from the same cohort who did not have osteopenia. Baseline characteristics and P values are shown in table 1. We compared sTNFR2 levels in case patients and control subjects. We used χ² and Fisher’s exact tests to compare categorical variables, and Student’s t test and Pearson’s correlation were used for analysis of continuous variables.

sTNFR2 levels were nearly identical in the 2 groups (mean level ± SEM, 0.5 ± 0.5 ng/mL among case patients and 5.2 ± 0.8 ng/mL among control subjects; P = .85). No correlation between sTNFR2 levels and osteopenia was identified, although levels were significantly elevated in the case patient group, compared with HIV-negative subjects (5.1 ± 0.5 ng/mL vs. 3.1 ± 0.3 ng/mL; P = .003). When t score and total BMD were analyzed for the 2 groups, we encountered similar results. We found no associations between antiretroviral medications and osteopenia, including nucleoside reverse-transcriptase inhibitors, nonnucleoside reverse-transcriptase inhibitors, and protease inhibitors.

The number of patients studied was small; however, 15% of this predominantly male, young, overweight cohort with mean CD4+ cell counts >350 cells/mm³, were osteopenic, by total z score. Elevated levels of proinflammatory cytokines have been classically demonstrated in patients with poorly controlled HIV infection or as a consequence of HAART. Before the advent of HAART, low BMD was rarely observed; however, studies performed since 1996 have demonstrated an association between osteopenia and HIV infection [3, 7].

Given these observations, and as suggested by Arnsten et al. [1], HIV-infected patients with osteopenia would be expected to have higher circulating levels of TNF; however, we found that not to be the case. It may be that serum sTNFR2 is not a sensitive marker, because levels may vary in response to extraneous sources of inflammation. Cytokine levels in other tissues, such as adipocytes or osteocytes, might be more indicative. Alternatively, other cytokines may be more helpful in answering this question. Based on our findings, sTNFR2 is not associated with osteopenia.

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References


Antibiotic Pricing: When Cheaper May Not Be Better

To the Editor—Antibiotics in India have always been cheaper in absolute terms thanks to weak patent laws that have been
in effect until recently. Because a direct translation of drug prices from US dollars to Indian rupees (INR) would have rendered most new antibiotics inaccessible to the vast majority of Indians, such patient violations were subtly encouraged. Even despite this, we were caught unaware when pharmaceutical representatives approached our primary care center in rural India, claiming that a 5-day course of levofloxacin would henceforth cost the patient ~INR 20 (<$0.50). Reluctant to accept such a statement at face value, we consulted the CIMS Updated Prescriber’s Handbook [1], a popular index of pharmaceutical drugs available in India. Here, we discovered that a 5-day course of oral levofloxacin (500 mg once daily) cost anywhere from INR 19.5 to INR 475 ($0.50–$10.50), with most companies pricing their brand at <$1 for a full course. The same course in the United States would cost >$100. Intrigued, we did some more research and came up with the following results. The cheapest 5-day courses of first-line antibiotics, such as oral amoxicillin (500 mg thrice daily) or oral erythromycin (500 mg 4 times daily), cost INR 45 ($1) and INR 90 ($2), respectively. On the other hand, the cost of a 3-day course of oral azithromycin (500 mg daily) was one-half that of a course of erythromycin. Despite the obvious price advantage to the patients, we find this trend troubling. Lower prices often lead to wider prescription of a given drug, especially in resource-limited settings. If second-line antibiotics—such as levofloxacin and azithromycin—are made available at lower prices than first-line antibiotics, there is a high probability of their overuse and subsequent development of resistance. In the face of very low costs of medication, patients are unlikely to complain of escalating medical expenses. The issue assumes more gravity when one considers the fact that levofloxacin is an important second-line drug for the treatment of tuberculosis [2]. Its widespread use in the community is likely to lead to emergence of resistance among mycobacteria and delayed diagnosis of tuberculosis [3]—an occurrence that India, with its large population of tuberculosis-affected patients, cannot afford. We believe we have encountered a situation where low prices of antibiotics are likely to cause more harm than good. In the post World Trade Organization treaty scenario, governments in resource-limited countries should use their privileges of essential drug control to ensure that the costs of first-line antibiotics remain lower than those of second-line drugs. Such a government-instituted ladder in antibiotic pricing is essential to prevent the misuse of antibiotics in the community and to ensure that antibiotic resistance is kept at low levels.

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Nitric Oxide and Endothelial Dysfunction in HIV Type 1 Infection

To the Editor—Solages et al. [1] addressed some involved issues regarding the pathogenic mechanisms of endothelial dysfunction in human immunodeficiency virus type 1 (HIV-1)–infected patients. It is conceivable to think that several factors, in a multifactorial way, may contribute to endothelial injury and dysfunction in persons with HIV-1 infection.

As shown in figure 1, nitric oxide (NO) and antiretroviral drugs play a crucial and predominant role in determining endothelial dysfunction in persons with HIV-1 infection; however, to a lesser extent, HIV-1 itself, along with its viral proteins and proinflammatory cytokines, may synergize to inhibit endothelial function. It has been demonstrated that NO production is increased in symptomatic patients with HIV infection and/or AIDS, as well as in asymptomatic patients, and that NO concentrations are positively correlated with plasma- and cell-associated viral loads [2, 3]. In addition, HIV-1 and its recombinant gp120 also stimulate NO production in human macrophages, and studies have shown that NO production in monkeys was greatly increased when systemic viral load was at its peak [4].

In viral infections, including HIV-1 infection, NO, through interaction with oxygen radicals, produces peroxynitrite, which, in turn, provokes nonspecific oxidative damage in virus-infected tissues [4]. Excessive production of NO is often detrimental during viral infection, and a major target of that damage is the vascular system [4]. In fact, the control of vascular tone is one of the most important functions of NO, which maintains basal vascular tone and alters vascular tone in response to bacterial or viral stimuli. As shown in figure 1, excessive production of NO, which is directly stimulated by HIV-1, and the production of oxygen radicals, which are stimulated by cardiovascular risk factors (including hypercholesterolemia, hypertension, insulin resistance, and diabetes mellitus) cause production of peroxynitrite [5]. This molecule causes impaired flow-mediated dilation and consequent tissue damage, which contributes to endothelial dysfunction.

HIV protease inhibitors, which have been implicated as a cause of cardiovascular complication, are able to provoke...