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Response

To the Editor:

Cook and Leventhal have correctly pointed out that decreased caloric intake is an important cause of the euthyroid sick syndrome. We agree that decreased caloric intake may account for the findings of decreased free and total T3 in depressed patients as compared with euthymic patients and normal controls. They have also provided a very comprehensive review of the effects of altered nutritional status on thyroid function tests.

Although we would also agree that the study of metabolic and nutritional state is important in determining the potential importance of altered thyroid function tests in depressed patients, we would be cautious about their statement that "successful treatment of depression with T3 may represent the first evidence of the potential efficacy of T3 administration in the low T3 syndrome." In fact, studies of T3 potentiation of tricyclic antidepressants have largely not addressed the relationship between baseline thyroid function tests and antidepressant response to T3 potentiation (Joffe and Post 1985). Goodwin and colleagues (1982) did, however, mention that patients had no evidence of thyroid dysfunction in their study of thyroid potentiation of a variety of tricyclic antidepressants, and Schwarcz et al. (1984) found no abnormalities of thyroid function tests, particularly T3 in three desipramine nonresponders who were converted to responders by the addition of T3. Clearly, further systematic studies are required to elucidate the relationship between baseline thyroid function tests and subsequent response to T3 potentiation of tricyclic antidepressants.

Russell T. Joffe
David W. Blank
Robert M. Post
Thomas W. Uhde
National Institute of Mental Health
Intramural Research Program
Bethesda, MD 20205

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Effect of Lithium on RBC Water Permeability

To the Editor:

The concentration of choline in the red blood cell (RBC) increases in lithium-treated patients at the same time that the choline carrier system appears to be inhibited (see Domino et al. 1981). Water permeates the RBC membrane primarily via hydrophilic protein channels, which also provide an important route for the passive flux of monovalent cations (Vieira et al. 1970). Hence, alterations in intracellular steady-state levels of choline may correlate with changes in the hydrophilic protein channels, therefore affecting water permeability. Our experiment measured RBC water permeability in lithium-treated patients and normal volunteers.

The mean lifetime of a water molecule in an av-

erage RBC (τ) was determined using a modification of the ^{1}H-NMR method of Conlon and Outhred (1982). Adding Mn^{2+} to whole blood diluted 1:4 with 0.9% NaCl shortens the plasma spin–spin relaxation time. This allows the water external to the RBCs to be "pulsed-away," using a Standard Carr-Purcell-Meiboom-Gil (CPMG) pulse sequence on a JEOL-FX90Q NMR spectrometer. The CPMG conditions were an 18.5-μsec pulse to induce a 90° spin flip, a 39.0-μsec pulse for a 180° spin flip, and an interpulse interval of 30 msec. The second half of the spin echo was Fourier transformed after an 8-Hz exponential apodization. The internal water peak line width ($\nu_{1/2}$) is related to τ by $\tau = \pi/\nu_{1/2}$.

Titrating blood samples with Mn^{2+} from 2.5 to 30 mM showed that the internal peak width depended linearly on Mn^{2+} concentration. Each blood sample was titrated with Mn^{2+}, and the titration curve extrapolated to 0 to determine $\tau_{1/2}$ without Mn^{2+}.

This method was applied to blood from eight lithium carbonate-treated patients and four normal volunteers. The lithium-treated patients had a mean water lifetime of 8.4 ± 1.2 msec, whereas the normal volunteers had a mean water lifetime of 8.1 ± 0.6 msec. The treated versus normal groups did not differ significantly by the Student's *t*-test. The two groups compare with the mean water lifetime of approximately 8 msec, reported by Solomon (Vieira et al. 1970).

No differences in water permeability were observed between lithium-treated patients and normal volunteers, suggesting that the choline accumulation is not due to modification of the membrane protein channels responsible for passive efflux of water. In fact, lithium may alter the properties of a specific RBC membrane choline carrier, or it may affect endogenous choline metabolism.

This investigation may be limited by the small sample size of the two groups studied, making the results vulnerable to type II statistical error. It would also be interesting to compare the same patients before and during lithium treatment.

Christian L. Ballast
Robert R. Sharp
Edward F. Domino

Departments of Pharmacology and Chemistry
University of Michigan
Ann Arbor, MI 48109-0010

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DST, Depression, and Anxiety

To the Editor:

In *What Does the Dexamethasone Suppression Test Identify?*, Ranga Rama Krishnan et al. (1985) claim to have shown that depression and its profile were more efficient discriminators of suppressors and nonsuppressors than anxiety. There was, however, a bias in their study against the identification of anxiety as the main determinant of DST nonsuppression by their incorrect use of the Hamilton Anxiety Scale in this context. This latter scale was designed for the rating of anxiety as part of an anxiety neurosis, rather than for the rating of anxiety symptoms occurring in the context of other psychiatric disorders. It would have been more appropriate to have used one of the many anxiety schedules that measure state anxiety independently of diagnosis.

D. Roger Thomas

Department of Psychological Medicine
University of Wales College of Medicine
Whitchurch Hospital
Whitchurch, Cardiff, CF4 7XB Wales

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