June 16, 1942

Dear Peters,

Do you remember my suggestion that, as the drug is only supposed to affect growth through its action as a disinfestant, it seemed unreasobable to make the same allowance for initial egg count to sheep at different dosage levels. I mentioned that, although regressions on egg count appropriate to different dosage levels could be obtained by comparisons within these, yet such regressions would not enable us to make allowance for differences in initial egg count when comparing sheep at different dosages.

I see now that the problem is theoretically simple, though complicated in respect of computation. If at the 7 dosage levels one regards initial egg count as a different independent variate, i.e. $x_1, \ldots, x_7$, and introduces initial weight as x_8, on the understanding that, for example with the control sheep, x_1 and x_8 have observable values, but $x_2 \ldots x_7$ are all zero, then the coefficients of the 8-fold regression equation 4

$$Y = b_1x_1 + b_2x_2 + \ldots + b_8x_8$$

may be applied comparably to sheep at all dosage levels, and will make allowance for egg count at each level at the appropriate rate, i.e. $\underline{b_1}$ will be large and negative, while b_2 to b_7 should presumably approach zero progressively.

In full this would only be practicable if we were in real doubt on an important issue. In the cases of our outside flocks, however, we already know that the response is nearly proportional to the weight of the drug, so that I have tried the simpler form of regression equation

$$Y = c + b_1 e + b_2 w + b_3 ed,$$

where d is the weight of the drug used in each case. This I have now done for all 6 outside flocks.

The chief pointoof interest is whether this formula, which makes the effect of the drug proportional to the initial egg count, gives in fact a better fit than the original formula of the form

$$Y = c + b_1 e + b_2 w + b_3 d .$$

Among the papers I sent you, Singer and Baker remark that in cases of heavy parasitic loads the drug is found to be less effkoacious than in light infestations. This conclusion, if true, must depend on the level of parasitic load at which the experiments are carried out; for, obviously, if the drug has any effect, this effect will increase when the load is increased from zero, though it may well rise to a maximum and then fall in the more heavily infested sheep. If, therefore, we were working on the near side of the maximum, we might expect the new formula to be an improvement on the old. Actually it does not fit the data so well, Using the same numbers of degrees of freedom. In fact, of the 6 flocks tested I get a lower mean square residual variance in two cases and a higher residue in four. The indicatioh is that, if we are below the maximum at all, we are not far below it, which suggests the important inference that with lower infestations than we have used, such as must exist in the bulk of the sheep population, the response to the drug might be higher, and should not be much lower than what we have found.

At all events, it is satisfactory that the method of analysis used in our report is justified by the actual data, in contrast with what might have seemed a more reasonable allowance for initial egg count. I can see now that it would have been instructive to use a four-variate formula, including e, d and ed, to examine more closely the nature of the responses, since, of course, the initial egg counts are not exact measurements of degree of infestation as it affects growth rate, and in so far as they are inexact one would expect there to be a visible effect of the drug, in addition to the effect represented by the term ~~[illegible]~~ in ed

I thought you would like to know and consider these possibilities in case they have a bearing on your future experiments.

Yours sincerely,

P.S. About egg counts their grand use seems to be as a preliminary observation to increase the precision of comparisons in other things. For this I suppose tapeworms &c might be counted in .