

September 16, 1947

Dear R C,

We're anxious to hear about your trip to Greenland and what you found, I hope that it was interesting. I'm glad that you are having a chance to travel in that way and hope that you will be able to go to Europe to supervise the field trial of the pro. I feel that you are the one to do it, for it is your baby, and you should have the opportunity. By now you should have seen the formal report that I sent up on the GC work to date, and it looks good to us here under the conditions of the experiment. It has been given a much more severe test, so it seems to me, than it would get normally. But to fit the circumstances more nearly to the usual modes we have begun now to wait one hour after application and to let the patient apply it. We shall do much more work on it and shall continue the normal exposure. We're getting another group ready for next week, the first normal exposures in some time. We felt that we would wait, for there had been a good deal of talk among the officers in the Guardia de Honor where we were working. But now we shall work for a while in another installation. The letter to Dr. Mahoney was written because Sacha said that Dr. <sup>W.</sup> wanted it to use in keeping other workers out of here, but the fear of too much talk is constantly with us, and ever so often we hear remarks from people, such as some of the American Army here, who should know nothing of it. But we can't avoid some talk, for the American Military mission is working here with the Guatemalans, as they are working with all other Latin-American groups, so that some talk must get around.

We are toying with the idea of using normal females for some of the contacts and then inoculating them afterwards so as to pile up a sizable group of treated and control patients. And, if Dr. Tejada approves, we could go to the Guardia and treat a portion of the 100 odd men receiving pro nightly with inoculation then prophylaxis further to increase our numbers. This would involve keeping a reservoir of infection, but we think that that could be arranged at the Military Hospital. That will have to wait for a while, but it is in our minds and will be pushed if at all feasible.

Dr. Salvado will be away for about 6 weeks, so that we shall be able to do no significant local studies during that time, but we want to try some three hour applications in mucin and to the unclean penis before he leaves if it can be arranged. While he is away we shall have the normal exposure going on, for the mechanics of that are arranged except for starting, as we are waiting for the girls to show a few xxx signs before starting them into actual work. Perhaps we shall be able to do that late this week, for I have a date to examine them tomorrow. We are beginning to have some hope for the application following scarification of the penile membrane, for on Friday several of the patients showed signs of small papules at the site which may be significant. But we shall have to wait another week, so do not get hopeful. We feel that there is probably a good deal of penile trauma during intercourse with breaks in the membrane, for our observations on the groups of men following the GC work have shown for the most part reddened and battered-looking penes suggestive of trauma and dissolution of continuity of the membrane. We have begun some studies using application of dye following exposure but are thus far working on with fluorescein and would appreciate your suggestions and sending of any dyes you think should be used, for they are hard to get, often non-obtainable here.

but we are all very sure that the reactions are not due to syphilis. We spent the last week end in Puerto San Jose and shall send you a more detailed analysis as soon as the reports are ready.

In the first group at the penitentiary inoculated with the Nichols strain all of those with negative cardiolipin and a positive and/or doubtful Kahn and Mazzini (up to 32 Kahn units) were effected, and six of the seven in the group developed secondary syphilis, but there was not one typical chancre formed. Of the twelve with positive cardiolipin, Kahn and Mazzini only three showed serologic evidence of infection as evidenced by significant increase in titre, and all of the three had three or less Kahn units as the initial titre. If we accept the hypothesis that a previous, untreated infection with syphilis confers some degree of immunity to re or superinfection then the fact that the group in which the cardiolipin reaction was negative showed no resistance to infection; while the group with positive cardiolipin showed significant resistance suggests that the cardiolipin reaction is much more nearly specific than the others. We are thus securing proof of the significance of the cardiolipin reaction in an immunologic manner.

With the opportunity offered here to study syphilis from the standpoint of pure science just as Chesney studied it in the rabbit it should be possible to justify the project in the event of the impossibility of resolution of the prophylactic program. But we feel that we shall be able to subject prophylaxis to a severe trial. Along the same line of thought of investigation in pure science I shall have a chance later to do a survey on a small group of pure Indians being worked by the Carnegie institution. If any interesting findings result it may give us new leads for investigation on a purely scientific basis. But from the small sampling of tests that have been taken from the new draftees in the Guatemalan Army, many of whom are Indians from the backwoods it is my guess that we shall find only a relatively small number of cardiolipin positive reactors, but a much larger group showing positive or doubtful Kahn and Mazzini reactions.

We think that there is justification, a gain for purely scientific reasons, for serologic investigation of the role of the liver in the false positive reactions. For there is a very high incidence of liver disease here. Knowing the effect of dietary deficiencies in the pathogenesis of liver disease, knowing the high incidence of deficient diet, knowing the incidence of chronic and acute malaria and the effect of malaria on liver disease, and knowing the high incidence of false positive reactions it seems that further study of the relation of these factors to the false positives is justified.

As we have indicated to you before it is our opinion, based on a growing body of evidence, that the VDRL Cardiolipin test will prove to be ideal for use in countries such as Guatemala and others having similar conditions. Thus we feel that a thoroughgoing study of the reaction should be carried out. With sufficient data it should be easy to secure general acceptance of the method throughout the Latin American countries who are badly in need of a simple, reliable method. Thus with the vast amount of fundamental work to be done in experimental syphilis in man and in serology it should be easy to justify continuation of the study even though we are not able to study simple prophylaxis as originally planned. But we feel that at the same time we shall be able to study prophylaxis by other methods and to subject it to much more severe tests than those occurring normally.

Sincerely,