3rd March, 1956.

My dear John,

Thanks for your letter of February 25th. At the moment I feel a little doubtful about the use of hospital patients, such as you and Bird have been using so fruitfully, in specific studies of blood groups and disease, for the opportunity that seemed to be afforded by the support of the Tobacco Manufacturers' Standing Committee seemed better fitted for getting blood group data on an unselected sample of the population such as might well be provided by now donors. It may be, however, that these are predominantly of age groups younger than would be suitable to get representative material of the different smoking classes. I presume that most people have classified themselves as non-smokers, cigarette-smokers, pipe-smokers etc., by the time they are 35 and perhaps earlier, and that persons of this degree of maturity would be suitable for an examination (preliminary rather than final) of the question whether these classes are genetically differentiated, or whether in any way they display differentiation in frequency of genotype.

From the point of view of genetics it would seem to have been an essential preliminary, before inferring that smoking habits have any causative influence on the development of lung cancer, to see whether the classes compared are apparently equivalent or apparently differentiated in respect of genotype.
Of course the problem can be approached from other points of view, and I have suggested (to Luca Cavalli in particular) that it might be looked at in the manner of Verschuer by the use of twin studies, and those have, I believe, been begun on a small scale in several countries. An examination of the same question, however, using the genetic markers provided by the blood groups, would seem to have the advantage of enabling blood-group serologists to examine a comparatively large and representative sample of the population. From this point of view the selection of hospital patients would be, on the whole, a disadvantage, and I wonder if more appropriate material could not be obtained from other sources.

Sincerely yours,