

# Hyperthyroidism In Adults: Variable Clinical Presentations And Approaches To Diagnosis

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**Background:** Hyperthyroidism is a disease that has various symptoms and can present in many ways. In the elderly patient hyperthyroidism often is not expressed in the classical manner. A case report of a middle-aged man who had hyperthyroidism with only one symptom is detailed.

**Methods:** A literature review utilizing MEDLINE files from 1988 to the present, as well as current textbooks of medicine and endocrinology, was used to prepare this report. Keywords for the search were "hyperthyroidism," "symptoms," "unintentional weight loss," and "differential diagnosis."

**Results and Conclusions:** The clinical presentation of hyperthyroidism can vary from almost asymptomatic to apathetic in appearance to a marked hyperdynamic physiologic response. Family physicians must be well informed of this variation in disease expression. Overlooking the diagnosis of this relatively easily treated condition can be detrimental to patient care and expensive. (J Am Board Fam Pract 1995; 8:109-13.)

Thyroid dysfunction is important to understand because it occurs often. The incidence of hypothyroidism when looked for in large elderly populations varies up to 17 percent. Women are affected more often than men, and subclinical disease is very common. Hyperthyroidism is also common but much less so than hypothyroidism, occurring in up to 3 percent of large elderly populations.<sup>1</sup> Most patients who have hyperthyroidism are white and female. Iatrogenic overuse of synthetic thyroid replacement was found in one study to be very common (making the percentage of true hyperthyroidism even lower).<sup>2</sup> A study of an African population in South Africa who had hyperthyroidism showed an annual incidence of 875 cases per 100,000 population for women and 70 per 100,000 for men.<sup>3</sup> Most studies also note that atypical symptoms and signs and presentations, such as apathetic hyperthyroidism, are not rare and could delay the diagnosis.<sup>4</sup>

The classic symptoms of hyperthyroidism reflect the ability of thyroxine to drive cell functions in all tissues. Some tissues are more strongly influenced by thyroxine than others, which accounts for the predominance of certain symptoms.

Common symptoms occurring in more than 50 percent of cases include nervousness, increased

amounts of sweating, heat intolerance, palpitations, dyspnea, fatigue, weight loss, and various eye complaints. Common signs of hyperthyroidism include thyroid gland enlargement and a thyroid bruit, exophthalmos, lid lag, tremor, tachycardia, hyperkinetic muscular activity, and warm moist hands. Less common signs and symptoms include hyperphagia, increased quantity of stools, eyelid retraction, and arrhythmias, such as atrial fibrillation. More unusual signs of hyperthyroidism include periartthritis, severe peripheral edema, heart failure, osteoporosis, proximal myopathy, encephalopathy, seizures, and abdominal pain with or without changes in bowel motility.

In an elderly population only a small percentage of persons with hyperthyroidism will exhibit the classical features. The common complaints in this age group more likely will mimic those associated with cardiac, neuromuscular, gastrointestinal, and neuropsychiatric diseases, making the diagnosis of thyroid dysfunction very difficult. The presence or absence of various signs and symptoms either greatly increases or greatly diminishes the physician's suspicions of hyperthyroidism. Various textbooks of internal medicine give concise descriptions of the clinical picture. One text assigns various diagnostic weights to certain symptoms and signs as an aid to making the diagnosis. For example, heat intolerance is given greater weight than nervousness to predict hyperthyroidism positively. Heat intolerance is also given greater negative weight than moist hands to rule out hyperthyroidism if that symptom is not present.<sup>5</sup>

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In 1931 Lahey<sup>6</sup> described a form of hyperthyroidism in which the patients appeared apathetic to their surroundings. These people were withdrawn and listless and had immobile facies and dulled eyes. They seemed to exhibit few, if any, signs of classic hyperkinetic hyperthyroidism. Their condition was more like that of patients with hypothyroidism. These patients were given the diagnosis of apathetic hyperthyroidism. Masked hyperthyroidism is the diagnostic descriptor of a patient in whom the classic signs and symptoms of hyperthyroidism are overshadowed by those classically due to other problems, such as cardiac or gastrointestinal diseases.<sup>7</sup> Monosymptomatic hyperthyroidism is the descriptor used when all symptoms of hyperthyroidism are referred to one organ system. In masked and monosymptomatic varieties it is possible that the symptoms and signs of hyperthyroidism are too subtle to be recognized. Estimates of the frequency of apathetic or masked or monosymptomatic varieties of hyperthyroidism are about 5 percent or less of cases. Some review articles even fail to mention the existence of these entities.<sup>8</sup>

In this case report our patient was a middle-aged man who experienced his usual state of health except for a 30-pound unexplained weight loss. This unusual expression should reinforce that hyperthyroidism can be difficult for family physicians to diagnose clinically and that a high index of suspicion must be maintained to diagnose properly this easily treated problem.

### Case Report

A 57-year-old man, a long-time patient, came to the office for his annual examination in June 1989. He stated that he was feeling well but had lost 30 pounds without really trying. He attributed the weight loss to his not being able to chew very well with a new denture. He denied a history of any peptic acid symptoms but stated that his bowel movements, although normal in quantity, were slightly darker than normal. He denied any cardiovascular symptoms. His genitourinary symptoms were nocturia once a night and a decreased ability to maintain an erection. He did not appear depressed and denied any vegetative symptoms.

His medical history revealed that he had a hemorrhoidectomy, a pilonidal cystectomy, a tonsillectomy, and the repair of a rectal fistula. He

was not taking any medications regularly and was not allergic to any medications.

His parents were diabetic. A brother had died at the age of 51 years of coronary artery disease. At that time a brother had hypertension and two sisters had cancer (breast cancer and leukemia respectively).

He worked as a quality control manager for a local creamery for longer than 30 years. He had quit smoking 14 months before his examination (he had smoked more than 30 pack years). His alcohol usage was minimal, and his caffeine usage was five to six cups of coffee per day. He tried to follow a cholesterol-restricted diet but admitted he liked to have his dairy products. He did some regular exercise.

Findings from a physical examination showed his blood pressure to be 108/64 mmHg. His weight was 166 pounds (his weight had been 196 pounds 15 months earlier). Examination of his head did not reveal any exophthalmus or lid signs. His mouth and pharynx, including the area of his new upper plate, were normal. His neck showed no thyroid enlargement or tenderness. He had a heart rate of 75 beats per minute with a regular rhythm and no murmurs or extra sounds. Results of an abdominal examination were normal, and a genital-rectal examination showed only mild testicle atrophy. Stool for occult blood was negative. His extremities did not show evidence of edema, decreased muscular strength, or changes in his deep tendon reflexes.

Laboratory studies disclosed the following values: a hemoglobin of 14.2 g/dL (1 year earlier it had been 17 g/dL), a white cell count of 6,000  $\mu$ L with a normal differential, and normal findings on a urinalysis. Results of a multichannel profile were entirely normal except for a cholesterol level of 168 mg/dL (1 year earlier it had been 228 mg/dL) and a blood glucose of 133 mg/dL (1 year earlier it had been 119 mg/dL).

### Follow-up

One month later the patient had a repeat blood glucose measurement and fortuitously a thyroid profile. The thyroid profile showed a thyroxine ( $T_4$ ) level of 13.7  $\mu$ g/dL (normal, 4.7 to 12.0  $\mu$ g/dL), a resin triiodothyronine ( $RT_3$ ) uptake of 45 percent (normal, 28 to 40 percent), a free thyroxine index calculated at 6.2 ng/dL (normal, 1.3 to 4.8 ng/dL), and an ultrasensitive thyroid

stimulating hormone (TSH) level of less than  $0.03 \mu\text{U/mL}$  (normal,  $0.4$  to  $4.0 \mu\text{U/mL}$ ). A free  $T_3$  level was subsequently obtained and was  $6.4 \text{ pg/mL}$  (normal,  $1.4$  to  $4.4 \text{ pg/mL}$ ). These thyroid parameters were consistent with a diagnosis of hyperthyroidism or exogenous thyroid hormone administration.

A 24-hour thyroid uptake and scintiscan using  $300 \mu\text{Ci}$  of iodine 123 (Figure 1) showed a uniform distribution of activity with a 2-hour uptake of 10 percent and a 24-hour uptake of 41 percent (normal range, 15 to 35 percent). Based on these findings and a telephone consultation with an endocrinologist, the patient was treated with  $8.1 \text{ mCi}$  of iodine 131 on 16 August 1989.

Since treatment the patient's thyroid hormone levels gradually returned to normal and eventually subnormal, with the TSH rising to greater than  $10 \mu\text{U/mL}$ . At that point he was prescribed a synthetic thyroid hormone replacement. He gradually regained the previously lost weight. In 1993 he developed adult-onset diabetes mellitus, which he could control by diet alone.

### Differential Diagnosis

A middle-aged man thought that he was in his usual state of health, except that he had an unexplained 30-pound weight loss (14 percent of body weight). There were no other symptoms or signs that could be attributed to a hyperthyroid condition.

Diabetes mellitus was considered in the differential diagnosis because of his mildly elevated blood glucose level and his family history. Cancer

of the lung was also thought a possibility because of his long-term smoking history. Other cancers that can cause extreme inanition were also considered: gastric carcinoma, pancreatic carcinoma, and colon carcinoma. Acquired immunodeficiency syndrome (AIDS) and other chronic wasting infections were not considered, primarily because the incidence of AIDS in our state is so low, and nothing suggesting an infection was present. Depression was not considered because there was an absence of vegetative symptoms and the patient had an outgoing appearance. Systemic collagen vascular diseases were also not considered because he lacked other corroborating symptoms. Hyperthyroidism was not initially considered in his differential diagnosis because he lacked the classic symptoms.

### Pathogenesis

A complete description of thyroid hormone production and regulation is beyond the scope of this article. Greatly simplified, inorganic iodide is concentrated in the thyroid gland. Oxidization to organic iodide occurs, and immediately organic iodide is incorporated into tyrosine residuals within thyroglobulin. Linkages occur eventually to form tetraiodothyronine ( $T_4$ ) and triiodothyronine ( $T_3$ ), the principal thyroid hormones.

Stimulation by the anterior pituitary by TSH results in the release of  $T_4$  and  $T_3$  into the circulation. A negative feedback loop stimulates the release of TSH. TSH is also influenced by the hypothalamus by means of the thyrotropin-releasing hormone (TRH), which alters the set point for feedback regulation (amount of  $T_3$  and  $T_4$  needed to stimulate TSH). Iodine stores in the thyroid gland also influence the secretion of  $T_3$  and  $T_4$ .

Unregulated production of excessive amounts of  $T_3$  or  $T_4$ , excessive oral intake of thyroxine, or destruction of thyroid gland tissue can all cause excessive thyroxinemia, which produces the symptoms and signs of hyperthyroidism. An autoimmune process causing continuous long-term thyroid stimulation is responsible for the thyroxinemia in Graves disease.

Once released from the thyroid gland,  $T_4$  and  $T_3$  are bound to serum proteins in a reversible equilibrium. Free (unbound)  $T_3$  and  $T_4$  enter individual cells by a diffusion process. In the



**Figure 1.** The patient's 24-hour thyroid uptake and scan: 2-hour uptake = 10.0 percent, 24-hour uptake = 41.0 percent.



cytoplasm  $T_3$  and  $T_4$  are again bound to proteins or other cell organelles.  $T_3$  and  $T_4$  can enter the nucleus, again by a diffusion process. The receptors for  $T_3$  and  $T_4$  are nuclear nonhistone proteins. By binding to their receptors,  $T_3$  and  $T_4$  can regulate the production of various enzymes, hormones, and proteins, which is why thyroid hormones have such a wide range of systemic physiological effects. The amount of  $T_3$  and  $T_4$  receptors in an organ indicates how much control the thyroid will have over that organ's function.

## Discussion

Since Lahey's original description, other authors have provided evidence that extrathyroidal manifestations could be the primary symptom for patients with both Graves disease and apathetic hyperthyroidism. These manifestations can include but are not limited to cardiac arrhythmias, severe peripheral edema, congestive heart failure, weight loss, peri-arthritis, osteoporosis, myopathies, encephalopathy, and seizures.

Apathetic hyperthyroidism has also been reported by Coe, et al.<sup>9</sup> as manifesting as a surgical abdomen. In that case surgery was performed without resolution of the patient's symptoms until the patient's hyperthyroid state was recognized and treated. Until recently apathetic or masked hyperthyroidism was thought to be a diagnosis of elderly patients (older than 65 years of age). In 1991, however, Teelucksingh, et al.<sup>10</sup> described a case of apathetic thyrotoxicosis in a 16-year-old girl who complained of a variety of nonspecific symptoms and who also had marked weight loss.

Rabinovitz, et al.<sup>11</sup> retrospectively reviewed 154 cases of unintentional weight loss. Unintentional weight loss was the primary complaint or a secondary serious problem. Excluded were voluntary weight loss, recent diuretic use, established gastrointestinal diseases, established psychiatric diseases, and known malignancies. Unintentional weight loss was found to account for 2.8 percent of patients admitted to an internal medicine department during a 2-year period. Of these patients, 36.3 percent had a neoplasm, and only 3.8 percent had endocrine disorders, including diabetes mellitus and hyperthyroidism.

Serum cholesterol in the patient in this case report had decreased markedly from 288 mg/dL to 168 mg/dL, in spite of the patient's admitted pref-

erence for regular dairy foods (he worked in a creamery). This magnitude of decrease is usually not associated with dietary treatment alone and perhaps should have signaled that hyperthyroidism be considered as a diagnosis earlier in the evaluation.

This case is an excellent example of the difficulty that can be encountered in the diagnosis of hyperthyroidism. Physicians must ensure they are sufficiently knowledgeable about the various expressions of hyperthyroid states, because the symptoms and signs can be extremely variable, particularly in elderly patients.<sup>12</sup>

## Summary

In this case report a middle-aged man was found to have hyperthyroidism, with unintentional weight loss as his only symptom. The lack of other classic symptoms, the patient's sex (male), and his relatively young age made the diagnosis more difficult.

The work-up of a relatively healthy patient of any age complaining only of weight loss must include a thyroid hormone assessment even if no signs or symptoms are present to suggest hyperthyroidism. Although unintentional weight loss is more commonly caused by a malignancy than by hyperthyroidism, screening for hyperthyroidism should be done initially in the evaluation. If the thyroid screening is normal, the longer and more expensive work-up for malignancy must be started.

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