

April 18, 1953

Dear Spice'

Esther and I were greatly distressed to hear of your bout with Brucella. We hope we shall not have to wait too long to hear of your permanent, complete and prompt recovery. You indicated this was a lab. infection: do you know how it happened?

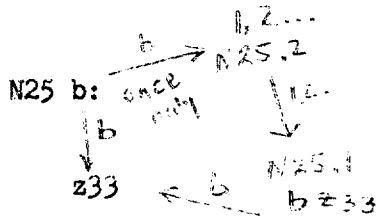
Evidently we were only lucky not to have picked up some other bugs around Atlanta! Witness Ike's recent attack of food poisoning (picked up at Augusta, just prior to his policy speech a couple of days ago— or do you get to hear such details in your press? I will admit one fish platter at Atlanta left me feeling rather dubious, but I terminated the experiment before the outcome was well-defined.

To turn to in vitro Salmonellosis, I agree with you completely about the futility of chasing every will-of-the-wisp of cross-reactions. I think, however, that Felix' statements (as opposed to his practice) are rather extreme and that we have to take and use the K-W scheme for whatever it is worth. It would be very helpful if someone more critical than K, but still sympathetic with the purposes of the scheme would review the whole question of the serological structure of the group. I suspect either JT or PNE could do a fine job, if they could be persuaded to do it. [I note, by the way, that a b/1,2... cross-reaction to a titer of 1:200 is recorded in Edwards & Bruner's Kentucky circular]. I don't want to go into this sort of thing myself any more deeply than I have to, to settle ambiguities that may arise in other problems. The only real point of the c-c' story is its bearing on monophasicity, and the selective or inductive effects of serums. Obviously, one has to be well aware of even the minor cross-reactions in using serums for this purpose. Edwards, at the moment, seems to suspect that c' is the somatic antigen, which would put the formalin effect more or less in line with your H901K. I am not too deeply concerned about this, except that in my single trial c' appeared to be thermostable. The more important point is that this reaction will explain the effectiveness of some serums and not others in provoking the c phase from Kunzendorf.

As time passes, my recollection for the details of your experiments becomes rapidly dimmer. But was not the O-inagglutinability of your 901K only part of the story? I thought you had a IV-V serum which agglutinated 901K, but did not agglutinate alcoholized or 0-901 in control titrations. Have you identified this reaction?

The anomalous 1,2 phase story gets more complex daily. There are two Java strains to keep in mind, N25 and N97. On a single occasion, each of these strains have given rise to 1,2.. phases, apparently serologically identically with the second phase of typical paraB. N25 ph2 is Edwards #157, has never shown any alternative phases in serum selections ($\frac{1}{1,2}$; $\frac{1}{1,5}$; $\frac{1}{2}$), and in all transductions, to and fro, behaves as if it were $H_1^{1,2} H_2'$, so that, for example, #157 —x S. miami ($\frac{1}{a,5}$) gives 1,2:1,5. I have not done much with N25 ph 1, but one experiment is consistent with its being H_1^b . N97 ph 2 has not been studied serologically as fully as #157, but appears to be the same. However, it fairly readily gives back a ph 1 when selected in 1,2 serum. These phases however show a strong but variable reaction with z33 which is unlike the original N25. (as well as $\frac{1}{b}$)

This may not mean too much: both the original N25 and the return bz33 will give rise to z33 phases more or less regularly after prolonged selection in b serum. The sequences can be diagrammed:



I would not place too much emphasis on the irreversibility of phases until the possibilities of interfering cross-reactions are worked out.

All of this would be entirely consistent with a set of mutations from one allele to another. One could in fact put the b complex down as:

b.z33.1,2,...., with the components usually expressed in the order given. This would have

nothing in particular to do with the typical phase variation of b:1,2 in paraB. I forgot to mention that N25.2 also behaves as $H_1^{1,2}$, e.g., in —x S. miami.

But last week I got another startling result which has been very upsetting:

SW 623 (= TM —x SW666, i:—) —x N25 gave an i transduction whose second phase proved to be b. As with N25.2—1, the b phase was not, however, reversible. But one still would represent this beast as IV V XII i:b. For a time I took this as evidence that N25 is genotypically $H_1^{1,2} H_2^b$, but with a very sluggish phase variation.

This was tested, however, by N25—x S. miami, and the result, IX XII b:1,5 shows that the b phase of N25 is a phase 1 homologue. We have the situation, therefore, where the b; 1,2; and (by some indirect evidence) z33 phases of N2 N97 are all homologous with the a phase of miami and the i of TM, i.e., are all H_1 alleles. This does not account for the b:i anomaly, unless N25 is $H_1^b H_2^b$, which seems unreasonable. Some further

tests have to be made with the b:i stock to determine whether it is actually undergoing typical phase variation, i.e., a shift between two loci. So far there is no specific evidence of the homology behavior of the b and i factors. It may be that too much emphasis is being placed on the single occurrence of this type, and that it plays no real part in the scheme: I have to see whether it can be obtained reproducibly.

We've just received the SGM preprints for the adaptation symposium. I'm really quite surprised at the numerical strength of the direct adaptationists. I hope someone pointed out Hinshelwood's improper application of indirect selection, (galley 15). It is a little hard to see how 2×10^7 cells could have given visibly single colonies! It is nowhere clear whether he had actually identified a mutant clone in his first plating; his second plating, in which one of a hundred colonies gave rise to a mutant must certainly have been a completely independent mutation occurring late in the development of this colony. On this basis it is not surprising that 2/107 of the cells in this colony were perfectly typical sensitive. It is altogether horribly muddled. Was anybody taken in by it? [P.S. We discover we have two copies of the SGM directory, dated 1951. Is one of these conceivably yours?]

Do you recall our discussing the chemical unity of the somatic antigen complexes? The paper seems to have been overlooked by subsequent reviewers, but K. Meyer did a job on TM which seems to indicate the identity of the IV and V components of TM (which seems unlikely on other grounds.) I haven't gone over the paper carefully: it's in Ann. Inst. Pasteur, 62:282, 1939.

I hadn't time to hear more from you about Bernstein, and have encouraged him to come over. I hope he doesn't get snagged on visa problems. It is almost impossible to find anyone with that kind of training to go into bacterial genetic research over here; most of them come from general biology and genetics rather than medical bact.

As my last letter indicated, we're getting rather low on some of our serums, particularly b, 1, enx and esp. 1,2,3. If there is any material way we can return your past and prospective generosity (e.g. bacitracin....) give us the word.

Yours,