To quote from Sir Francis Bacon (1561 to 1626): “For what a man had rather were true he more readily believes. Therefore he rejects difficult things from impatience of research; sober things, because they narrow hope; the deeper things of nature, from superstition; the light of experience, from arrogance and pride, lest his mind should seem to be occupied with things mean and transitory.” Novum Organum, Aphorisms, XLI

Our responsibility is not only to our patient but to our community. Tuberculosis is a disease of both and drug-resistant disease is a threat to both. Davidson’s results carry a clear message: it is indeed time for all physicians to recommend directly observed therapy as the first approach to the treatment of tuberculosis. Only when it is not available should we consider allowing a patient to self-administer treatment.

However, Davidson’s results also raise a second question. Why did only 70% of patients complete their course of directly observed therapy? What program elements must we create to achieve yet higher rates of completed treatment?

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Adjunctive Corticosteroid Therapy for Pneumocystis carinii Pneumonia

Case reports regarding the efficacy of adjunctive corticosteroids for the treatment of HIV-related Pneumocystis carinii pneumonia (PCP) began to appear in the late 1980s. Three controlled trials documenting the efficacy of adjunctive steroids for moderate and severe PCP infection were reported in 1990.1-3 This led to the development of the NIH consensus statement regarding use of adjunctive steroids for HIV-related PCP.4 Routine use of adjunctive corticosteroids for moderate to severe PCP in this group of patients has since become the standard of care.

Initially, many clinicians were wary of the use of immunosuppressive agents, such as corticosteroids, in a group of patients who were already profoundly immunosuppressed. The incidence of subsequent life-threatening opportunistic infections in HIV-infected patients given adjunctive corticosteroids for P carinii infections was unknown. The initial controlled trials of adjunctive steroids reported few complications of steroid therapy,1-3 however, follow-up of these patients was limited. Subsequent case reports5,6 of patients who developed severe fungal or mycobacterial infections following courses of adjunctive corticosteroids for PCP added to the concern and confusion regarding steroid therapy for PCP.

Two previous studies have specifically addressed the risk of developing tuberculosis following the use of adjunctive steroids for PCP. Jones and colleagues7 reported on a group of 144 HIV-infected patients treated for PCP in Los Angeles. After 16 months of follow-up, there was no difference in the rate of development of tuberculosis between patients who did or did not receive adjunctive corticosteroid therapy for their PCP. Similarly, Martos and colleagues8 reported no effect of adjunctive corticosteroids on the subsequent development of tuberculosis in a group of 129 patients with HIV-related PCP. These two reports provided convincing data that treatment of HIV-related PCP with adjunctive corticosteroids was not associated with an increased risk for development of tuberculosis. Nonetheless, the data regarding the incidence of other opportunistic infections in this patient group was lacking.

In the current issue of CHEST (see page 1258),
Gallant and colleagues have reported on a group of 174 patients with HIV-related PCP, comparing the incidence of 11 common HIV-associated opportunistic infections in patients treated with adjunctive corticosteroids vs those patients treated with antibiotics alone. These patients were followed for up to 7 years after their initial diagnosis of PCP. Of the 11 opportunistic infections studied, only esophageal candidiasis and tuberculosis were noted to occur significantly more often in patients treated with adjunctive corticosteroids. The increased incidence of tuberculosis was likely a spurious result, as there were only two cases of tuberculosis in the steroid treated group, and these were diagnosed at day 1 and day 963 following diagnosis of PCP. Therefore, it is highly unlikely that either case of tuberculosis was directly related to the use of adjunctive corticosteroids.

Gallant and colleagues noted no differences between the two groups of patients (steroids vs no steroids) in age, race, sex, HIV transmission category, stage of HIV infection, CD4 count, use of antiretroviral therapy, or prophylactic antibiotic usage. Since the National Institutes of Health guidelines for use of adjunctive corticosteroids in PCP were used to determine whether patients received steroids, it is likely that the patients who received steroids had more serious P. carinii infections as manifested by more severe hypoxemia than did those patients who did not receive steroids. In spite of this, there was no difference in either short-term or long-term mortality following steroid therapy, further supporting the lack of significant deleterious effects of adjunctive corticosteroids in the treatment of HIV-related PCP.

When reporting on the development of opportunistic infections, Gallant and colleagues only included patients who had not been previously diagnosed with that specific infection. The concern with this approach is that for many HIV-associated infections, especially those caused by fungi, patients may remain chronically infected following treatment for their acute illness and may require long-term suppressive therapy to keep these low-level infections from recurring as an acute illness. Any recurrences of these infections in the steroid-treated group would not have been identified in this study. However, as noted above, there was no significant difference in survival between the steroid treated vs untreated groups. Therefore, it is unlikely that recurrent infections were a significant unreported problem in the steroid-treated group.

An additional concern was that the incidence of histoplasmosis and coccidioidomycosis infections, which are very common HIV-related infections in some parts of the country, was not addressed. This is likely due to the fact that the study was performed in Baltimore where these two fungal infections are relatively uncommon. Further data will be needed from areas where these organisms are endemic to draw conclusions regarding their incidence in patients treated with adjunctive steroids.

Overall, the data presented by Gallant and colleagues represent the most thorough and comprehensive evaluation of the risks of opportunistic infections in patients with HIV-related PCP who are treated with adjunctive corticosteroids. The previously documented improvements in the acute outcome of this group of patients following steroid therapy more than makes up for the relatively small increase in incidence of opportunistic infections reported in this study. For this reason, adjunctive corticosteroid therapy should remain an essential part of the therapy for moderate and severe PCP in HIV-infected patients.