

cellular cyclic adenosine monophosphate and protein kinase activation. The relationship of this to the symptoms in our patient is unknown, but our case does indicate the need for caution in administering beta-blockers to patients with skeletal muscle disease.

We thank Professor M F Oliver for permission to report this case and for advice in the preparation of the manuscript.

<sup>1</sup> Robinson, B F, *Side Effects of Drugs Annual*, ed M N G Dukas, 3rd edn. Amsterdam, Excerpta Medica, 1979.

<sup>2</sup> Satya-Murti, S, Heiman, S, and Martinez, L B, *New England Journal of Medicine*, 1977, **297**, 223.

<sup>3</sup> Blessing, W, and Walsh, J C, *Lancet*, 1977, **1**, 73.

<sup>4</sup> Barrett, A M, *Recent Advances in Cardiology*, ed J Hamer. Edinburgh, Churchill Livingstone, 1973.

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## Effect of sustained-release lithium tablets on renal function

The ability of the kidney to concentrate urine may be impaired in patients treated with lithium; this impairment may persist after stopping the drug in some patients who have had long-term treatment.<sup>1,2</sup> Disagreement exists as to the severity of the effects of lithium treatment. Donker *et al*<sup>3</sup> and Hullin *et al*<sup>4</sup> found less effect than in previous studies<sup>1,2</sup>; this may have been because they used smaller doses of lithium. Bucht *et al*<sup>2</sup> found greater impairment in patients whose plasma lithium concentrations were slightly above the recommended therapeutic range than in those whose plasma concentration was within it. This suggests that the therapeutic range of plasma concentrations must be narrow. We therefore hypothesised that it might make a considerable difference whether readily soluble lithium carbonate tablets or sustained-release tablets were prescribed: more stable plasma concentrations and less pronounced peaks might reduce the toxic effect. We have tested this hypothesis and describe our results.

### Patients, methods, and results

We used 28 pairs of patients who were being treated long-term with lithium (median duration of treatment 63.5 months) and in whom plasma lithium concentrations had always been within the therapeutic range. The patients were paired for age, sex, and total intake of lithium. One patient in

each pair had been treated with lithium carbonate tablets and the other with sustained-release tablets (Lithionit<sup>®</sup> or Litarex<sup>®</sup>). We measured the urine concentrations in each patient after 24 hours without drinking. The patients were given an intramuscular injection of antidiuretic hormone (vasopressin tannas 5 IE) at the beginning of the 24 hours, and during the test lithium treatment was suspended for 48 hours. The mean maximum urine concentration in patients taking sustained-release tablets was 846 mosm/kg; significantly higher ( $P < 0.03$ ) than the 747 mosm/kg of the patients taking lithium carbonate tablets (table).

*Comparison of mean maximum urine concentration after 24 hours without drinking in patients taking lithium carbonate tablets and patients taking sustained-release lithium tablets*

	Sustained-release tablets (n = 28)	Lithium carbonate tablets (n = 28)
Mean age (years)	46.1	46.6
Mean total lithium intake (mols)	64.3	64.7
Mean maximum urine concentration (mosmol/kg)	846	747

Wilcoxon's matched pairs test;  $Z = 2.16$ ;  $P < 0.03$ .

### Comment

This comparison showed that during long-term treatment sustained-release lithium tablets produce less impairment of the ability of the kidney to concentrate urine than do lithium carbonate tablets. The sustained-release tablets used in this study are completely absorbed, and give more stable plasma concentrations and fewer concentration peaks than lithium carbonate tablets.<sup>5</sup> We believe that this is why they produce less impairment of the ability of the kidney to concentrate urine.

We believe that lithium treatment is an irreplaceable prophylactic measure for patients with periodic affective disorders. The therapeutic range of plasma concentrations does, however, seem to be narrower than was previously thought, and therefore close attention should be paid to keeping the plasma concentration as low as is compatible with a prophylactic effect. We suggest that, when selecting the type of tablet, preference should be given to the sustained-release form.

<sup>1</sup> Bucht, G, and Wahlin, A, *Lancet*, 1978, **1**, 778.

<sup>2</sup> Bucht, G, and Wahlin, A, *Nordisk Psykiatrisk Tidsskrift*, 1978, **32**, 445.

<sup>3</sup> Donker, A J M, *et al*, *Clinical Nephrology*, in press.

<sup>4</sup> Hullin, R P, *et al*, *British Medical Journal*, 1979, **1**, 1457.

<sup>5</sup> Amdisen, A, in *Lithium Research and Therapy*, ed F N Johnson, p 197. London, Academic Press, 1975.

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## Vancouver style

All manuscripts submitted to the *BMJ* from now on should conform to the uniform requirements for manuscripts submitted to biomedical journals (known as the Vancouver style).

The *BMJ*, together with many other international biomedical journals, has agreed to accept articles prepared in accordance with the Vancouver style and will be introducing the system from January 1980. The style (described in full in *BMJ*, 24 February, p 532) is intended to standardise requirements for authors and covers text format, presentation of methods and results, use of SI units, and the form of tables and illustrations. All the participating journals have also agreed to introduce a standard form of references.

In future references to papers submitted to the *BMJ* should include: the names of all authors if there are fewer than seven or, if there are more, the first three followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated

according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter.

Examples of common forms of references are:

<sup>1</sup> International Steering Committee of Medical Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1979;**1**:532-5.

<sup>2</sup> Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;**294**:687-90.

<sup>3</sup> Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology: mechanisms of disease*. Philadelphia: W B Saunders, 1974:457-72.

Up to the beginning of October some 100 journals had agreed to accept articles in the Vancouver style, and a full list will be printed early in 1980.