In recent years, patients receiving thyroid hormone have been told by pharmacists that the medication should be taken on an empty stomach. This advisory is found in a number of sources that pharmacists use for administration details. For example, Micromedex Drug information for levothyroxine reads:

Administer tablets and capsules with water on an empty stomach, preferably one-half hour to an hour before breakfast. Administer four hours apart from antacids, iron, and calcium supplements (Prod Info Tiro-sint oral capsules, 2006; Prod Info Synthroid oral tablets, 2005; Prod Info Levoxyl oral tablets, 2004). Levothyroxine tablets may be crushed and suspended in 5 to 10 milliliters of water prior to administration. The suspension should be given immediately by a spoon or dropper. The crushed tablet may also be sprinkled over a small amount of food (applesauce or cooked cereal). Foods containing large amounts of soybean, fiber, or iron should not be used for administering levothyroxine (Prod Info Synthroid oral tablets, 2005).

Similarly, the Product information for Synthroid brand of levothyroxine reads: “Synthroid is administered as a single-daily dose, preferably one-half to one hour before breakfast.”

Specifically, the Product Information indicates:

Consumption of certain foods may affect levothyroxine absorption thereby necessitating adjustments in dosage. Soybean flour (infant formula), cotton seed meal, walnuts, and dietary fiber may bind and decrease the absorption of levothyroxine from the GI tract.

Foods that decrease absorption of levothyroxine, such as soybean infant formula, should not be used for administering levothyroxine tablets.

Tracking down the source of these recommendations turns out to be surprisingly difficult. The only study that specifically addresses the absorption of levothyroxine relative to food intake used double isotope methodology and reported that absorption of a 100-μg dose of levothyroxine was reduced from 79.3% ± 7.2% in the fasted state, compared with 63.9% ± 10.5% with simultaneous food intake. No subsequent studies examining this question have been reported. There are a number of reports addressing the effect of soybean flour on levothyroxine absorption. However, these reports represent a total of 12 cases and are all retrospective. A single report addresses the effects of dietary fiber on levothyroxine absorption, and this report consisted of 3 adult patients receiving dietary fiber supplement capsules who had changes in levothyroxine requirement when they were and were not taking the capsules. No articles could be found supporting an effect of either walnuts or cotton seed on levothyroxine absorption.

Recent articles reviewing levothyroxine therapy either do not refer to effects of stomach contents on levothyroxine absorption or refer to the limited case reports discussed above.

Therefore, although information available to pharmacists and in the Product Information supplied by the manufacturers indicates that levothyroxine should be taken on an empty stomach, the evidence supporting this recommendation is limited, even for soy. Conversely, particularly in the infant, the therapeutic window for levothyroxine is sufficiently narrow that possible effects of food in general, or specific components of meals on levothyroxine absorption could be potentially important. Therefore it is understandable that the manufacturers and pharmacists choose to err on the side of caution in providing recommendations for dosing.

However, pediatric endocrinologists have expressed concerns that this recommendation has potentially deleterious effects on adherence, particularly in smaller children and infants. Although there are no studies addressing the effect of the recommendation that levothyroxine be taken on an empty stomach on patient adherence, anecdotal evidence from a number of pediatric endocrinologists indicate that patients find this advice burdensome. In infants, expecting a family to wait 30 to 60 minutes before feeding the infant on awakening hungry is potentially harsh. In the older child and adolescent, recommending that the levothyroxine will be taken 30 to 60 minutes before eating raises substantial risk that the dose will be missed in the rush to head out to school in the morning or to prepare dinner in the evening.

The American Thyroid Association, in their consensus guidelines for the treatment of hypothyroidism, do not recommend that levothyroxine be taken on an empty stomach. Rather, the guidelines indicate that absorption of levothyroxine may be influenced by the presence of food and recommend that levothyroxine be taken consistently in both time of day and presence or absence of food. Dosage should then be adjusted on the basis of routine measurement of thyroid stimulating hormone to determine appropriate dosing in this setting. Avoidance of soy and calcium is also recommended. Similarly, the American Academy of Pediatrics...
and American Thyroid Association joint statement on the management of congenital hypothyroidism states only that concomitant ingestion of soy, calcium, and iron should be avoided.13

On the basis of the above review, the Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society recommends that even though the absorption of levothyroxine on an empty stomach may be better than the absorption with or after meals, the more important aspect in the treatment of hypothyroidism is consistency in medication administration and regularity in the performance of thyroid function tests, followed by appropriate dose adjustment. A limited number of reports indicate that soy formula may impair levothyroxine administration. Consequently, clinicians should remain cognizant of feeding practices in infants and frequent thyroid function testing may be required, particularly when there are changes in formula.

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