2nd July, 1956.

My dear Arthur,

I have just been looking through your article which arrived here this morning. I think it will be worth while giving it some further revision, in view of the complexity of the history and of the many misleading statements issued by, or on behalf of, Wiener.

In looking over your account I was led to draft a possible insertion on page 2, at the end of the short paragraph on the Rh antigens.

I did not know that Wiener had thought he found a cD chromosome, that is an R_o or R_2 without E or e. Has it been tested with anti-f?

On page 4 you refer to the possibility of what I have called a "clover leaf" gene, and I suppose you are thinking of such discussion as Stormont's. Of course, if such a view were true one would still need symbols for the elementary antigens of the different classes. In your last sentences before the section on the antibodies, you seem to imply that the CDE notation of elementary antigens is intended to obviate the need for short symbols for the antigenic compounds. This certainly has never

been its intention, and I hope that younger blood-group workers also, even in Britain, whether they have heard of Wiener or not, will still use what you have called the "abbreviated British notation".

On page 5 I suggest the word 'apt' instead of 'flexible' for the quality that makes it possible for a notation specifying the elementary antigens to incorporate more of these. The notation is not in any sense "bent" in order to do this. There is some little obscurity in the last sentence on page 5 before the section on the genetical background. It seems to me an advantage of paternity testing using the elementary antigens separately, that ~~but~~ a possible recombination will not affect the diagnosis, i.e. that paternity will only be excluded of men lacking the genes necessary, and not on the ground that having these genes they would need to be reassembled to supply the genotype of the child.

Forensically the point is that so long as any school of genetic thought considers a recombination a possibility, even if some other school regards it as impossible, its possibility must be admitted by the Court, though evidence of its infrequency would be entirely pertinent. On page 6, "Wiener's strongest arguments against the theory", "the theory" is ambiguous. After recognizing that the elementary antigens needed a specific notation, we noticed some evidence, though not fully conclusive, indicating a linear order of the corresponding loci. At the time

of proposing that these loci were, as in most genetic situations, arranged in order on a chromosome, we were naturally well aware that crossing-over was so infrequent that although it might have recognizable effects in Population Genetics, where 500 generations is not very much, it would not easily be demonstrated among the smaller numbers subject to critical serological analysis. For example, Bentley Glass at the Stockholm Congress announced a case which he regarded as quite decisive, but so far as I know, no user of the CDE notation has taken the same view of it. My own reaction was that half a dozen such cases might well be decisive. It was the distribution of Rhesus chromosomes that led to the addition to my theory of the notion of linear order of genes.

Such close linkage as is required was not unique in Genetics at the time it was proposed for the Rhesus factor, though it was said to be unknown in other organisms by opponents of my notation. The linkage of short ear with dilute in the house mouse must have been reported a long while ago. More relevant, and even longer ago, Ernst in Switzerland suggested three closely-linked genes as responsible for the heterostyle segregation in Primula, the three differences being functionally harmonious and inherited together, yet rare recombinations had been found showing the some dominance relations, but of course making a grave disturbance of the breeding system.

In aleurone colour in maize, and in leaf spot in cotton, large series of multiple alleles ~~have~~ been found, which on examination were capable of cross-classification as though dependent on more than one gene, and indeed the origin of new combinations, nominally of new alleles, had been reported in culture following crossing-over. Of course, in all these cases there had been the discussion of alternative interpretations, and of these alternatives I have uniformly preferred that of closely-linked factors. However, I was not unaware of the alternative of very numerous multiple alleles, but perceived that when capable of unequivocal cross-classification, as was clearly the case with the Rhesus alleles, then names or symbols should be found for the whole classes so definable.

In fact, in my view the appropriateness of having symbols for the elementary antigens does not depend on the multiplicity of the loci, and was put forward before such multiplicity could be clearly recognized. It is evidence since that time which has led us to this extension of the original theory.

Sincerely yours,

Enc.

The primary purpose of Fisher's notation was to provide a distinct designation for each elementary antigen, and therefore for the antibody by which each may be detected. There has never been doubt as to the need also of symbols for the antigenic compounds which occur and which react each with a number of different testing fluids. These were of course the first to require symbols. At a time when the M.R.C. department working at Cambridge under G. L. Taylor had discovered seven such distinct "allelomorphs", and succeeded in identifying six of these with the six known at this time to Wiener, a group of British serologists, with some generosity, decided to adopt the same symbols as Wiener was using for those compounds known to him. These, with later extensions, are listed in Table 1 as the "abbreviated British notation". It has always been regretted that Wiener should have rather frequently changed his symbols from those adopted here with a view to avoiding international confusion. The existence of a parallel notation for the elementary antigens has, however, made it possible to recognize these antigenic compounds under their various disguises.