9th July 1954

Dear Professor Lederberg,

Thank you for your letter. I quite agree with your remark about the possible prevalence of cross purposes. Among reprints which I am sending you separately you will find one by A.A.Eddy on yeast and galactose which describes behaviour quite different from what Baskett found with D-arabinose and from what Dean and I have recently found with Bact. coli mutabile and lactose. Moreover, Brenner, who has been working on phage resistance here, finds very sharp contrasts between the phenomena which he has observed (or confirmed) and the behaviour of aerobacter with proflavine. We both felt that much phage resistance is the result of a destructive mutation, though the establishment of lysogenic systems I believe to be another example of the "gearing" of metabolic systems.

I might explain that for a very long time my aim was to show chemists that the machinery of living systems could be of interest to them. That a cell should only gradually develop its capacity to attack a sugar did not seem to me necessarily to have more evolutionary significance than that hexane vapour and oxygen show a long induction period before visible reaction sets in. I think I should still be surprised to find that simple substrate adaptations were of great ultimate significance (except of course as clues to cell mechanism). I agree that resistant forms are harder to judge. I feel pretty sure the mechanisms of resistance are varied. To mention only one point ; proflavine resistant cells of aerobacter take up more drug than normal forms, whereas phage resistant coli cells may not adsorb at all.

The strain of Bact. lactis aerogenes will be sent to you as soon as it can be prepared for transport. As to the strain trained to D-arabinose this may take a little time to culture since we do not normally preserve sub-strains of this type. The adaptation to arabinose is pretty persistent after 5-10 passages in an ammonium sulphate-phosphate medium with this carbon source. The lag in a liquid medium always lengthens by a few hours (as compared with the initial days) out of contact with arabinose, or the plate lag by perhaps half a day.

You raise a question about the paragraph on replication. The 2×10^7 cells of the inoculum were not counted of course on the resulting plate but inferred from a parallel roll-tube count on a dilution. The statement that single colonies were visible on the plate is, I am afraid, a little confusing and irrelevant. Reference to the records shows that all that was meant was that the practically confluent growth did show under magnification the kind of appearance which a newspaper photograph would show rather than the kind of pellicle one gets with "spreaders" like B. subtilis.

Yours sincerely,

C. N. Hinshelwood