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Mendelian Genetics Today

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The purpose of this first " Round-table Conference " could well be to present the historical development of human genetics from the early days of Mendelism to the elaboration of modern genetic research. The refinement of methodological possibilities and the unfolding of problems indicate to us the proper lines for further study. With this introduction I should like to restrict myself to a few remarks concerning the role of the gene analytical system of Gregor Mendel in human genetics. If as a result of corrent research the concept of the gene has undergone important alterations and is no longer the closed unit of the classical formulation, it still remains a useful concept for practical research. Every investigation of a genetically active factor immediately begins with the determination of a segregating unit or a mutating unit. Determining an allele relationship or a series of multiple alleles will remain the principal result. Quite often in human genetics it has not been possible to demonstrate these relationships as pseudoallelal or with other methods to achieve a differentiation of the gene concept into its subunits: the cistron, recon and muton. So far the objectives of human genetics the employment of the gene concept as classically formulated is methodologically necessary.

The ideal goal of the gene analytical method is to determine the function of all genes which take part in the heredity of an organism, the preparation of theoretical chromosome maps for the various linkage groups, the determination of the relationships between the genes and their alleles to visible or measurable characteristics of the organism, and the establishment of relationships between phenotypic expression and dominance or epistasis. Its further area of interest is in the genetic analysis of natural populations, the question of spontaneous mutability, the problem of genetic diversity and the polymorphism caused by it in populations, and the equilibrium between all alleles. These questions lead necessarily to general problems of population dynamics, adaptation and evolution.

These ideal goals of a genetic analysis lie far in the future even in the most favourable objects for experimental genetics. In humans in which planned crosses are not feasable, and which display a number of other unfavourable characteristics for genetic analysis, we are naturally far from this goal and will probably never achieve it. Yet on the other hand, humans offer certain methodological advantages which are not available in other organisms. I allude, for instance, to the possibilities offered by twin research and the extensive fund of information available on human physiology, biochemistry and pathological relationships which offer a wealth of fundamental information and can be used as a basis for genetic research. Recently the examination of human chromosomes, which had long been ignored, has come to the forefront of interest despite of its technical difficulties. Today it is no longer necessary for the human ge-

neticist to simply wonder at the results of experimental geneticists. On the contrary, human geneticists have been able to produce very decisive contributions on important general problems in genetics and will certainly continue to do so on an increasing scale. Besides, by virtue of close connection with medicine, they will always be able to offer practical service to public health.

The heredity of morphological and physiological characteristics within the normal range of variation and the natural racial connections in humans have been examined to only a slight extent. The environmental lability of many characteristics and the polyfactorial basis of most of these hinder their analysis. From a genetically better orientated anthropology, further progress could be expected. The genetics of pathology is in better conditions where already a large accumulation of analytical material is available; for instance, in the area of ophthalmology and the promising area of metabolic anomalies. The expanding interest of medicine in posing genetic questions leads one to expect that the abundant material of the clinic will be better evaluated from a hereditary point of view in future. Applied medicine profits from genetics not only through the increasing possibilities to recognize a hereditary disease and its etiology, thereby gaining a rational basis for therapy, but also through the convincing demonstration of the heterogeneity of a unitary medical picture and allowing the important differentiation between outwardly similar but functionally different syndromes. As an example I should like to cite the results of our chairman, Prof. Lamy, in the classification of different types of Dysostosis. A heredity register similar to that one in Denmark would be desirable in all states and it should be considered whether this Congress should put forward a relevant proposal to the competent authorities. For the further elaboration of human genetic pathology we have even more to expect from comparative genetic pathology of vertebrates which unfortunately is as yet only in its infancy.

The mapping of linkage groups in human has progressed slowly, because of difficulties due to the large chromosome number and the high chiasmata frequency, and with the exception of the sex chromosome pair it has not been possible to assign any linkage group with security to a particular chromosome. Here also further progress is to be expected where well known gene markers with environmentally stable manifestations such as serological characteristics may serve as a basis.

The population genetics of humans has rested to the present on the analysis of easily obtainable and environmentally stable characteristics which in humans show a high degree of polymorphism as for example, the various blood groups and the haemoglobin types. In the structures present today in this polymorphism, we look back on the long racial history of mankind, and so this field of human population genetics has become an important adjunct for anthropological, ethnographic and prehistoric research. The polymorphism of the serological and haematological characteristics has given us the first indication of positive selection processes within human populations. In addition we are indebted to this field of human genetics for the most beautiful examples of the co-operative function of various genes, which can also be assumed for all normal and pathological processes, but which is not always so clearly demonstrable. In the light of the enormous importance of serological research in human genetics, the 8th Congress of the European Society for Haematology which met in Vienna in August of this year discussed the establishment of a center for gathering genetically important

serological data. I wish to urge that our Conference too supports the proposal of the Haematology Congress.

Negative selection against genetically determined defects is considerably weekened in the highly cultured populations of today. The practical problems of eugenics and of biological population dynamics have a scientific basis in considerations of population genetics. In the light of the immense increase in the world population in which the former selective pressures continually diminish, a role of responsibility falls to human genetics. The problem of the genetic load of the human population has been discussed from many aspects, in connection with the question of the frequency of spontaneous mutations as compared to mutations induced by mutagenic agents. The danger to genetic health from radiations in the areas of medicine, industry, industrial atomic energy and nuclear armament has been frequently emphasized, often without factual basis. The scientific basis for all of these actual considerations must reside in Mendelian based population genetics and mutation analysis. And so the gene analytical system of Gregor Mendel forms the basis of all research in human biology.

I should like to limit myself to these considerations derived from the standpoint of general biology and genetics. The main stress of this Congress will, however, be put on the discussion of specialized problems.