September 23, 1953

Dear Bruce:

This is in answer (I have to admit) to your letter of the 19th marked "urgent— re reprints", but I have been waiting for an opportunity to write you anyhow, about nothing in particular. I am surprised to realize that my last letter dates from about the first of June-- not entirely a matter of conscience, but also the appreciation of how many months have gone by without any particular happenings worth talking about. This time was consumed partly in summer indolence:: it was one h' of a hot summer here, and partly in frustration on such matters as getting our space remodelled. It has not been, and we are almost as cramped as ever. However, we did make a trip to San Francisco, unfortunately too hastily and by car. There was some compensation in visiting Tatum and van Niel and other old friends; much less in the S.A.B. meetings and connected business which obliged us to come. We thought often of your remark that there were stretches of 200 miles or more with no sight worth seeing, and did our best (perhaps not successfully) to deny it to ourselves. We also thought how entertaining it would have been to have you in the back seat reading pig-Greek letters out of the BMJ while we drove, as in times past.

One reason we did not insist on writing sooner was our confusion about your moving and travel plans. How long did you spend in Europe, and when are you going over to Lister? I suppose if we adopted the scheme of a circular letter to our multifarious friends abroad, you might hear from us more often, but I am not sure I wholeheartedly approve of such an arrangement.

Helen Byers was abroad this summer, as you probably know. But among her souvenirs was a good case of Entamoeba histolytica, as the doctors here finally diagnosed it. She will, I trust, get over it fairly soon. By way of other news, Aleck Bernstein arrived a week ago, and is already well started in some recombinational essays with E. coli O-55 and O-111. Esther had previously gotten some encouraging results in test crosses with K-12; the only serious point that can now be foreseen is the separability of the O and K antigens. But after this introduction, I expect he will be working on some of the Salmonella problems already started and mentioned in earlier letters. Dave Skaar just completed his term here and has taken a job at Cold Spring Harbor in Bryson's lab; neither of us knows just what for. Larry Morse just completed his certification (i.e., most of his courses) and is slugging along admirably in the E. coli (Gal) transduction. The matter is too detailed just now to be summarized briefly; the most interesting aspects are the correlation of transduction with lysogenization, and a special system in which nearly every phage particle is effective (sic). However, the transduction continues to be limited to a cluster of closely linked "pseudo-alleles" concerned with galactose fermentation. Also in E. coli, Tom Nelson (whom I do not think you met) has been accumulating more data along lines previously discussed [cross-over hemizygotes for the Mal/S segment in diploids] which quite conclusively require a post-zygotic elimination from a complete diploid heterozygote. This does not directly rule out the Watson-Hayes proposal for a prezygotic elimination as well (i.e. deficient gametes) but makes it superfluous. There were several other features of this proposal that could not meet all the facts, e.g., aberrancies in the segregation ratios of markers from diploids already heterozygous for them, and to leave the diploid story, the expectation that the two complementary cross-over classes for any "unselected" chromosome has not been met in any studied case. I have had some encouragement in cytological studies with Hfr x F- and am beginning to spend the larger part of my time in this work. This covers most of our staff; Esther will possibly be writing an additional letter of her own. Susan Beveridge has quit

school, cut her long yellow hair, and is engaged to be married to an ex-Marine, art-student, once-divorced man rather older than herself. [I recall her tender concern about your nutrition!].

We were pleased to have a visit from Hayes about two weeks ago, just after we had settled to a new house (still rented) not far from where Jim Crow lives. He was as affable a chap as everyone had told us, and I think we were soon agreed that there were more terminological than substantial differences in our discussions of E. coli recombination. There are two major differences, however: 1) whether defects in the zygotes stem from already deficient F+ gametes, or subsequent to mating and meiosis, and 2) whether there is an F+ agent, separable from the bacterium, which has at once the properties of converting an F- recipient and occasionally of transducing a substantial (if in fact not the whole) part of the genotype of the F+ to the F- cell. I already mentioned some of the evidence that inclines us to our particular views with respect to 1). As to 2), all of the known properties of the "F+ agent" correspond to what we have so far been able to identify only with the entire cell, and there has so far been no shred of evidence for a sub-cellular agent with the two crucial properties (or, in fact with either). Until the agent has been separated from the cells, I doubt that 2) has any real substance, and I am pleased that Hayes intends to devote considerable more attention to this so far unrewarded task. When (and if!) such a separation is made, it will be possible to test the putative role of the agent in recombination itself.

As to Salmonella, I spent altogether too much time on S. abortus-equi, and on the java H_1^b $H_1^{1,2}$ duplication without any particular advances of understanding. S. gallinarum --x H-901 finally did work as well as the previous --x IX XII a:— to bring out the gm: the trick is to use a recently motilized culture of H-901. Edwards finds (by the usual reciprocal absorptions) that the gm transduced from gallinarum is identical with that of S. enteritidis; there is no other very obvious biological link between these. I am satisfied that S. pullorum (Edwards #75) will also transmotilize O-901 (tracks, very occasional swarms) but have not yet found any evidences of H transduction. In some few other experiments on miscellaneous phages, k (determinative in S. typhi for Vi type K) and B.A.O.R. (typing phage for S. para(B) are both reasonably competent in transduction, but with rather restricted host-ranges, so they are not much use, except for trials of S. typhi—x.... I am not at all happy about any rationale for the host range of PLT22 (as well as BAOR) in view of occasional plaques on group C cultures. These have not been accompanied by any transductions, and I have still to verify that some other phage is not responsible.

You may have heard some odds and ends (e.g. from Kauffmann) concerning the coincidental transduction of I and V somatic antigens. We have run across these too, but I don't trust them as true bills. In similar experiments, we have also seen losses of the same antigens, and neither event has seemed to be correlated with the presence or absence of the corresponding antigen in the transducing source. I would (tentatively) conclude that the somatic antigens may play a secondary role in the dynamics of selection on semisolid agar, and that they are involved only in spontaneous variation.

(carriage included)

As to reprints, I think we can afford to pay up to $120 for our share. I suggest you order any number (up to 1000) that can be covered by our joint contributions. It would help then to have 100 shipped directly to Norton, and the residue here. If you are able to share evenly in the costs, naturally so much the better, but a proration (with this Department also covering Nortpn's share) would be equally acceptable. If the JGM follows the practise of most other journals, the unit cost should be substantially less on an order of 1000 than the price quoted for 100. If possible (and not prohibitively expensive) I would suggest shipment by post rather than ocean freight, from the angle of saving both time and customs formalities. Quite likely the reprints will be large enough to qualify as "books" for which the rates are fairly reasonable. If the bulk shipment is to be made by freight, can you arrange to have a sample (say 25 or 50) sent by post? Please let me know just what order is placed so I can pre-arrange payment.

I would indeed like to accept your offer of the abstracts of the Rome meetings. However, to avoid having to send these back, would it be possible to purchase them from or through you? I have a credit at the Bank of Bushey Heath (Spicer) to the amount ca. L.3:-- available for such a purpose. Do you know anything of abstracts of the Bellagio meetings? I had remitted $10 for advance registration in hopes of receiving these abstracts: did any appear?

Various people have told us that your position at Lister is quite a prize. The very best wishes to you! Our only regret is the diminished likelihood that you might ever be persuaded to abandon England in favor of a post closer to our own hand.

Yours,

Joshua Lederberg

P.S. Thanks for the various cultures received over the summer (The TM's and the typhi and paraA 0-forms). Have you made up a comprehensive chart of the motility interactions? I may have mentioned some other miscellaneous cultures in NCTC in past letters, but I will communicate directly with Colindale about these. I have not heard from Spicer about SW-684 (the possible Gal y). Could you simply return the culture (or a sub from it) without checking?

If I haven't mentioned it before, the paper with Edwards has been accepted by Journal of Immunology, and is scheduled for October or November 1953, if you want to correct the reference.

In re Q. yours of 6/30: I never have seen a swarm initiating from a trail, but I doubt if it would be visible: the microcolonies of the trail would probably be scarcely larger than those of the immigrating motile cells. One would have to judge from an apparent extra-marginal center of a swarm and this is dubious. So there is not necessarily any contradiction in of the manipulation with the agar experiments. For all we know, the trails might represent a phenotypic lag in the effects of a Fla^+ factor transduced to a cell which later segregated Fla^+ but inviable (possibly lysed) and viable Fla^- karyonides. To account for the failure of branching, we would have to suppose that the phenotypic effect was localized and not proliferative, viz. a flagellar bundle, or anlage thereof. This picture might account for the production of nonmotile, temporary motile and stable motile individuals in a single clone.