

What caused this case of asymptomatic hyperthyroidism?

Everything pointed to an exogenous cause, but our patient denied taking anything. Only later did she mention a diet aid.

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Practice recommendations

- When taking a medication history, always ask specifically about the use of all nonprescription products—including all over-the-counter remedies, vitamins, “natural” herbal supplements, and dietary aids (C).
- Counsel patients about the need for caution when taking dietary supplements and herbal remedies, which lack regulation and standardization and may contain ingredients not listed on the label (A).

Strength of recommendation (SOR)

- A Good-quality patient-oriented evidence
- B Inconsistent or limited-quality patient-oriented evidence
- C Consensus, usual practice, opinion, disease-oriented evidence, case series

When Mary J,* an overweight 47-year-old Caucasian woman, came in for an annual physical examination, she appeared to be in good health. She denied any recent illness, and reported that an oral contraceptive was the only medication she was taking. The patient’s only complaint: She was having difficulty losing weight despite complying with a low-calorie diet and exercise regimen for the last 6 months. Her comments prompted her physician (CC) to order a thyroid-

stimulating hormone (TSH) test to rule out hypothyroidism.

The test showed a TSH of 0.2 mIU/L (normal range is 0.35-5.0 mIU/L). Her physician ordered retesting a week later and this time, Mary’s TSH was normal (1.99 mIU/L). The laboratory report also showed elevated free triiodothyronine (T₃) of 8.1 pmol/L (normal range 2.6-5.7 pmol/L) and free thyroxine (T₄) >70 pmol/L (normal, 10-20 pmol/L); negative antithyroid peroxidase and antithyroglobulin antibodies; normal complete blood count, calcium, and alkaline phosphatase; and low levels of thyroglobulin. The patient had no symptoms and no personal or family history of thyroid disease. She also denied taking thyroid medications.

In search of an explanation

On examination, her physician found no significant thyroid enlargement or tenderness. However, the patient’s thyroid was somewhat boggy on palpation. There was no exophthalmos or pretibial myxedema. Mary’s blood pressure was 144/98 mm Hg (with no prior history of hypertension), her heart rate was 84, and she was afebrile. Her physician

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Our patient hadn’t mentioned the European dietary supplement she was taking to increase her metabolism because she assumed it was safe.

* The patient’s name has been changed to protect her privacy.

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Chromium is a popular weight-loss supplement whose efficacy and long-term safety are uncertain.

found no obvious tremors, hyperdynamic apex, or hyperreflexia on physical exam.

To rule out laboratory error from the second set of tests, her physician ordered yet another round of blood work. A diagnosis of hyperthyroidism was confirmed by elevated T_4 (>70 pmol/L) and T_3 (6.2 pmol/L). As in the previous test, the patient's TSH was in the normal range (1.54 mIU/L).

Detailed questioning solves the mystery

At follow-up, the patient was again asked about exogenous thyroid intake, which she had initially denied. After further questioning about what she was ingesting, Mary acknowledged that she had been taking *Pu Erb*—a European dietary supplement marketed as a means of increasing metabolism to help with weight loss—3 times daily for more than 3 months. She hadn't mentioned it before because it hadn't occurred to her to question its safety.

Her physician advised her to discontinue the supplement immediately, and to have her blood work retested in a month. Within 5 weeks, all her lab values returned to normal. (For more on lab values, see "Investigating thyroid dysfunction: What to test for" on page 205.)

Natural does not = safe

With an ever-increasing overweight population, there is growing concern about the misuse of diet aids. It is important for patients to be cautious when using dietary supplements because of the lack of regulation and standardization. Yet such products are often marketed as "natural," which may be interpreted as an assurance of safety.¹ Family physicians can play a crucial role in primary prevention by inquiring about the use of over-the-counter substances including "natural" herbal supplements and dietary aids, advising patients of the

risks associated with their use, and being alert to potentially dangerous side effects.

Thyrotoxicosis factitia: An exogenous cause

Thyroid hyperactivity can occur when excessive quantities of thyroid hormone are ingested. The excessive intake may be associated with treatment for hypothyroidism, or, as in Mary's case, may be linked to overuse (or abuse) of a diet aid in an attempt to lose weight.² Often, the condition can be traced to an iodine-containing substance such as kelp—a widely used dietary aid that we'll discuss in greater detail in a bit.

Iodide is an inorganic salt that is absorbed through the gastrointestinal mucosa and transported to the thyroid gland, where it is trapped and concentrated for thyroid hormone synthesis.³ Consuming large quantities of foods or other products that contain iodine—such as iodized salt, shellfish, cough syrups, multivitamins, or medications such as amiodarone and interferon alpha, as well as kelp—can cause hyperthyroidism.

What's in that weight-loss aid?

Pu Erb, the dietary supplement Mary was taking, was not available for analysis; it was purchased in Poland and the patient had exhausted her supply by the time her physician told her to stop taking it. Each capsule contains 400 mg of red tea extract with 15 mcg chromium, according to the label.

Red tea and chromium. There are no reports associating red tea with thyroid dysfunction, but chromium is a popular weight-loss supplement whose efficacy and long-term safety are uncertain.⁴ It is unlikely that Mary's hyperthyroidism was associated with chromium intake, however, as multivitamins often contain 100 mcg of chromium—nearly 7 times the quantity in each *Pu Erb* capsule—with no reported thyroid side effects.

Did the supplement contain a thyroid extract? It's possible, of course, that the supplement contained a thyroid extract, which would explain the resolution of symptoms after Mary stopped taking it. But without analysis of the product, we can't be sure. Our suspicion, of course, is that it did.

Another possible, but unlikely, explanation. Theoretically, the fluctuating TSH could have been related to silent or subacute thyroiditis, in which T_4 can remain elevated for 1 to 3 months. The fact that Mary had no history of cold or flu symptoms in the month preceding the initial TSH was inconsistent with this alternative diagnosis, however. Painless thyroiditis is also unlikely, as it is autoimmune in origin and the patient's antithyroid antibodies were negative. The low thyroglobulin level supported an exogenous cause of hyperthyroidism.

■ Other supplements and thyroid dysfunction

Mary's presentation is a single case indicating a possible link between a weight-loss supplement and asymptomatic hyperthyroidism—a clinically important condition that may be associated with disorders such as paroxysmal atrial fibrillation and osteoporosis. This is only one of a number of case reports of patients taking dietary supplements who have developed thyroid dysfunction.

Kelp. Long used as a dietary supplement, especially in Asia, kelp has been linked to thyroid dysfunction. One case report describes a 72-year-old woman with a history of thyroid disease having typical symptoms of hyperthyroidism while ingesting 4 to 6 kelp tablets daily for 1 year. Her TSH concentration was low, while total T_3 and T_4 levels were high. After discontinuing the kelp tablets, the hyperthyroidism resolved, and thyroid function tests returned to normal.⁵ Another report describes an

TABLE

Investigating thyroid dysfunction: What to test for

The single most useful screening test for thyroid dysfunction is serum TSH. Normal TSH levels effectively rule out hyperthyroidism and hypothyroidism, and obtaining serum T_3 and T_4 levels is usually not indicated.⁸ Circulating levels of free T_3 or T_4 are increased in hyperthyroidism and thyrotoxicosis, while TSH levels are low to immeasurable (<0.01 mU/L).⁹

The term "thyrotoxicosis" is used to denote the excess of thyroid hormone levels without thyroid hyperfunction or increased biosynthesis—ie, excess intake, excess release without synthesis, or syndromes of pituitary resistance to thyroid hormones.¹⁰ Low thyroglobulin in association with hyperthyroidism is a hallmark of exogenous thyroid intake, also known as thyrotoxicosis factitia.¹¹

instance of probable transient hyperthyroidism in a patient taking kelp in 2 different diet supplements.⁶

Tiratricol (Triac), a substance that has weak thyromimetic effects, resulted in a case of documented hyperthyroidism secondary to its use.¹

Other reports. In Japan, the weight-reducing herbal medicines, *Dream Shape* and *Ever Youth*, became available in 2000. Twelve patients subsequently developed thyrotoxicosis after taking these herbal medicines, both of which were found to contain triiodothyronine and thyroxine.⁷

As early as 1986, researchers have described several patients who developed thyrotoxicosis from *Enzo-Caps*, a nonprescription diet aid manufactured in Peru. The product was touted as "a natural food product of papaya, garlic, and kelp" to assist with weight reduction. Researchers obtained the supplement for biochemical analysis and found that it had been adulterated with thyroid hormones, which led to thyrotoxicosis factitia.²

Patients in the report complained of palpitations, weakness, fatigue,

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headache, diaphoresis, irritability, and nervousness, and had elevated serum T₃ and T₄ levels. Thyroglobulin levels were not determined, but would have been useful in differentiating thyrotoxicosis factitia from hyperthyroxinemia (Graves' disease, thyroiditis, nodular goiter).²

These reports, as well as our own experience, leave little doubt as to the importance of asking pointed questions about all prescription and nonprescription products a patient is taking. As we can attest, a little persistence goes a long way when it comes to identifying that agent your patient didn't think was worth mentioning. ■

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Disclosure

The authors reported no potential conflict of interest relevant to this article.

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