Thyroid Disease in the Elderly:

November 01, 2002

ABSTRACT: Age-related anatomic and physiologic alterations in the thyroid gland have a variety of clinically important effects. Hypothyroidism, which is common in older persons, raises cholesterol and triglyceride levels; hyperthyroidism may be masked by the severity of the cardiac problems it causes. In younger persons, depression may accompany hypothyroidism but not hyperthyroidism; however, in the elderly, it may be a feature of either condition. Papillary carcinoma-the most common type of thyroid cancer-is more aggressive in older persons. All these factors necessitate a cautious and deliberate approach to the management of thyroid disorders in elderly patients.

A variety of changes in thyroid function occur naturally as a person ages. Thyroid physiology and microscopic anatomy are altered, and the rate at which thyroid hormone is secreted and cleared is reduced. Some thyroid diseases (eg, hypothyroidism) are considerably more likely to develop in elderly persons than in younger ones, and the manifestations are often less typical. This can make it more difficult to diagnose thyroid disease in an older patient.\(^1\,\,2\)

As the number of elderly patients grows, it is crucial to understand the effects of an aging thyroid gland, which I will describe here. The relative frailty of older persons also mandates a more cautious and deliberate approach to management, as I will also discuss.

MICROSCOPIC CHANGES

The aging thyroid gland is characterized by several microscopic changes. Prominent among these is an increase in interfollicular connective tissue. The size of the follicles themselves decreases, however, as does their content of colloid (the matrix or form in which thyroid hormone is stored). Some areas become completely devoid of colloid, while follicles in other areas contain only very pale colloid, indicating reduced stores of hormone. At the same time, the glandular epithelium undergoes atrophy: the lining cells become flattened and reduced in size. The total weight of the thyroid gland may decrease as well, although the volume may increase slightly.

PHYSIOLOGIC CHANGES

Some reduction of thyroid function is suggested by a number of age-related physiologic changes. Basal oxygen consumption per unit of surface area declines, for example, just as it does in patients who have hypothyroidism. Increases occur in the levels of both total serum cholesterol and low-density lipoprotein cholesterol, which again parallel the effects of hypothyroidism. Thus, it is not surprising that at one time a number of researchers postulated that hypothyroidism might be a normal development of the human aging process, or even that a relative degree of hypothyroidism-in and of itself-might contribute to aging. Indeed, some early researchers reported that after desiccated thyroid hormone was administered to older patients, their basal metabolism rate (BMR) appeared to rise. It turns out, however, that the BMR does not decline with age if it is corrected for an age-associated decline in lean body mass.

The BMR, however, is a crude parameter, and researchers soon turned to radioactive iodine \(^{131}\)I and similar radioactive tracers to study age-related changes in thyroid function. Their investigations revealed the following effects of aging\(^3\):

- The thyroid's uptake of iodine (as \(^{131}\)I) declines somewhat.
- The half-life of thyroxine \((T_4)\) increases.
- The rate of \(T_4\) degradation declines.
- The thyroid gland reduces its secretion (output) of \(T_4\).

These researchers hypothesized that the reduced \(T_4\) distribution space (the fraction of body tissues penetrated by thyroid hormone) present in the aged may result from a reduction in overall "metabolic mass." Despite reduced \(T_4\) output, elderly persons remain euthyroid because this lower \(T_4\) level is matched by a reduction in \(T_4\) turnover and in the need for thyroid hormone.\(^3\)

The advent of radioimmunoassay gave rise to additional studies of thyroid hormone levels in elderly persons. The general consensus is that aging does not significantly alter either free \(T_4\) or total \(T_4\) levels in either direction. This concept is consistent with the finding that the reduced secretion of hormone from the gland is matched by the reduced rate of its clearance from the blood.
An age-related decrease in triiodothyronine (T₃) levels, however, has been suggested by some investigators. Theoretically, this could be a variant of the "low T₃ syndrome" seen during a variety of acute and chronic illnesses. (A patient with the low T₃ syndrome remains euthyroid despite having reduced plasma levels of T₃, which result from a decrease in the conversion of T₄ to T₃ in peripheral, extrathyroidal locations.) But most researchers now believe these low T₃ levels reflect a coexisting illness unrelated to the thyroid, rather than an effect of aging.

The levels of thyroid-stimulating hormone (TSH) do not change with normal aging, although the amplitude of nocturnal TSH secretion does decrease somewhat as the years pass. Elevated levels of TSH, however, are increasingly widespread among the elderly population, an observation believed to reflect a true increase in the prevalence of hypothyroidism with aging. Several studies confirm that population TSH levels rise with age, especially among women. Nevertheless, it appears that the elevated TSH concentration seen in some elderly persons is not a normal accompaniment of old age per se but rather a reflection of subclinical hypothyroidism, the incidence of which increases among the elderly.

All patients with elevated TSH levels—even those who have no symptoms—should be given replacement thyroid hormone. The TSH response to injected TSH-releasing hormone does not decline with age.

**THYROIDITIS AND ANTITHYROID ANTIBODIES**

Patches of thyroiditis are seen frequently when "normal" thyroid glands are examined at autopsy, as was first reported in 1913. These foci may be the precursors of a more diffuse, chronic form of thyroid inflammation called Hashimoto thyroiditis, which can eventually lead to hypothyroidism. Such localized patches of thyroiditis are both age- and gender-related: they are much more common among middle-aged and elderly women than among younger women or among men. Postmortem examination of the thyroid glands of women older than 60 years revealed thyroiditis in 45%; in autopsy studies of women younger than 40, 22% had thyroiditis. Similarly, among men older than 60 years, a rising incidence of thyroiditis is seen in autopsy specimens. At every age, however, the incidence of thyroiditis among men is lower than that among women.

The number of circulating antithyroid antibodies also increases with aging in women. In an English community survey, antithyroglobulin antibodies were found among 7.4% of women older than 74; the overall incidence for females of all ages is 3%. The incidence of antimicrosomal (antithyroid peroxidase, or anti-TPO) antibodies was 8.8% among women older than 75, compared with 7.6% among the overall female population.

**HYPOTHYROIDISM**

A number of large surveys reported a high incidence of hypothyroidism in elderly patients. Again, gender appears to be a factor: high TSH levels were found among more women than men older than 75 (17.4% of women older than 75, compared with 7.5% of women overall; 3.5% among men older than 75, compared with 2.8% of men overall).

The presence of circulating antithyroid antibodies also appears to be important: mean TSH concentrations were significantly higher among those persons who had such antibodies. This finding implies that antithyroid antibodies play a causative role in producing thyroiditis and ultimately hypothyroidism.

The clinical manifestations of hypothyroidism in elderly patients (Table) may differ greatly from those encountered in younger persons. In an older patient, the following clinical features should heighten your index of suspicion for hypothyroidism:

- Unexplained elevations in plasma cholesterol or triglyceride levels, which occur because of reduced uptake of lipids by tissues deficient in thyroid hormone.
- Congestive heart failure, especially if the patient shows evidence of restrictive cardiomyopathy.
- Fecal impaction, caused by retarded movement of stool through the bowel.
- Macrocytic anemia, which may result from the hypothyroidism itself or from associated pernicious anemia.
- Vague arthritic complaints, which may be the primary presenting symptoms of hypothyroidism among elderly patients.
- Mild psychiatric disturbances, especially depression.
- Psychiatric manifestations of hypothyroidism are common among the elderly. Although these changes in mentation are described classically as "myxedema madness," frank psychosis is actually a far less common presentation among elderly hypothyroid patients than is depression. Other age-related presenting symptoms of hypothyroidism include syncope, seizures, and impaired cerebellar function.

In addition, the history and physical examination of an older patient may point to other factors that
suggest hypothyroidism, such as the following:
Thyroidectomy scar.
Previous treatment with radioiodine.
Goiter.
Family history of thyroid disease.

Patients who have undergone surgical or radioiodine therapy for hyperthyroidism are especially vulnerable to hypothyroidism. One study found that more than 15% of all patients who had previously undergone thyroidectomy had stopped taking their thyroid hormone replacement medication—and 50% were taking inadequate doses.\(^{11}\)

Many elderly patients are required to take a number of drugs for various, often unrelated conditions. Either out of confusion or frustration, such patients may discontinue their replacement thyroid hormone. For these reasons, exercise considerable diligence in monitoring hypothyroid elderly patients and checking their compliance.

**THYROID HORMONE REPLACEMENT THERAPY**

The prevalence of coronary artery disease increases with age. Significant cardiac disease, therefore, is more likely in an older hypothyroid patient than in a younger one. This means that you must use great caution in treating elderly hypothyroid patients. Too vigorous a schedule for replacing thyroid hormone can precipitate angina pectoris, rhythm disturbances, or even a myocardial infarction.

For the older patient with nonemergent hypothyroidism, the most conservative approach is to begin by giving levothyroxine, 25 µg/d for 1 to 2 weeks, followed by 50 µg/d for another 1 to 2 weeks, and then by 100 µg/d. If the last dosage is tolerated, it becomes the long-term therapeutic dosage. Check thyroid function after 6 weeks on the 100 µg/d dosing schedule. The 6-week interval is necessary because thyroxine has a long half-life (6.6 days).

If the free \(T_4\) value is still not in the normal range, the daily dose of levothyroxine may be increased to 125 µg. The usual replacement dosage for younger adults is 100 to 150 µg/d, but elderly patients generally need less hormone. In one group of elderly hypothyroid patients, the average replacement dose was 118 µg/d (compared with 158 µg/d given to younger patients).\(^ {12}\)

Measurements of thyroid hormone levels 6 weeks after reaching the projected long-term replacement dosage is critical, because elderly patients seldom can tolerate iatrogenic hyperthyroidism for very long. At that time, make sure that the TSH level is in the normal range and not suppressed. This distinction is readily made with an immunoradiometric assay for TSH. Even if the free \(T_4\) level is within the normal range, a suppressed TSH implies chemical hyperthyroidism, a condition that should be avoided because of its probable effect on accelerating osteoporosis, particularly in elderly women.

Occasionally, when an elderly patient with severe coronary artery disease is given incremental doses of thyroid hormone, such severe angina results that only partial replacement is possible. Thus, the patient continues to have hypothyroidism, even though of modest degree. This is particularly unfortunate, because the increased cholesterol levels associated with hypothyroidism can lead to acceleration of coronary artery disease.

**HYPERTHYROIDISM**

In general, the signs and symptoms of hyperthyroidism or thyrotoxicosis, which often are striking in younger patients, are muted in the elderly. The hyperthyroid state, however, imposes such a burden on the heart that in an elderly patient, the most prominent symptoms may be those of congestive heart failure. This phenomenon was first described in 1924 by Levine and Sturgis,\(^ {13}\) who used the term "masked hyperthyroidism" to designate elderly hyperthyroid patients who presented with congestive heart failure. In these patients, the cardiac symptoms so predominated that the diagnosis of hyperthyroidism, which was the underlying cause of the heart failure, was initially overlooked. Another term for thyrotoxicosis in the elderly is "apathetic hyperthyroidism." Coined by Frank Lahey\(^ {14}\) of the Lahey Clinic, this term described certain older patients whose thyroid glands were small and who lacked such typical hyperthyroid features as exophthalmos; tachycardia; and smooth, moist skin. These patients did not appear to be severely ill; nevertheless, Lahey\(^ {14}\) observed that if they were subjected to physiologic stress, these fragile, elderly persons could "quietly and peacefully sink into coma and die."

Another early (1949) study found that only 16% of 124 elderly patients with hyperthyroidism showed the increased nervousness described by the authors as being "among the earliest and most consistent manifestations of the disease in younger patients." As Bartels and Kingsley\(^ {15}\) further noted, "The relative infrequency of nervousness and emotionalism is indicative of the altered response of the elderly to hyperthyroidism."

Among younger hyperthyroid patients, such symptoms as weight loss, increased appetite, muscle
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Published on Physicians Practice (http://www.physicianspractice.com)

weakness, palpitations, rapid pulse, and exophthalmos often are prominent, but according to what may be the definitive report in this area, these are far less often found among elderly hyperthyroid patients.\textsuperscript{16} Some of the specific findings from this and the Bartels and Kingsley study are detailed in the \textbf{Box}.

An elderly patient with thyrotoxicosis is much more likely than a younger one to present with apathy and depression. Although weight loss may be a prominent symptom in an elderly hyperthyroid patient, it is as likely to reflect reduced food intake as increased catabolism resulting from the excess thyroid hormone. Such elderly, depressed hyperthyroid patients often appear sad and lethargic and have little interest in either themselves or their surroundings. Be sure, therefore, to consider the possibility of hyperthyroidism in any elderly patient who exhibits such symptoms. A recent change in mental status thus can be an important sign.\textsuperscript{17}

\textbf{TREATMENT OF HYPERTHYROIDISM}

The principal therapy for hyperthyroidism in an elderly patient is radioiodine, which should be given after pretreatment with β-blockers to prevent the development of thyroid storm. Neither propylthiouracil nor methimazole is as effective as radioiodine, although it may be appropriate to pretreat the more severely ill patients with these drugs before giving radioiodine. These agents induce permanent remission in only a relatively small fraction of younger patients; among elderly thyrotoxic patients, the proportion of those who respond adequately is even smaller. Furthermore, compared with younger patients, a somewhat higher proportion of elderly hyperthyroid patients have multinodular toxic goiter (\textbf{Figure}) rather than Graves disease as the cause of their hyperthyroidism, although Graves disease remains the most common cause. Multinodular toxic goiters do not respond well to antithyroid drugs.

As with younger patients, the most significant problem encountered with radioiodinetherapy is the late development of hypothyroidism. Since the manifestations of hypothyroidism may be quite subtle in an elderly person, regular follow-up is critical for patients who have received radioiodinetherapy. Obtain thyroid function tests (free $T_4$ and TSH) at least every year, and more frequently (twice or even 3 times a year) if you suspect the patient has hypothyroidism.

Most thyroid specialists recommend initiating replacement thyroid hormone therapy whenever the TSH level is above the normal range, even if the free $T_4$ level is still normal. The TSH level is believed to be the most sensitive indicator of the body's true thyroid status.

Elderly hyperthyroid patients with a toxic nodular goiter typically have a somewhat lower uptake of diagnostic radioiodinethan patients with Graves disease; the 6-hour and 24-hour uptake values may be toward the upper end of the normal range or only modestly increased. The therapeutic dose of radioiodineneeds to be somewhat higher in these patients. For patients of any age with diffuse toxic goiter (Graves disease), a fairly standard total dose of radioiodines is 10 to 15 mCi, whereas a patient with multinodular toxic goiter usually requires a total dose of 25 to 30 mCi.

\textbf{THYROID CANCER}

In all age groups, papillary carcinoma is the most common type of thyroid cancer, but it is more aggressive in the elderly. According to one study, the 10-year survival rate among patients older than 50 was only 60%, compared with 90% among those younger than 50. The authors reported that the tumor progresses more rapidly in several respects in older patients than in younger ones: rate of growth, metastasis to distant sites, and recurrence after surgery.\textsuperscript{18}

Relative mortality rates for several types of thyroid carcinoma considered together were calculated in 2 other studies. Cady and colleagues\textsuperscript{18} evaluated 792 patients with differentiated carcinomas (including papillary and follicular carcinomas and mixed papillary-follicular tumors). Of the patients older than 50, 34% died, compared with 5% of patients between ages 20 and 40, and 8% of those between ages 41 and 50.

In the oldest age group, the mortality rate was higher in men than in women. These findings were borne out by Halnan's study,\textsuperscript{19} which analyzed all types of thyroid carcinoma. There was a consistent inverse correlation between age at diagnosis and survival. Thus, the prognosis is rather unfavorable for older patients who have thyroid cancer.

For older as well as younger patients, the management of thyroid carcinoma is controversial. Several different approaches are advocated in the literature-some more aggressive than others.

\textbf{References:}

\textbf{REFERENCES:}

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