13th. June 1950.

Dear Henningsen,

Thanks for your letter.    I should, of course,
have made it clear that the proportions I have calculated  of
heterozygotes among persons whom you have classified in the
three broad categories of strong, medium and weak $P$ reaction
are valid without regard to the genetic interpretation which
you chose to give to these differences in reaction strength.

E.g. so far as my work on your data is concerned, there
might be a continuous distribution of $P$ strengths of which (in
heterozygotes) proportions fixed by arbitrary bounding ordinates
are labelled strong, medium and weak respectively.    A higher
level of strength would, however, be obtained from the
corresponding homozygotes, or heterozygotes between two alleles
of similar strength.

Equally, of course, the data could be represented by as
few as two positive $P$ alleles, though not perhaps very satis-
factorily, or by three or four without any supposition that
these corresponded to the phenotypic strength classes you have
used.    Whatever the allelic basis it would, I think, on your
data, (which must stand until they are contradicted by better
data,) be true to say that two-thirds of the persons classified

as $\underline{P}$ strong have received positive $\underline{P}$ genes from both parents, while one-third have received a $\underline{P}$ gene only from one parent. In the latter case I think your pedigree evidence indicates that it must have been rather a good $\underline{P}$ gene, rather than an ordinary $\underline{P}$ gene dolled up with favourable modifying factors.

If the number of alleles were large, or if each of a few alleles were liable greatly to be modified by factors at other loci, then data similar to those you have published, if reclassified in different broad classes, e.g. 1) containing about half (the strongest) of the strong, 2) the rest of the strong and some of the strongest of the medium, 3) the rest of the medium and some of the weak, while 4) has only the weakest of the weak, then on examining the frequency of heterozygotes you might find something like 15%, 50%, 90% and 100% heterozygous in the four classes.

I entirely agree that the discrepancies between our estimated percentages must be due to the fact that the phenotypic classes are not genotypically homogeneous, but this is manifest in any attempt to calculate such percentages. With respect to the children, if age of donor affects only the strength, and does not influence judgement of positive and negative, then the percentages I have calculated will not be influenced by the age factor.

With my kindest regards,

yours sincerely,