

November 18, 1951

Dr. Harry Eagle,
Microbiological Institute
National Institutes of Health
Bethesda 14, Md.

Dear Harry:

Thanks for letting me see your ms., which I return herewith.

Unfortunately, Table 3 seems to be missing: I hope you have it.

I think that the factual content is so clear as to obviate any discussion, and I was pleased by the rather clear statement of alternative interpretations. I might wonder at the extensiveness of the general discussion in this clearly preliminary paper, but it is obvious that you are preparing your readers for more and better to come. I had not seen Gibson and Gibson's note: their suggestion seems to be very plausible. As you point out yourself, however, the data of the present paper offers no basis for a decision as to different hypotheses.

Without Table 3, my critical machinery is somewhat impaired, but I take it that the main conclusion is that the resistance of selected types is related to the concentration at which selection was exercised. But it is only at moderately low survivorships that the experiments can give any definite information. It would be of interest to know just how precise the generalization can be made, e.g., with comparisons of replicates of the same isolate, of different isolates from the same concentration, and of isolates from slightly different concentrations, to determine just how smooth the "stepless" distribution of resistance increment really is.

The one point that confuses my thinking the most is a lack of apprehension of what is being measured when a cell suspension is plated with an antibiotic. The interplay of bacteriostatic and bactericidal effects will have to be clarified before I can pretend to understand such experiments.

Since I cannot be very useful with respect to content, I wonder if you would be interested in some poor suggestions on form, offered for whatever you care to do with them.

1. Lederberg '52 should be Lederberg, J. and Lederberg, E.M. 1952 (Replica plating and indirect selection of bacterial mutants. J. Bact. In Press.) The editor would probably complete the reference from page proof. We returned the galleys a week ago.

2. Do you prefer or distinguish "adaptative" from "adaptive"-- the latter is in more general use.

3. (p.6 line 10) What are "several logs"? Do you mean decades, e-kades? How about proportional for linearly related.

4. Annals (de l'Institut Pasteur) should be Annales, or Ann.
5. May I suggest some references that may illustrate your points as well and perhaps be more accessible or up-to-date than some that you cite, especially with regard to induced genetic effects:

Sonneborn 1943 is not apropos. May I suggest instead a comprehensive review article:

Sonneborn, T.M. 1950 The cytoplasm in heredity. *Heredity*,
4; 11-36. or
1951 The role of the genes in cytoplasmic
inheritance. In, *Genetics in the 20th Century*, MacMillan.

For Ephrussi's work:

Ephrussi, B. 1951 *Remarks on Cell Heredity*. Loc. Cit.

In connection with both of these, you might be interested in Provasoli, et. al., 1948 Streptomycin-induced chlorophyllless races of *Euglena*. *Proc. Soc. Exptl. Biol. Med.*, (N.Y.) 69: 279-282

Brown, C.H. 1950 Elimination of kappa particles from "killer" strains of *Paramecium aurelia* by treatment with chloromycetin. *Nature*, 166, 527. (9/23/50).

The one other promising case I know of is the induction of parabasal forms of trypanosomes with various dyes. You must know this literature better than I do. If you know of a modern treatment of the problem would you let me know about it?

Yours sincerely,

Joshua Lederberg