PENTOXIFYLLINE IN TREATMENT OF ACQUIRED IMMUNODEFICIENCY SYNDROME?

To the Editor:

In a recent provocative paper in Blood, Fazely et al1 reported that the methylxanthine derivative, pentoxifylline (Px), may have several effects in human immunodeficiency virus-1 (HIV-1) infection. It blocks tumor necrosis factor α production, which in turn (1) upregulates HIV-1 production in tissue culture, (2) decreases the therapeutic efficacy of zidovudine (AZT), and (3) contributes to
cachexia. We found additional data through which Px may interact with HIV-1 infection. In HIV-1–infected patients, there is an initial increase in interferon α (INF) production that later decreases, and an INF inhibitor appears in the circulation. This inhibitor interferes with both the production and the action of INF. We also found that INF production is cAMP dependent and is inhibited by prostaglandin E (PGE). Px increases intracellular cAMP levels and increases INF synthesis. PGE inhibitors Indomethacin and sodium meclofenamate also increase INF synthesis and potentiate the effect of Px. Details of the biochemical mechanisms of action of Px were discussed in a recent review. Px causes the release of PGI2, which stimulates adenylate cyclase and inhibits cAMP phosphodiesterases. Thus, the production of cAMP is increased and its decomposition decreased. On the basis of all of these data, a clinical study of Px in acquired immunodeficiency syndrome appears justified.

J.L. AMBRUS
M.A. LILLIE
Departments of Medicine and Pediatrics
Roswell Park Cancer Institute
State University of New York at Buffalo
Buffalo, NY

REFERENCES

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JL Ambrus and MA Lillie