unique characteristic not applicable to protozoa or even to all other mycobacteria[7].

In view of the clear immunological changes produced in pre-lepromatous indeterminate patients and persistently Mitsuda-negative contacts, we consider that this vaccination procedure would be very effective for application to susceptible persons in endemic areas for leprosy.

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Mechanism of Action of DDS

We are fortunate to begin the decade of the 1980s with a group of excellent original articles in this issue among which is the authoritative article by Professor Seydel, *et al.* concerning the mechanism of action of dapsone (DDS). Molecular mechanism of action studies are, by their very nature, complex biochemical puzzles, frequently seeming beyond the grasp of those of us engaged in more pedestrian efforts such as patient care, leprosy control, rehabilitation, and editing. This work stands on its own merit, of course, as meticulous basic science, but we would like to point out and emphasize that, additionally, work of this sort has profound implications for all leprosy workers.

The fundamental question being addressed by Professor Seydel, *et al.* is why is dapsone so uniquely useful in leprosy? If it were an "ordinary" sulfonamide and *M. leprae* were an "ordinary" microorganism, we would undoubtedly have been deluged with dapsone resistant cases within a few years after the introduction of the sulfones in 1941. We were not, and, indeed, it was not until after almost a quarter century of use that the first cases of sulfone resistance were documented in leprosy. Providence looked over us in our ignorance as we empirically dispensed this cheap and relatively innocuous chemical to our patients. As more and more cases of secondary sulfone resistant leprosy accumulate, and now that patients with primary resistant disease are appearing, it is clear that we can no longer comfortably rest on our empirical good fortune. If the almost unique efficacy of dapsone against *M. leprae* is due to a unique mechanism of action, it is indeed imperative that this mechanism of action be elucidated, for only in so doing can we hope to develop rational alternatives to, or rational companion drugs for, the sulfones.

In *E. coli* model systems, necessary because of *M. leprae*'s reluctance to propagate *in vitro*, Professor Seydel, *et al.* have shown systematically that, by and large, dapsone behaves like a sulfonamide in its mechanism of action, i.e., it inhibits the enzyme dihydropteroic acid synthetase. There are some clues, however, (e.g., the two phases of inhibition of growth of *E. coli* caused by dapsone) that there may be something different about the way dapsone works. The likely possibilities are outlined, and some sound familiar to leprologists, e.g., the ideas that dapsone may act in some fashion in leprosy completely unconnected with the bacterial synthesis of folic acid or that it may perhaps uniquely accumulate in leprosy bacilli. The other likely possiblities involve dapsone, either directly or through a "false" folic acid precursor acting to inhibit the other enzyme (dihydrofolate reductase) involved in manufacturing the useable form of folic acid (tetrahydrofolate). Although Professor Seydel, *et al.* show that dapsone does not seem to work that way in *E. coli*, the possibility remains that dapsone may work that way in *M. leprae*. The prospect that answers may be forthcoming to these questions is exciting not only from a basic biochemical-microbiologic-pharmacologic standpoint but from the standpoint of every frustrated clinician and paramedical worker who has longed for more effective drugs for his leprosy victims.

—RCH