

Patient No.	Levothyroxine Dose, µg*	TSH Level Before Calcium, mU/L	Simultaneous Administration of Levothyroxine and Calcium		Separate Administration of Levothyroxine* and Calcium†	
			Calcium, mg	TSH, mU/L	Calcium, mg	TSH, mU/L‡
1	125	0.08	1200§	13.3	None	0.68
2	325	0.03	1000	7.31	100	0.13
3	175	0.04¶	1000	8.4	1000	0.02

*Taken while fasting in morning.

†Calcium given in 2 doses after lunch and dinner.

‡TSH measured 3 weeks after medication change for patient 1, 8 weeks later for patient 2, and 10 weeks later for patient 3.

§Tums.

||Os-Cal.

¶Patient 3 took Giant calcium carbonate with levothyroxine before changing to Os-Cal.

Calcium Carbonate and Reduction of Levothyroxine Efficacy

To the Editor.—I would like to report an interaction between 2 commonly prescribed drugs, levothyroxine sodium and calcium carbonate, which reduces levothyroxine efficacy. This inhibition may be reversed by separating the administration of these 2 medications.

In a recent evaluation of 3 women with thyroid cancer who were receiving levothyroxine to suppress serum thyroid-stimulating hormone (TSH) levels, it was noted that simultaneous ingestion of some calcium formulations reduced levothyroxine effectiveness (Table). For example, patient 1 took levothyroxine (125 µg/d) and had a baseline serum TSH concentration of 0.08 mU/L (normal, 0.5-4.0 mU/L). She subsequently began to take calcium carbonate (in the form of Tums) for prevention of osteoporosis, often taking it together with levothyroxine. She experienced fatigue and a 4.5-kg weight gain over the next 5 months, and her serum TSH level was found to have risen to 13.3 mU/L. She then stopped taking calcium carbonate but maintained her levothyroxine regimen. Three weeks later her serum TSH level had declined to 0.68 mU/L.

In patients 2 and 3 (Table), there was also loss of efficacy of levothyroxine when it was taken simultaneously with oyster shell calcium carbonate (in the form of Os-Cal). In both patients, levothyroxine activity was restored by administering it in the morning and administering calcium carbonate after lunch and dinner. Interestingly, patient 3 previously took a different form of calcium carbonate (Giant brand) with levothyroxine without affecting TSH suppression.

Decreased bioavailability induced by simultaneous intake of other medications (eg, aluminum-containing antacids, iron, cholestyramine, sucralfate) is a well-known occurrence with levothyroxine therapy.¹ Decreased absorption could similarly account for the calcium carbonate effect. Calcium carbonate itself or, alternatively, excipients or contaminants in the preparation² could form insoluble chelates with levothyroxine.³ Differences in excipients or contaminants or variations in rates of dissolution² could explain the discrepant effects of the 2 calcium carbonate preparations used by patient 3.

Given that both calcium and levothyroxine are used together in a large number of patients, this phenomenon is likely

to be widespread. Special attention should be directed toward postmenopausal women, as these individuals most frequently use calcium supplements to prevent osteoporosis and, in addition, often require therapy with levothyroxine.⁴ Separating administration of these medications by at least 4 hours should provide a simple method for maintaining levothyroxine efficacy.

Christine R. Schneyer, MD
Sinai Hospital of Baltimore
The Johns Hopkins School of Medicine
Baltimore, Md

I thank Prina Schwartz, RN, for assistance in evaluating these patients; Ralph Shangraw, PhD, Stephen Sherman, MD, and Paul Englund, PhD, for valuable discussions; and David Cooper, MD, for much advice and encouragement.

1. Sherman SI, Malecha SE. Absorption and malabsorption of levothyroxine sodium. *Am J Ther.* 1995;2:814-818.

2. Levenson DI, Bockman RS. A review of calcium preparations. *Nutr Rev.* 1994;52:221-232.

3. Kendall EC, Osterberg AE. The chemical identification of thyroxine. *J Biol Chem.* 1919;40:265-334.

4. Kaufman SC, Gross TP, Kennedy DL. Thyroid hormone use: trends in the United States from 1960 through 1988. *Thyroid.* 1991;1:285-291.

CORRECTIONS

Incorrect Statement.—In an Editor's Note (for the Original Contribution entitled "Trends in Drug-Resistant Tuberculosis in the United States, 1993-1996"), published in the September 10, 1997, issue of THE JOURNAL (1997;278:798n), an incorrect statement was made. The fourth sentence of the Editor's Note should read: "Even physicians outside the epicenters of the epidemic are urged to use 4 first-line drugs for initial treatment regimens until susceptibilities become available, because of the resistant organisms in nearly every state."

Incorrect Statement.—In the Medical News & Perspectives article entitled "Health Care Leaders Form Drug Policy Group," published in the August 6, 1997, issue of THE JOURNAL (1997;278:378), an incorrect statement appeared in the eighth line of the second paragraph. The meeting was held at the New York Academy of Medicine (not the New York Academy of Sciences).