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Thyroid Disease in the Elderly

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ABSTRACT

Thyroid dysfunction and benign and malignant neoplastic changes in the thyroid gland occur frequently in the general population but are more likely to result in undesirable clinical consequences in the elderly, usually because of coexistent pathology such as diminished cardiovascular reserve. This review will highlight the common problem of thyrotoxicosis in nodular thyroid disease in the elderly; such thyrotoxicosis frequently has an iatrogenic basis and is therefore potentially preventable. The treatment of thyrotoxicosis and the relative advantages/disadvantages of therapeutic modalities such as antithyroid drugs, radioiodine and surgical intervention tend to vary between younger and older patients. Radioiodine is often the treatment of choice in the elderly. Monitoring and treatment of hypothyroidism is also discussed, and the substantial risks of rapid correction of low thyroid hormone levels in elderly patients with coexistent ischaemic heart disease. Also emphasised is the need to potentially adjust dosage of other pharmacological agents frequently used by elderly patients (e.g. digoxin, warfarin) in states of as yet uncontrolled hypothyroidism or thyrotoxicosis.

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INTRODUCTION

Apart from diabetes, thyroid dysfunction is a common endocrine disorder, especially in the elderly, with a 2 to 5% prevalence of clinically significant disease reported in geriatric institutions.¹ Subtle biochemical abnormalities occur more often, with subclinical hypothyroidism (raised thyroid stimulating hormone [TSH], normal triiodothyronine [T_3]/thyroxine [T_4]) present in 15% of females over 60 years and subclinical thyrotoxicosis (suppressed TSH, normal T_3/T_4) in 2% of people over 55 years.² Therefore, a low threshold for screening for thyroid disease should be considered in the elderly.

Although there are no differences in clinical presentation, diagnosis or management of thyroid disease in the elderly, there are some specific issues, such as more subtle clinical manifestation, need for early treatment and best form of treatment which require discussion.

SPECTRUM

In order of frequency of occurrence but in reverse order of clinical impact and urgency for intervention, thyroid dysfunction in the elderly usually takes the form of nodular disease, hypothyroidism (spontaneous or iatrogenic) and thyrotoxicosis.

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Nodular Thyroid Disease

The development of thyroid nodules with ageing is extremely common, with prevalence exceeding 90% in females over 70 years and 60% in males over 80 years.³ Although many of these nodules are not clinically evident, imaging and scanning the neck, often for other indications, will reveal their presence. The need for further specific thyroid assessment then becomes an issue, with inappropriate investigations sometimes initiated in otherwise asymptomatic people. The question of neoplastic changes in nodular goitres is raised as justification for such investigations and although thyroid cancers have a high morbidity and mortality in the elderly, their incidence remains extremely low.⁴ A clinical challenge relates to making a decision on the need for fine needle aspiration or surgical intervention on suspicious nodules. The majority are eventually found to be nonmalignant, but the fear of missing a potentially treatable malignancy leads to unnecessary interventions in a proportion of cases. A rapid increase in the size of an existing nodule or the appearance of new dominant nodules with characteristics of malignancy would warrant more aggressive intervention such as a fine needle or open biopsy.

The functional autonomy of thyroid nodules (independence from pituitary TSH control) and potential for developing thyrotoxicosis is an important issue, probably more relevant in most instances than malignancy. Spontaneous thyrotoxicosis is unpredictable but iodine-induced thyrotoxicosis, frequently seen following exogenous iodine loads such as radiological contrast agents or iodine-containing medications (e.g. amiodarone, cough mixtures, topical antiseptics) is a common form of thyroid dysfunction, difficult to manage and potentially preventable, e.g. by minimising the use of iodine-containing radiological contrast agents unless definitely necessary.⁵ Contrast radiography was responsible for 25% of cases of iodine-induced thyrotoxicosis in a geriatric hospital in Melbourne.⁶

Hypothyroidism

Hypothyroidism has a prevalence of 5% and an annual incidence of 0.1 to 0.2% in middle-aged females.⁷ In people over 70 years, TSH > 4.5 mU/L was found in 14%.⁸ This hypothyroidism usually occurs *de novo* from autoimmune damage to the thyroid gland (Hashimoto's thyroiditis) or can become manifest following earlier episodes of Graves' disease, with or without surgery or radioiodine. It is particularly important to consider the likelihood of hypothyroidism after radioiodine treatment.⁹

Thyrotoxicosis

Toxic nodular goitre, iodine-induced thyrotoxicosis and excessive thyroxine replacement therapy are common aetiological factors responsible for raising circulating

levels of thyroid hormone in the elderly. Graves' disease and subacute thyroiditis also occur in the elderly.

Appropriate changes in therapeutic approach are required in the elderly, such as the earlier consideration of radioiodine rather than prolonged trials of antithyroid drugs (e.g. carbimazole, propylthiouracil). Radioiodine is the preferred option in Graves' disease and toxic nodular goitre, although in both these conditions, a short course of antithyroid drugs may be required to achieve control of thyrotoxicosis and reduce the impact on cardiovascular function prior to the use of radioiodine.

Iodine-induced thyrotoxicosis presents a specific challenge since radioiodine is likely to be ineffective because of very low uptake by the thyroid gland and antithyroid drugs are not particularly effective.

Subacute thyroiditis (including a form of amiodarone-induced thyrotoxicosis) is particularly difficult to manage, with no response to antithyroid drugs, no effect of radioiodine and occasionally the need to resort to emergency surgical thyroidectomy. In such cases, glucocorticoid therapy may have a place, with control of local thyroid pain in subacute thyroiditis and limitation of disease progression in amiodarone-induced thyroiditis.

CLINICAL MANIFESTATIONS

Both hypothyroidism and thyrotoxicosis may manifest with different clinical features in the elderly (Table 1).¹⁰ 'Apathetic thyrotoxicosis' is a well-recognised entity, with the cardiovascular system predominantly affected and presentations such as new-onset atrial fibrillation +/- thromboembolic complications or congestive heart failure. The heat intolerance and nervousness noted in young patients may be absent in the elderly and weight loss may be masked by fluid retention related to the heart failure. Proximal muscle weakness is often missed or attributed to other pathology or to the ageing process *per se*.

Hypothyroidism is often missed in the elderly, especially

Table 1. Symptoms and signs of thyrotoxicosis in the elderly

	Study 1* (n = 25)	Study 2† (n = 247)
Age (mean and range)	81.5 (75-95)	40 (5-73)
Symptoms		
Weight loss	44%	85%
Palpitations	36%	89%
Weakness	32%	70%
Nervousness	20%	99%
Heat tolerance	4%	89%
Signs		
Pulse >100	28%	100%
Atrial fibrillation	32%	10%
Tremor	36%	97%

*Tibaldi JM, Barzel U, Albin J, Surks M. Thyrotoxicosis in the very old. *Am J Med* 1986; 81: 619-22.

†Ingbar SH, Woeber RA. The thyroid gland. In: Williams RH, editor. *Textbook of endocrinology*. Philadelphia: WB Saunders; 1981. p.117-247.

in the early stages, and associated symptoms (tiredness, memory loss/confusion, skin dryness, cold intolerance, constipation) attributed to ageing or co-morbidities.

The American Thyroid Association recommend that routine screening for hypothyroidism at 5-year intervals over the age of 35 years may be cost effective, whereas the American College of Physicians reserves such screening for women over 50 years.¹¹ Even if this is not generally accepted, there should be a very low threshold for screening for thyroid hypofunction in the elderly, especially when presenting with deteriorating mental function.

LABORATORY DIAGNOSIS

Current guidelines indicate that the measurement of serum TSH levels should be the first test for both hypothyroidism and thyrotoxicosis. Significant elevation of TSH levels (>10 mU/L) indicate thyroid failure, while suppression of TSH levels (<0.1 mU/L) possibly indicative of thyrotoxicosis will need further assessment by measurement of free levels of T₄ and T₃. However, T₃ levels should be interpreted with caution since there is evidence that T₃ production may be reduced in the healthy elderly¹² but more importantly the low T₃ syndrome related to the effect of intercurrent illness on T₃ levels is well-recognised.¹³ There is a very low likelihood of missing significant thyroid dysfunction due to pituitary disease by relying on TSH measurements alone; such disease should be considered in specific cases where low levels of T₄/T₃ are associated with apparently inappropriately low levels of TSH.

Measurement of thyroid antibodies is of relatively little value in most instances, although the presence of antithyroid peroxidase antibodies in the elderly patient with mild elevation of TSH points to a much higher likelihood of progression to more significant, clinically relevant thyroid failure, of the order of 5% per year,¹⁴ thus indicating the need for ongoing monitoring and possibly early intervention with thyroxine replacement therapy.¹⁵

Imaging of the thyroid gland is most commonly performed with ultrasound and as mentioned earlier, nodular changes are very often detected. The usefulness of information gained is sometimes limited.

Radioisotope scanning to assess the functionality of nodules can be very helpful, especially as a guide to radioiodine ablative therapy but its potential is strictly limited in the setting of iodine-induced thyrotoxicosis. Low or absent uptake is seen in subacute thyroiditis.

TREATMENT

Options for intervention do not differ significantly between younger and older patients, although the use of prolonged (12 to 24 months) courses of antithyroid drugs for Graves' disease, is less likely to be successful in the older patient where radioiodine ablation may be more acceptable after an initial control of the thyrotoxicosis with antithyroid drugs and concomitant careful use of beta-blockers for early symptom relief. Surgery is commonly reserved for large goitres complicated by obstructive symptomatology or when malignancy is suspected.

A common problem is the timing of initiation of therapy in subclinical hypothyroidism and thyrotoxicosis.

Subclinical Hypothyroidism

Modest increases in serum TSH levels (5 to 10mU/L), with free T₄ or T₃ in the reference range occur frequently. It is tempting to initiate thyroxine replacement therapy, especially if there are symptoms which may be attributable

to thyroid hypofunction. As progression to clinical hypothyroidism is not universal (<5%/year), early intervention may be unnecessary. In such cases, continued monitoring at 6 to 9-month intervals may be more logical.

Subclinical Thyrotoxicosis

A commonly encountered situation is suppressed TSH levels with free T_4 and T_3 in the reference range, often with some nodular changes. Prevalence has been reported to be of the order of 4% in the elderly population.¹⁶ Some symptoms could be attributable to thyroid hyperfunction, such as nervousness, weight loss and palpitations. If reversible causes of these biochemical abnormalities are excluded (e.g. transient subacute thyroiditis, over-replacement with thyroxine, transient iodine-induced thyrotoxicosis), the adverse clinical consequences of subclinical thyrotoxicosis may point towards the need for intervention. This state is associated with a significant risk of atrial fibrillation¹⁷ and an increased likelihood of osteoporosis.¹⁸ Although one would anticipate some beneficial effects from therapy, no studies have been reported in which such benefits are indeed seen.

Thyroxine Replacement in Hypothyroidism

The rapid introduction of thyroxine in a significantly hypothyroid elderly patient may be associated with potential risks, such as precipitation of cardiac ischaemia. Reports of increased early mortality in patients treated in such a fashion¹⁹ indicate the need for caution. To minimise the risks it is recommended that initial doses of thyroxine be limited to 25 micrograms daily, with increases by a similar amount at 6 to 8 week intervals.²⁰ Such an approach needs to be modified in cases of severe hypothyroidism (myxoedema coma) when rapid correction with intravenous T_3 is essential.

The thyroxine dose is likely to be low in the elderly (20%) because of reduced metabolic clearance of thyroxine. The dose should therefore be determined by monitoring TSH levels, as occurs in the younger patient.

Concomitant use of other medications may effect the thyroxine dosage required for adequate replacement. Phenytoin, rifampicin and carbamazepine increase thyroxine clearance and lead to increased requirements for T_4 , whereas drugs such as cholestyramine, aluminium hydroxide, calcium carbonate, soy preparations and ferrous sulphate may interfere with intestinal absorption and lead to increased requirements for T_4 . The most common reason for inadequate thyroxine therapy in elderly patients is likely to be poor compliance with medications.

THYROID DISEASE AND OTHER MEDICATIONS

Hypothyroidism and thyrotoxicosis can significantly effect the metabolism of other drugs commonly used in elderly patients, potentially resulting in either reduced efficacy or potential toxicity.²¹ In general, thyrotoxicosis increases metabolic clearance rates of drugs whereas hypothyroidism will reduce such rates. It is well recognised that achieving therapeutic levels of digitalis and therefore control of atrial fibrillation requires higher dosage of digoxin in thyrotoxic patients. Similar increases in cortisol requirements are also seen. Conversely a decrease in the biological half life of vitamin K dependent coagulation factors means that warfarin dosages are usually lower in the thyrotoxic state. Sedatives will have a greater effect in hypothyroid individuals and this is

commonly observed following surgery in an untreated hypothyroid patient where recovery from anaesthesia can be quite prolonged.

CONCLUSION

Thyroid dysfunction is common in the elderly and is often associated with greater morbidity than in younger patients. Thyroid failure from Hashimoto's thyroiditis or from an iatrogenic cause requires regular monitoring and careful replacement therapy. Thyrotoxicosis and the associated cardiovascular dysfunction is relatively common, especially after administration of iodine-containing material to patients with nodular goitres and some degree of thyroid autonomy. It is strongly suggested that a low threshold for assessing thyroid status be maintained, as prevention of decompensation is preferable to the sometimes difficult treatment. Finally the influence of thyroid dysfunction on other concomitant pathology and relevant treatments needs to be considered in the elderly. Unresolved issues relate to appropriate timely interventions in subclinical hypothyroidism and thyrotoxicosis; these are areas where well-designed clinical trials would be of clear benefit in choosing therapeutic options.

Competing interests: None declared

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