etanercept. They concluded that the risk of TB is greater with infliximab than with etanercept.

The authors base their conclusion, in part, on comparing the incidence rates of reported TB cases associated with these drugs. We agree that, as presented, the data suggest a greater risk of TB with infliximab, but we call attention to a potential misunderstanding in the methods. Wallis et al. [1] state that the denominators for their incidence calculations contain only persons who initiated treatment with infliximab or etanercept in the United States, but they do not state whether the numerator is similarly limited to TB reports from the United States. Although the FDA adverse events database is in the United States, the system accepts adverse event reports from both within and outside the country, and many of the cases of TB collected in this database are from outside the country. Having recently reviewed this database, we suspect that Wallis et al. [1] included case reports from both the United States and other countries in the numerator and included only persons who initiated treatment in the United States in the denominator.

This possibility leads to an overestimation of TB risk associated with any of these agents, and it underscores the difficulty in drawing conclusions about a risk difference between agents. Although other reports [2] also suggest that infliximab carries a greater risk of TB disease, to date, there has been no study directly comparing the rates of TB disease associated with these 2 agents while controlling for potential differences in TB risk factors among patients. Fewer TB cases have been reported with etanercept, but the clinical features of these cases (with the exception of a shorter time to disease onset with infliximab, as noted above) resemble those associated with infliximab. With either agent, TB is often extrapulmonary and disseminated [3].

We consider both agents, as well as other TNF-α antagonists, as immunosup-

pressive drugs that confer a risk of TB. Any person who is a candidate for TNF-α antagonist therapy should be screened for latent *Mycobacterium tuberculosis* infection with a medical history, a tuberculin skin test, and a chest radiograph, in accordance with CDC guidelines [4–6]. Persons who have latent infection diagnosed should begin preventive therapy before starting treatment with TNF-α antagonists, and clinicians should remain vigilant for TB in any patient who has a febrile or respiratory illness while receiving any TNF-α antagonist.

Acknowledgment

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Correction regarding Adalimumab Labelling

SIR—In the recent article by Wallis et al. [1], the authors state incorrectly that the "black box" warning on the US label for adalimumab (Humira; Abbott) addresses risks for tuberculosis "and other opportunistic infections" [1, p. 1264]. Only tuberculosis is addressed on this portion of the label. As with other labels for TNF blocking agents, the warnings section addresses the potential risks for "opportunistic infections," including tuberculosis.

Acknowledgment

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Clinical Hyperthyroidism in Chinese Patients with Stable HIV Disease

SIR—Only 2 cases of subclinical hyperthyroidism were found in the prevalence study of thyroid dysfunction by Beltran et al. [1]. We, however, found no cases of hypothyroidism and 9 cases of hyperthyroidism in a retrospective study of symptomatic thyroid disorders in patients attending an HIV/AIDS clinic until the end

Table 1. Demographic, clinical, and treatment characteristics of 9 Chinese patients with hyperthyroidism and HIV disease.

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age in years, sex	29, M	44, M	40, M	33, F	40, M	46, M	34, M	48, F	41, F
Family history of thyroid disease (relative affected)	No	No	Unclear	No	Yes (sister)	No	No	Yes (sister)	No
Percent weight loss over 6 months prior to diagnosis of hyperthyroidism	10	7.6	9.5	0	13.9	9	7.5	11.5	7.9
Laboratory values									
Free thyroxine, pmol/L (NR, 9.0–19.1)	52.27	45.60	57.50	56.70	57.20	57.90	16.00[a]	29.00	>77.2
Thyroid stimulating hormone, mIU/L (NR, 0.35–4.94)	0.01	<0.01	<0.05	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Anti-microsomal antibodies, IU/mL (NR, <100)	Negative	Negative	NA	100	Negative	100	Negative	1600	1600
Anti-thyroglobulin antibodies, IU/mL, (NR, <0)	Negative	Negative	NA	Negative	Negative	Negative	Negative	Negative	80
CD4 count, cells/µL									
Nadir	6	5	15	69	1	216	71	226	305
At diagnosis of hyperthyroidism	233	538	234	185	459	320	522	423	426
Increase	227	533	219	116	458	104	451	197	121
CDC stage at diagnosis of hyperthyroidism	B3	B3	C3	B3	C3	B2	C3	B2	A2
Antiretrovirals received	3TC, D4T, FTV, and RTV	CBV, NFV	3TC, AZT, NFV	CBV, EFV	CBV, IDV	AZT, DDI-EC, NVP	CBV, IDV	3TC, D4T, EFV	…
Time from initiation of HAART to diagnosis of hyperthyroidism, months	39.9	62.9	12.5	52.4	61.8	64.6	36.6	24.3	…

NOTE. AZT, zidovudine; CBV, combivir; D4T, stavudine; DDI-EC, didanosine, enteric-coated; EFV, efavirenz; FTV, fortovase; IDV, indinavir; NA, not available; NFV, nelfinavir; NR, normal range; NVP, nevirapine; RTV, ritonavir; 3TC, lamivudine.

[a] Free triiodothyronine level, 6.9 pmol/L (NR, 3.0–6.2).

of 2003. Two more patients gave a history of thyrotoxicosis before diagnosis of HIV infection; they were excluded from the analysis. The incidence of clinical hyperthyroidism was 0.28 cases/100 patient-years (0.22 cases/100 patient-years for males and 0.55 cases/100 patient-years for females). The overall cross-sectional prevalence was 1.1% (0.9% for males and 2.0% for females). As shown in table 1, all 9 patients were Chinese, the ethnic group that constitutes 80% of our clinic's population. Weight loss was the most prominent feature of the clinical presentation, with a median decrease in body weight of 7.9% (range, 0%–13.9%) relative to body weight 6 months prior to the diagnosis of hyperthyroidism. Other classic thyrotoxic symptoms—for example, palpitation, tremors, and sweating—were also present in some patients but were not as marked. Goiter was only found in 4 patients.

Biochemical testing revealed that all patients had markedly suppressed levels of thyroid stimulating hormone, of which most were below the detection limit. All patients had grossly elevated serum levels of free thyroxine, except one who had elevated levels of free triiodothyronine. Unfortunately, because of the retrospective nature of the study, the etiology of hyperthyroidism could not be identified in patients for whom there was inadequate information. None of the patients had been investigated using thyroid scanning or tests for antithyrotrophin receptor autoantibodies. Of the 4 patients who tested positive for antimicrosomal antibodies, 2 patients had high titers (1600 IU/mL). Only 1 patient tested positive for antithyroglobulin antibodies. According to the available information, Graves disease was the cause of hyperthyroidism in 6 patients. The clinical and biochemical conditions of all 9 patients improved promptly after treatment with antithyroid drugs.

At the time of diagnosis of hyperthyroidism, all patients except one were receiving HAART for a median duration of 57.6 months (range, 12.5–64.6 months). Also, most patients had experienced a substantial increase in CD4 count above the nadir (median, 223 cells/μL; range, 104–533 cells/μL), especially those patients with low baseline levels. However, in our study, only 3 patients were AIDS patients (patients 3, 5, and 7) and 1 never had symptoms of HIV infection (patient 9) (table 1), which is in contrast to another study [2] in which all cases of hyperthyroidism were found in AIDS patients. The occurrence of clinical hyperthyroidism in our patients could be coincidental or related to HAART. The higher prevalence of overt disease in our HIV cohort study, compared with studies reporting overt disease in 0.5% and 0.2% in general Chinese [3] and Japanese [4] populations, respectively, suggests an association. The fact that almost all patients were treated with HAART and experienced good immune recovery further supports this notion. Immune restoration due to HAART [5, 6] might have precipitated or hastened the manifestation of thyrotoxicosis in some individuals. Yet the delay between initiation of HAART and onset of clinical hyperthyroidism in our patients was much longer than that of another study, in which the median time until onset of Graves thyrotoxicosis was 20 months [2]. The severely abnormal biochemical profile and the marked weight loss might have been caused by severe disease or delayed diagnosis.

In summary, we have found that overt hyperthyroidism is an uncommon but clinically important event in HIV-infected Chinese patients. Presentation mostly occurs in patients receiving HAART and is often delayed for years after treatment. Weight loss, which may be the only obvious feature, in a patient with otherwise stable HIV disease should prompt examination for the diagnosis or exclusion of hyperthyroidism. Awareness of the ever-increasing nonconventional complications in HIV/AIDS patients is essential for their timely diagnosis and management.

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Testing for HIV to Destigmatize and Improve Diagnosis of HIV Infection

SIR—In her recent article, Stone [1] suggests that there are 5 major ways to enhance the care of underserved minorities with human immunodeficiency virus infection and AIDS: provision of culturally competent HIV/AIDS care; enhancement