509) on Dr K Raghus's letter (3 November, p 1147) with respect to aggressive patients with increasing unease and incredulity.

If I have grasped the meaning of Dr Bailey's comments correctly, do I now have to make meaningful inquiries as to the psychological status of the person demanding a visit for another person, accepting that this is an "indication of the intermediary's agitation"—however rude, objectionable, or threatening that "agitated intermediary" may be?

Let me ask this. If you had a burst pipe, your house was rapidly filling with water, and in your "state of agitation" you asked your neighbour to send for the plumber, whereupon he rang the aforesaid person at, perhaps, 2 am with the request "Send the bloody plumber," would you really expect him to come?

JOHN P LEWIN

Cockerham, Lancaster LA2 0EP

Mebendazole and hydatid disease

SIR,—I have followed with great interest the recent reports of pyrexia following mebendazole therapy for hydatid disease. We have recently excised a 2-litre hydatid cyst of the liver in a young woman. Full-dose mebendazole therapy was started five days preoperatively and samples of venous blood and intact daughter cysts were collected at operation for mebendazole levels, which we have been unable to measure. In the postoperative period a swinging pyrexia developed, which we attributed to infection in the residual cavity. However, fluid from the closed suction drain was sterile on aerobic and anaerobic culture.

The hypothesis of Mr I M Lyon and Mr K W Reynolds (3 November, p 1111) that the pyrexia is due to drug-induced cyst necrosis is difficult to accept. There is no good evidence in man that mebendazole penetrates intact, established cysts in sufficient levels to produce destruction. Heath¹ had great difficulty in destroying experimental cysts in mice and Reisin's experiments² showing that mebendazole entered cysts by simple perfusion were conducted in vitro.

A full course of mebendazole costs the NHS £185. Unless the drug can be shown to penetrate cyst fluid in therapeutic doses sufficient to destroy viable daughter cysts its use in established hydatid disease must be open to question—especially as Benex³ showed that only a small amount of living germinal tissue is required to produce a new *Echinococcus granulosus* cyst.

D R OSBORNE

Academic Department of Surgery,
Royal Free Hospital
School of Medicine,
London NW3 2QG

¹ Heath DD, et al. *Parasitology* 1975;70:273.

² Reisin IL, et al. *Int J Parasitol* 1977;7:189.

³ Benex J, *Ann Parasitol (Paris)* 1968;43:573-82.

Snail-eating mummy?

SIR,—As a parasitologist I was most interested in the review "Buried treasure" by Dr John Cole (1 December, p 1412), which mentioned the finding of a calcified worm of *Dracunculus* (guinea-worm) in the abdominal wall of a mummy. However, without wishing to appear