

July 8, 1975

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Dear Egon,

It was certainly a pleasant surprise to see you at the WHO restaurant. I am sorry we did not have just a bit longer to chat together. I hope you may have at least a few minutes while you are in Palo Alto if you in fact receive this, before you are again on your way.

You asked me to put down in writing some of the comments I passed to you about the possibilities and some research needs with respect to passive immunization against sperm.

The main point is that by anyone of a number of methods it is a very reasonable prospect that some time in the next five or perhaps ten years it will be possible to produce large quantities of specific human antibody globulins. My own favorite candidate of technology for this purpose is DNA insertion, and I have written a little piece about that which I am enclosing with this letter. Perhaps you will have noticed the article by Stanley Cohen in the current issue of Scientific American which gives a rather nice review of the background of this whole story.

At any rate, the possible advent of such antibodies puts a new wrinkle on the prospect for immunocontraception. I am sure that there have been a number of people who would share my own concern about establishing active auto-immunity as a mass technology in this particular field. But if we can really get fairly cheap antibody protein, I think it does open up a somewhat different approach although, of course, it is likely to be more costly to provide the actual delivery of the material than a single active immunization. Even in that context I think that there is likely to be better general acceptability of the active approach if there has been wide experience with passive immunization for that.

If you will just grant me the stipulation that such materials will be available, then it is fairly obvious that there are a number of experiments that should be done fairly soon. The most cogent, and I am not aware of any report of it, would be to demonstrate the passive transfer of sterilizing anti-sperm immunity from man to man. Since you should be able in favorable cases to establish a diagnosis of autoagglutination as a way of monitoring the effect, this of course will mean a much simpler experimental design than a more complete demonstration of male sterilization. The information would

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also be very important in enabling us to learn something about the dynamics of secretion of the antibody or subsets of the antibodies of various types into the seminal fluid. And I am sure you can use your imagination to look into the question of various sources of such antibodies which may include women as well as men and perhaps vice versa.

One point that I do not think anyone has considered is the potential bearing of the rather prevalent autoimmunity that we already know about on the distribution of blood for transfusion. I am not suggesting that this is an urgent risk but I think that people should be at least aware of the possibility, and of course it does mean that the experiment that I am advocating may already be being done as a byproduct of other clinical measures! And I certainly think somebody should look into the anti-sperm component of the pooled gamma globulin which is used in a variety of prophylactic ways.

Since there is still a great deal of confusion about the distribution of IGG versus IGA activity in these cases, I hope that you will be able to keep a lookout for that!

The same principles might of course apply with respect to antigonadotrophic hormone activity by passive transfer. I do not know if you have seen very many in human sera having that component.

I might mention to you that I am trying to get a number of people interested in the actual (and that probably means commercial) development of these ideas. So, it seems to me that it would be a very useful bench mark to look for the production of a diagnostically valuable immunological reagent before undertaking the very difficult steps involved in validating therapeutic efficacy and safety.

I wonder if it would not be particularly useful to attempt to get a clonal antispecific antibody preparation directed against the active site of either LH or ICSH or whatever other candidate hormone you would like to recommend! If you have any ideas about the most pressing needs in this direction, I would be happy to hear them.

Along the same, if you can refer me to any literature on the more detailed immunochemistry of the antibodies that have been studied so far in this general arena, I would be most grateful to you. We have to try to find an antibody whose active site is mostly located on a single chain, probably preferably the light chain of the gamma globulin. I just do not know if anyone has carried studies of the specificity of these antibodies to that degree of refinement. It just seemed to me that it would be important to first establish some groundwork with material that would be useful in a diagnostic sense before taking the more courageous steps that would be involved in the development of therapeutic preparations.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

JL/rr

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