DRAFT

Minutes of meeting of a panel of genetic experts to develop a plan for genetic analysis of Collaborative Study data.

A panel of genetic experts and members of the Perinatal Research Branch and the Perinatal Research Committee met on Thursday, June 19, 1969, in the conference room of the Branch headquarters in the Wiscon Building, to discuss problems of genetic analysis of Collaborative Study data and to develop a comprehensive plan for analysis of these data.

Present were:

Dr. C.S. Chung, University of Hawaii

Dr. James Crow, University of Wisconsin

Dr. Joshua Lederberg, Stanford University

Dr. William J. Schull, University of Michigan

Dr. Dorothy Warburton, College of Physicians and Surgeons, Columbia University

Dr. Patrick Bray, University of Utah, representing the Perinatal Research Committee

Dr. Heinz Berendes, Dr. John Churchill, and Dr. Michael Davies, representing the Perinatal Research Branch

Dr. Ntinos C. Myrianthopoulos, Dr. Valerie Cowie, and Dr. Alfred Naylor, representing the Section on Epidemiology and Genetics, Perinatal Research Branch.

The Meeting convened at 9:00 a.m., under the chairmanship of Dr. Myrianthopoulos.

Dr. Myrianthopoulos reviewed briefly the history of the Collaborative Study, stated the broad objectives of the Study, described the sample and

and the sampling procedure, the protocol, and the variables collected in each case. Dr. Myrianthopoulos drew attention to the fact that the last Study child was born in September, 1966, and that collection of the data will be completed in 1974. The Section on Epidemiology and Genetics is responsible for the collection, processing and analysis of the collected genetic and socioeconomic information. As the data-collection phase of the Study is coming to a close, the Section is now ready to turn its attention to the problem of analysis. A skeleton plan for analysis of the genetic and socioeconomic material has already been produced but the Section is anxious to have the panel's advice and help to develop the plan further and make it comprehensive, and also to oversee its implementation.

Dr. Crow at this time asked Dr. Myrianthopoulos to describe in some detail the current efforts of the Section on Epidemiology and Genetics in data analysis, for the information of the panel. Dr. Myrianthopoulos, Dr. Cowie, and Dr. Naylor took turns describing the projects now carried out in the Section, including those in collaboration with individuals and institutions outside the Collaborative Study. Among them was a study of macrosomia on which Dr. Lederberg, who had done a preliminary analysis of data, reported at some length.

Following specific inquiries, Dr. Berendes informed the panel about mechanisms for reviewing proposals, the possibility of obtaining certain blocks of data, arrangements for financing the analysis of such data, and

arrangements for collaboration and authorship with members of the Perinatal Research Branch. Dr. Berendes emphasized that it is the policy of the Branch to invite qualified individuals or groups of individuals from outside the Collaborative Study, to participate on a collaborative basis in the analysis of the data. The Branch is willing to support such arrangements to the extent of producing the necessary tapes and financing the analyses by contract, in some cases.

It appeared obvious that if large blocks of data are to be contracted out for analysis, this could be done best at centers where computer facilities exist to handle large masses of data which require complex programming. Among the panel members, Dr. Lederberg, Dr. Chung, and Dr. Schull indicated that their computer facilities were capable of handling any size job involving Collaborative Study data. Dr. Crow indicated that smaller scale operations were possible at his facility, also.

Dr. Myrianthopoulos then asked for a critique of the genetic analysis plan presented by the Section on Epidemiology and Genetics and for suggestions and discussion to make the plan comprehensive and workable. There was no major critism of the design of the plan but several specific recommendations were made, as follows:

1. Any and all genetic factors which are known or are suspected to influence IQ should be utilized in analysis. Environmental information can be used to account for variance.

2. Studies should be made of associations of ABO and Rh blood groups, and every identifiable single gene factor, with IQ. In this context all existing cord blood samples from Study children now in storage should be analyzed for blood antigens and serum proteins. This would yield a large number of genetic markers which should be made part of the data file.

3. Genetic analysis should include obstetric variables such as site of implantation, size of pelvis, and length of labor.

4. Repeat pregnancies should be utilized to full advantage.

5. Half sibships should be analysed for the detection of maternal effects.

6. Comparison should be made of concordant and discordant IQ performance at four and seven years, particularly in twins.

7. Studies should be made of the effects of ABO and Rh incompatibility on IQ.

8. Micro-effects, such as minimal malformations, should be used to construct an index for epidemic teratology; for example, observation of symmetry, or asymmetry, like that usually found in dermatoglyphics, may turn out to be a useful teratology alert.

It was recognized that the main efforts should be made in the direction of genetic analysis of Collaborative Study data which have been collected and are now available. Some discussion, however, was devoted to consideration of direct extensions of the Study, should time and funds become

available. The following were considered as most profitable and interesting extensions of the study:

1. Taking of finger and palm prints of all children during the seven-year battery of tests.
2. Taking of blood samples during one of the seven-year examinations in order to type for blood antigens and serum markers.
3. Chromosomal survey of seven year olds for epidemiologic study of chromosomal anomalies and especially of the XYY phenotype.
4. Study of possible genetic component of lead poisoning.

Dr. Myrianthopoulos asked if, at this point, the panel was ready to express an opinion about priorities for analysis of already existing data. Dr. Lederberg pointed out that it would be difficult to establish priorities without some kind of cost analysis of each major project, and without some indication of the extent to which the Branch would be capable of providing funds to finance the analysis. With these reservations in mind the panel recommended that the following projects be given high priority in analysis:

1. Establishment of record linkage file.
2. Study of half sibships for maternal effects.
3. Determination of genetic markers from cord blood and/or blood drawn at the seven-year examination.
4. The utilization of repeat pregnancies and twins in studies of IQ.

Attention was drawn again by Dr. Lederberg to the problem of funding. This was considered to be the crucial item on which the success of genetic analysis would depend. It was recommended that the Perinatal Research Branch provide in the near future a cost analysis program for review by the panel. It was also recommended that the members of the panel forward to the Section on Epidemiology and Genetics a summary statement of their thoughts concerning the program of genetic analysis, ways of implementing such a plan, recommendations as to who is best qualified to carry out certain parts of the analysis and as to centers which are well equipped to undertake such analysis.

The meeting adjourned at 5:30 p.m.