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 satisfactorily, 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 P strong have received positive P genes from both parents, while one-third have received a P gene only from one parent. In the latter case I think your pedigree evidence indicates that it must have been rather a good P gene, rather than an ordinary 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 of the strongest, 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 pheno-
typic 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,