



THE COLORADO FOUNDATION FOR RESEARCH IN TUBERCULOSIS

GERALD B. WEBB MEMORIAL BUILDING

4200 East Ninth Avenue
Denver 20, Colorado

June 1, 1956

Dr. Joshua Lederberg
Professor of Genetics
The University of Wisconsin
College of Agriculture
Madison 6, Wisconsin

Dear Joshua:

Just got back from the New York trip. I was gone two weeks this time, stopping for a visit with my family and with my wife's family and also spending two days in Dallas for a medical meeting enroute home. Your letter of May 17th was very welcome. I am delighted to hear that you are pursuing the study of antibiotic inhibition of enzyme synthesis.

The latest on the individual variation and metabolism of isoniazid is as follows: Gardner and his associates published in the Proceedings of the Society for Experimental Biology and Medicine in March, 1956, Vol. 91, p. 409, and Larry's brother Clint, presented their data at the February V.A. Conference at St. Louis, the transactions of which will be available in the near future. Clint made a presentation at the annual meeting of the American Trudeau Society in New York this past week and this also will appear in the transactions. The essential facts are these, we still do not have easily applicable and dependable tests for the difference between individuals. For instance, the Cincinnati group who began all this work, make a counter-current distribution study of isoniazid and its metabolites from the 48 hour urine collection, during which time the individual being studied receives two daily doses of isoniazid for two days running and has been on the drug for some time past. They have an arbitrary dividing line being high and low but they admit that there are a number of people in between. We are making the same sort of examination by determining the level of free isoniazid in blood serum at 2, 3, and 6 hours after the administration of a single test dose, and are doing it by bio-assay since there is a high blank value for free isoniazid in blood serum and we have not solved the technical problems of making the examination by paper chromatography, which is under investigation at the present at Fitzsimons. In short, we are not sure that we have been studying the same individuals as yet and we are not sure what the size of the test dose should be, we are not sure whether we can confine our examination to one at 2 and 6 hours or just to 6 hours or whether we need an entirely different type of analysis. In short we need a bit more information and data on how to distinguish between the individuals in order to cope with the problem, and we will have to have a method of handling the individuals that fall in between the extremes. In other words there is no clear cut dividing line.

I will be delighted to hear from you further in the light of the above information which is all I can give you at present. Would certainly love to visit with you about it in person when the opportunity presents itself.

My very best to you and Esther.

Very sincerely,


Roger S. Mitchell, M.D.

RSM:ch