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Adler

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH

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NEW YORK 21, N. Y.

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Dr. Joshua Lederberg
Professor of Genetics
Stanford University
Stanford, California

Dear Joshua:

Your letter was most interesting and I belatedly reply.

It is true that in my mind's eye I saw this originally as a disease of generalized hyper-responsiveness. This was so despite absence of specific evidence of antibody formation to foreign, non-human antigens. However, now I think the true story may be somewhat different. E.g., we have immunized a group of patients who were in remission and off steroids to typhoid and compared their response to supposedly normal controls. Despite three booster shots, these persons did not develop titers in excess of the controls. We are now beginning a study of T agglutinin titers in lupus patients. At this time it must be said that there is no solid evidence of an excessive response to antigens other than those from human tissues. If future studies confirm this, then the hyper-responsiveness of the patients will be limited to their own tissues (and perhaps other human tissues as in the blood group reactions). Such a situation might represent an interesting application of clonal selection with the ever-present autologous tissues acting as the antigens which stimulate growth of the clones.

It would indeed be interesting to titer sera against rare Salmonella antigens and perhaps we should do that as a part of this study.

Your thoughts about the relationship between SLE and agammaglobulinemia are quite interesting. We are in the process of attempting to conduct tissue culture and transplantation experiments, using tissues and cells of these patients. I anticipate a great deal of difficulty, but if we can succeed in crossing the species barrier for any period of time, we may be able to examine more closely the growth characteristics, protein synthesis, and cyto-toxic effects of some of these presumably abnormal lymphoid cells. Perhaps I am wrong, but research in this field seems stymied by the lack of an experimental model. Transplantation may give us some leads.

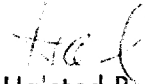
One interesting facet that seems fairly well established is the existence of bizarre rheumatoid-like serologic abnormalities in clinically normal relatives of patients with SLE. This, coupled with the high incidence of rheumatoid arthritis in other relatives, suggests that there is some sort of familial immunologic abnormality which may express itself as either disease or only as a peculiar immunologic responsiveness devoid of symptoms. In such families we may also find fertile tissue for study.

I look forward to your results with the fluorescence experiments.

Under separate cover I will send the reprints you requested.

With best regards.

Sincerely yours,



Halsted R. Holman, M.D.