June 19, 1952

Dear Dr, Inoki:

Thank you for your letter and the papers which arrived a day or two ago. Your account of antigenic variation in Trypanosoma was very interesting indeed. You certainly should seek to present it at the International Congresses next year, if you can find funds to travel to Europe. I do not see just how I can assist you in this respect. If you travel via the U.S. I hope you will have an opportunity to visit Madison, and to discuss the possibility of working here for a time. I am doubtful that this laboratory would be the most suitable, as we are mainly interested in bacteria, but I trust you are also in correspondence with Professor Sonneborn.

On the face of it, your interpretation of the antiserum-induced variation seems entirely correct, although it seems incredible that such changes could occur so rapidly in a medium that will not support growth of the trypanosomes. It should be noted that some of the Paramecium transformations will occur in a few hours, before any fission has occurred, but you should consult Sonneborn for the details.

Your note on Trichomonas was most interesting, but I regret that I am not competent to evaluate it. For your trypanosome work, I think that it would be desirable to report some more experimental details, especially the controls which show that , in vitro, the induced return to the original serotype gives trypanosomes which react specifically with serum for the O- and none of the others, I appreciate the limitations of using mouse-serum for the reagents. Would it not be feasible to vaccinate rabbits to obtain larger quantities of antiserum for each of the serotypes, especially for the in-vitro experiments?

It is indeed surprising that, in your vaccination experiments, trypanosomes which respond in a few minutes to antiserum in vitro remained unchanged for many days in vivo! Have you tested freshly drawn blood mixed with trypanosomes? Can you inoculate a heavy dose of O- trypanosomes in an O-immune mouse, and then remove blood samples, keeping them in vitro for various length of time to look for the change?

Metallagy is as good a word as any. Before introducing it into the literature, itb might be better to wait until the mechanism is more thoroughly understood.

Are you acquainted with other work on antigenic variation in trypanosome relapses (and with the comparable studies on Borrelia)? They are reviewed by Harrison in the Ann. Rev. Microbiol. 1947. I did not understand the reference 15. in your paper from the Osaka Un. Med. J.

Sincerely,