CORRESPONDENCE

This department is provided for the publication of informal communications which are of interest because they are informative or stimulating, and for the discussion of controversial matters.

To the Editor:

In view of the fact that an occasional case of leprosy improves under sulfone treatment, perhaps even to the point of bacteriologic negativity of skin smears, and then—after a period of quiescence—undergoes reactivation not controlled by further treatment, I am asked to comment on the proposition: "How can it be said that, when the patient becomes unresponsive to treatment, it is because the *bacilli* have become sulfone resistant? May it not be that the body, the tissues, have become incapable of metabolizing the drug to a form that can act on the bacilli?"

From one point of view the question of "sulfone-resistant" bacilli comes in the same category as "living *vs* dead" bacilli. Delightfully, neither can be proven bacteriologically, so that only speculation is at hand, not truth capable of experimental substantiation. However, assuming that this is recognized, then the question is, "Is the state of drug resistance in the patient a matter of sulfone-resistance by bacilli?"

Most of the experimentally provable examples of drug resistance by bacteria are phenomena of persistence, or of the development of genetic variants which are not drug-sensitive. Quite possibly this occurs in leprosy. Again, I am safe in arguing this, because no disproof can be marshalled. Electron microscope evidences of deterioration, degeneration, or death of bacilli are acceptable, even though direct biologic evidence is not available. No light on the present question is provided here.

I am not knowing enough to know whether or not tissues (i.e., cells) lose their ability to acetylate sulfones, but I doubt it. Perhaps, on the contrary, their ability is increased over the years. There is some (rather small) evidence that sulfones, as sulfonamides, are reduced by acetylation. But—is the favorable action of the sulfone an integral part of this biochemical reaction?

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Comment.—Although, as stated, there is no way of proving, bacteriologically, that *M. leprae* actually acquires resistance to a drug, there is collateral evidence in findings with *M. lepraemurium*. Although general experience indicates that that bacillus, like *M. leprae*, is not cultivable, it is transmissible. Hart, Rees and Valentine reported that although that mycobacterium is at first responsive to treatment with isoniazid, it soon acquires resistance to that drug. (Isoniazid-resistant and dependent strains of *Mycobacterium lepraemurium* studied *in vivo* and *in vitro*. J. Path. & Bact. **84** (1962) 105-111). In that case bacterial resistance can be demonstrated, because lesions induced by transfers of the resistant strain resist isoniazid from the outset.—H. W. W.