

November 6, 1952

Dr. PrR. Edwards  
Box 185  
Damblee, Georgia

Dear Dr. Edwards:

Your note of the 4th on your prospective review for Bact. Rev. just came in. I shall be looking forward very intently for a review based on such an outline. Your decision to omit a consideration of nutritional variation seems appropriate, not because of any question of personal qualifications, but because these are primarily laboratory tools. The Salmonella group gives one an unexampled opportunity to contrast laboratory findings on the mechanisms of variation with the natural occurrences of the variant types, and the geneticist is just as anxious as the bacteriologist to see an emphasis on this. The only biochemical variation that might still be worth thinking about would concern those markers that do seem to ~~have~~ have some taxonomic value-- xylose and rhamnose fermentation, and anaerogenicity. It is quite a puzzle that these should be correlated with serodiagnosis even as well as they seem to be. It should be within 3 months that I will have an opportunity to ask you many more questions on your views on these questions.

The PS. to your note has set me off on a bit of a guessing game as the special "niceness" of the last batch of cultures. By way of retaliation, I will set down some of the things that would be worth looking for. First let me mention that I have been getting some perplexing results on the apparent b-agglutinability of the "O-form" ~~aka~~ Kauff. #248 from which many of the new cultures have been derived. Incipiently rough suspensions have reacted quite specifically with my b reagent (used in slide agglut. at 1:100 tube titre), but when cultures were made from purified rough colonies, no specific agglutination was seen. It seems to me that there might be some residual b substance in these cells, with or without flagella, that cannot be detected in the normal O cells. This would be consistent with our genetic conclusions, namely that #248 has the apparatus for producing the b substance, but not for putting it on to active flagella. Agglutinogenicity and mirror absorption tests should give a definite answer, but I want to discuss this with you in greater detail. SW-672 turns out to be b-1,2 (according to my test), i.e., a serotypic paratyphi B from typhimurium X-abony. I have since done this experiment on a larger scale, and it looks as if only one phase is transduced at a time, so that from abony X-typhimurium, as well as the converse, b-1,2 and the new serotype IV,V,XII ~~item~~ have been engendered. Spicer brought a few addnl. sera with him, so I have been able to check up, by crude slide agglutination, on some of the other cultures I sent you. SW-675 (#248 X-altendorf) is evidently not c. I do hope that the "j" phases [e.g. also 676] turn out to be recognizable. However, I do have a new S. typhi X-altendorf which seems to be IX,XII;c:+ and another, X-heddelsberg with r:-. I may have interchanged SW-680 and 681, or one of them may be impure b/i. They had been through one single-colony isolation.

To return to the guessing game, the following possibilities run through my mind as things that would have to be looked for. The odds are even as to genetic predictability:

1. Phase variation gp--1 or gp--1,2 in SW-674. [Unlikely on grounds of absence of natural occurrences].
2. Somatic recombinations
3. Separation of components of gp, gm, or enx [Conceivable on basis of
4. Monophasicity of SW-668 [probable] [I have, in this connection, a #248 X- san diego, which may be either eh-- or eng--, more likely the former. If so, it may be the counterpart of your #150. It is being sent as SW-664.]

A rather striking finding has been that, as a rule, phase II is not transducible to #248 (e.g. in tests of FA from S abony<sup>2</sup> and typhimurium<sup>2</sup>). The outstanding exception to this has been the second phase of your #157. In our hands, this has been monophasic 1,2. Do you know its previous history, and how it comes to have the specific label paratyphi B? Is there anything distinctive about the serology of the flagellar phase, aside from its stability? Our sub. of your #3 sometime picked up an immigrant, quite likely since it was first received. I did not immediately identify it, but am returning it as SW-703CONT., on the unlikely chance that it may interest you (and for id~~id~~ curiosity on my part).

Dr. Spicer has been trying to do transductions in group C and E with homologous phages, but so far no luck. Different phages may, however, have some individuality in their effectiveness for these experiments.

The abony-typhimurium experiments are leading towards some sort of genetic theory of phase variation, quite different from anything that I had anticipated. The alternate phase is latent in the cells of a given phase, but is not expressed in the FA from it. This leads to the notion that there are genetic factors for each of two phases (probably at different genetic loci) in either phase of a diphasic type, but that, for lack of a better way to express it, one is "active" and one is "suppressed" at any given time. The surprising thing is that the "suppression" is very closely connected with the genetic factor itself, and is not a matter of changes elsewhere in the genetic or physiological makeup of the cell. There is nothing quite like this in physiological genetics to date, although it does resemble some speculations on the genetic basis of embryological development and differentiation. I don't expect that this condensed discussion makes much sense.

I am sending a further group of cultures under separate cover, as listed herewith.

Sincerely,

Joshua Lederberg

P.S. Thanks for the last sera, but the cultures never did arrive. However, as I could not yet prepare an FA from eastbourne, which we had gotten before, this combination of strains would not have been as useful as I had hoped. Please let me withdraw this request for the time being. JL