chronic cough: the treatment in patients with nasal disease should be tailored to the specific otolaryngologic condition. Data from randomized, controlled trials of specific therapies for nasal disease in patients presenting with chronic cough are lacking, and only uncontrolled observational data provide support for the efficacy of ipratropium bromide, nonspecific antihistamines, and decongestants in this patient group. Nonpharmacologic interventions have been shown to be effective in treating typical symptoms of gastroesophageal reflux disease such as heartburn and regurgitation, and these approaches are mentioned in recent guidelines for the management of chronic cough. We did not emphasize these maneuvers in our brief review because of the lack of data showing efficacy in patients with reflux-related chronic cough.

Graves’ Disease

TO THE EDITOR: We wish to clarify some statements made by Smith and Hegedüs (Oct. 20 issue) regarding the serologic diagnosis of Graves’ disease and the role of autoantibodies in relation to the thyrotropin receptor. The guidelines on hyperthyroidism from the American Thyroid Association strongly recommend measurement of thyrotropin-receptor antibodies for accurate and early diagnosis as well as management of Graves’ disease. Functional stimulating thyrotropin-receptor antibodies are causative factors in the hyperthyroidism and the extrathyroidal manifestations of Graves’ disease, and these antibodies can be sensitively and exclusively measured with validated bioassays that are available worldwide. In particular, the analytical performance and clinical utility of a stimulatory thyrotropin-receptor bioassay in patients with Graves’ disease have been demonstrated. In addition, a multicenter trial confirmed the very high specificity, sensitivity, and positive and negative predictive values of this tool for the diagnosis of Graves’ disease in children. Finally, the incorporation and early use of stimulating thyrotropin-receptor antibodies in current diagnostic algorithms have been shown to shorten the time to the diagnosis of Graves’ disease by 46% and to achieve a cost savings of 47%.

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TO THE EDITOR: In the review of Graves’ disease by Smith and Hegedüs, we found that the following sentence — “therapy with alemtuzumab, a
CD52-targeting monoclonal antibody, can induce Graves’ disease” — was too short a summary of the issues they raised. Coles et al.1 reported the frequent occurrence of Graves’ disease months after the cessation of anti-CD52 treatment during immune recovery in patients who had undergone a durable and profound depletion of T lymphocytes, an observation that allowed an interesting comparison with studies of lymphopenia-induced organ-specific autoimmunity in animals.

We2,3 and others4 have described the occurrence of Graves’ disease during immune restoration in severely immunodepressed patients infected with the human immunodeficiency virus (HIV) who were receiving antiretroviral therapy. In these patients, thyroid autoimmunity has been linked to the quantitative recovery of naive CD4+ T cells that were recent thymic emigrants.4

These observations define a specific context in which Graves’ disease can occur: lymphopoiesis–thymopoiesis after prolonged T-cell depletion, probably leading to errors in the recognition of self versus nonself by new T cells. We believe this phenomenon sheds an interesting light on the pathogenesis of Graves’ disease and is worthy of attention.

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THE AUTHORS REPLY: In our article, we needed to determine which of the issues related to Graves’ disease should be covered and how to apportion our allotted space. In response to the comments of Kahaly and Olivio: we maintain that thyrotropin-receptor antibody assays are not always necessary for making the correct diagnosis of Graves’ disease. These assays are unavailable in some parts of the world, partly because of their cost. When used, they provide a reliably accurate diagnosis. When the diagnosis is in doubt and the assays are available, they should be used. We would add that although there is overwhelming evidence that anti-thyrotropin–receptor antibodies underlie the hyperthyroidism in Graves’ disease, the role of these antibodies in thyroid-associated ophthalmopathy is considerably less well understood.

We appreciate the point raised by Viard and Gilquin regarding the complexities involved in the development of Graves’ disease in association with the anti-CD52 treatment used in multiple sclerosis. They point to the clinical setting of immune-function restoration after antiretroviral therapy in patients with HIV who have severe immunodepression. Although both situations represent examples of immune reconstitution, it remains uncertain whether the underlying mechanism is identical. Each scenario represents a clinical process that engenders unusual immunologic challenges. In our view, more detailed characterization of these two clinical events is warranted. We agree that these examples of iatrogenic Graves’ disease may shed important light on disease pathogenesis and the roles played by specific T-cell populations.

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