Thyroid Abnormalities

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KEYWORDS

• Thyroid function • Infective thyroiditis • Immune reconstitution
• Inflammatory syndrome • Graves disease • Non-thyroidal illness

KEY POINTS

- Most patients with early human immunodeficiency virus (HIV) infection with no weight loss have normal thyroid function.
- As disease progresses, subtle abnormalities in thyroid function occur in some patients, including subclinical hypothyroidism and isolated low free thyroxine levels.
- Immune reconstitution in the first 3 years after highly active antiretroviral therapy is associated with the development of Graves disease and other autoimmune disorders in a small number of patients.
- In advanced HIV infection, unusual opportunistic infections may cause acute or subacute thyroiditis.

Many endocrine and metabolic abnormalities have been identified after infection with human immunodeficiency virus (HIV), typically comprising endocrine gland involvement by neoplasms or after opportunistic infection, hormone abnormalities resulting from the associated illness, and side effects from treatment.[1,2] As chronic HIV infection becomes the norm, prolonged inflammation and immunodeficiency can combine to produce new disease associations, such as cardiovascular complications, and extended treatment may also induce novel side effects[3]; it is likely therefore that there is a still evolving pattern of endocrine abnormalities. This review focuses on thyroid abnormalities, which are usually asymptomatic or mild, but may cause diagnostic problems (**Table 1**). Approximately one third of patients with HIV infection may have biochemical disturbances of thyroid function, whereas only 1% to 3% develop overt thyroid disease.[4]

THYROID FUNCTION TESTS IN HIV-INFECTED INDIVIDUALS

In most patients with recent HIV infection, thyroid function tests are normal. However, as disease progresses and complications such as opportunistic infections ensue, a wide

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Table 1
Summary of the main types of thyroid disorders in HIV-infected individuals

Disorder	Description
Infective thyroiditis	Caused by opportunistic infections that do not affect the thyroid in non–HIV-infected individuals
Thyroid neoplasm	Kaposi sarcoma; lymphoma
Nonthyroidal illness	Especially in the terminal phase in AIDS patients
Isolated low free T4	In treated individuals, especially children
Subclinical hypothyroidism	In treated individuals
Reconstitution disease	After treatment; especially Graves disease

Abbreviations: HIV, human immunodeficiency virus; T4, thyroxine.

variety of asymptomatic disturbances may occur, which are part of the spectrum of disorders termed nonthyroid illness or sick-euthyroid syndrome (SES). Any acute, severe illness may cause SES, including anorexia and psychiatric disorders. The alterations seen in thyroid hormones are primarily owing to the effects of cytokines on thyroid hormone deiodination and on the pituitary, and teleologically have been regarded as an adaptive mechanism to conserve energy and limit catabolism. It is increasingly clear this view is overly simplistic, with significant variations in the presentation and outcome of SES that depend on etiology, end-organ responses, and chronicity.[5]

Weight-stable patients with HIV have normal serum free tri-iodothyromine (FT3) levels, in contrast with those who lose weight, in whom serum FT3 and reverse T3 levels can decrease rapidly, in close relationship to nutritional status.[6,7] The lowering of reverse T3 is unusual, because altered thyroxine (T4) deiodination in SES is usually accompanied by an increase in reverse T3 production, which works together with reduced clearance to elevate serum levels of reverse T3. This increased production results from a decrease in 5'-deiodination of T4, leading to a decrease in T3 production and reverse T3 metabolism and an increase in 5-deiodination of T4, leading to an increase in reverse T3. The pattern of reduced levels of reverse T3 seen in HIV infection has been replicated in other studies, but the reasons for it are unknown.[8,9] Any decline in T3 levels in HIV-infected individuals probably occurs later than would be expected in typical SES, and is associated with an increased mortality.[9] It is conceivable that the failure of T3 to decrease in the SES associated with HIV infection contributes to weight loss.

Another distinctive feature of HIV infection is that serum levels of T4-binding globulin progressively increase; cortisol-binding globulin and sex hormone-binding globulin remain unaltered.[6,8,10] The reason for this increase in T4-binding globulin is unknown, but seems unrelated to estrogen levels or clearance of the protein. The only relevance of the change in T4-binding globulin is that alterations in the level of this protein have a significant effect on biochemical tests that measure total rather than free thyroid hormones; however, these tests are used rarely. Serum thyrotropin (TSH) levels in HIV-infected individuals are typically normal, but more detailed study has revealed that the response to thyrotropin-releasing hormone is exaggerated and there is an altered pattern to the normal circadian rhythm of TSH, with higher pulse amplitudes and a higher mean 24-hour TSH level.[11] These changes again differ from typical SES, in which serum TSH levels may decline or (less commonly) increase, and indicate a mild underlying subclinical hypothyroidism.

Most studies preceded effective treatment for HIV and more recent work has focused on thyroid abnormalities in treated patients. However, a recent study of