

TWIN FAMILY STUDY OF CHRONIC DISEASE¹

FOR many years the family has been considered a basic unit for epidemiological investigation of the acute infectious diseases. Chapin introduced the method—a quantitative description of familial aggregation of disease—as early as 1888. In recent years the concept of epidemiology has broadened and now includes the study of some of the chronic diseases, such as tuberculosis and rheumatic fever. Frost experimented with and described the use of the family as the unit of study of differences in the risk of attack of tuberculosis for persons in familial contact with the disease compared with the general community risk.

The “family method” of epidemiological investigation used by Chapin and Frost and his students had the specific purpose of describing the spread of infectious disease in the immediate environment of an index or primary case. The “family method” has recently been combined with the “twin method” and used as an effective means of exploring the possibility of genetically determined resistance factors which may affect the incidence of chronic infectious disease and other chronic conditions.

The “Twin Family Method,” as pointed out by Kallmann and Reisner, is the best available method for clarification of the part played by genetic factors in the variability of the pathologic effect produced by a specific microorganism, the tubercle bacillus. This method provides six categories of sibship pairs; namely, monozygotic twins, dizygotic twins of the same sex, dizygotic twins of opposite sex, full siblings, half siblings, and step siblings.

The material used for analysis by Kallmann and Reisner consisted of 308 complete twin families with 616 twin partners, 930

¹ a. Kallmann, J. Franz and Reisner, David: Twin Studies of the Significance of Genetic Factors in Tuberculosis. *The American Review of Tuberculosis*, June, 1943, XLVII, No. 6, pp. 549-574.

b. _____: Twin Studies on Genetic Variations in Resistance to Tuberculosis. *Journal of Heredity*, September, 1943, 34, No. 9, pp. 269-276 and 293-301.

c. Kallmann, J. Franz: The Genetic Theory of Schizophrenia: An Analysis of 691 Schizophrenic Twin Index Families. *American Journal of Psychiatry*, November, 1946, 103, pp. 309-322.

d. Kallmann, J. Franz and Sander, Gerhard: Twin Studies on Aging and Longevity. *Journal of Heredity*, December, 1948, 39, No. 12, pp. 349-357.

full siblings, 74 half siblings, 688 parents, and 226 marriage partners of twin patients. The proportion of monozygotic to dizygotic twin pairs was about 1:3, a ratio consistent with that found for twins in the general population.

The method used for classification of twin partners in respect to their zygotic origin was the "modern similarity method," that is, similarity in certain anatomical traits. The clinical data required for a diagnosis of tuberculosis included complete histories, chest x-ray films, and sputum examinations.

The care with which the study was done is revealed by the authors. "The diagnostic aspects of the study were strictly a matter of the investigators' research, since it was advisable to ascertain them beyond reasonable doubt and in accordance with a uniform system of classification. Whenever possible, therefore, the diagnosis of both tuberculosis and zygosity was made on the basis of personal examination and extended observation."

Some of the significant findings of this investigation are as follows:

The chance of developing tuberculosis increases in strict proportion to the degree of blood relationship to a tuberculous index case. The difference in morbidity between dizygotic and monozygotic twin partners amounts to a ratio of 1:3.5.

The difference between dizygotic and monozygotic co-twins increases to a ratio of 1:16, if the similarities in extent, course and eventual outcome of the disease are taken as additional criteria of comparison.

The consistent differences in tuberculosis morbidity among the various sibship groups of the twin index cases *cannot* be adequately explained on the basis of a simple correlation between closeness of blood relationship and increasing similarity in environment with correspondingly intensified opportunity for infection.

The analysis of the morbidity distribution in the sibship groups indicates that resistance to tuberculosis is modified by a heredoconstitutional mechanism which seems to be multifactorial in its genetic nature.

The "Twin Family Method" was used also by Kallmann in a

special study of schizophrenia (3). Twin index cases were collected from the resident populations and new admissions of all mental hospitals under the supervision of the New York State Department of Mental Hygiene. The requirements were that the index cases be born by multiple birth and that they were admitted with a diagnosis of mental disease. All were reported by twenty institutions within a period of nine years. The twin diagnosis was based on findings obtained by the "similarity method."

The frequency of schizophrenia in the different population groups which comprised the families of the twin index cases is of considerable interest. The data are as follows:

<i>Relation to Index Case</i>	<i>Per Cent Diagnosed as Schizophrenia</i>
Parents	9.2
Husbands and Wives	2.1
Step Siblings	1.8
Half Siblings	7.0
Full Siblings	14.3
Dizygotic Co-twins	14.7
Monozygotic Co-twins	85.8

The similarity of full siblings and dizygotic co-twins is of special interest. According to Kallmann, "If the assumed genetic factor exists and the part played by the twinning factor is negligible, the statistical expectation will be that the morbidity rates for full siblings and dizygotic twin partners should be about the same, but they should clearly differ from the rates for the other sibship groups."

For monozygotic co-twins, Kallmann indicated that a rate of 100 per cent would be expected theoretically in regard to a strictly hereditary trait. Since the rate among monozygotic co-twins in this study (85.8 per cent) was somewhat below the expected, he concluded that "from a biological standpoint, the finding classified schizophrenia as both preventable and potentially curable." It is difficult to accept Kallmann's line of reasoning at this point because it seems to be based upon complete confidence that there can be no possibility of error in the

diagnosis of either monozygosity or schizophrenia; that is, there were no missed cases in either category.

One of the chief conclusions from the study was "The predisposition to schizophrenia; that is, the ability to respond to certain stimuli with a schizophrenic type of reaction, depends on the presence of a specific genetic factor which is probably recessive and autosomal."

Kallmann is using the "Twin Family Method" also in an investigation of aging and longevity (d). During a period of three years a total of 1,602 twin index cases, both of whom survived to 60 years of age, were studied. "In a comparison of the life spans of the same sexed twin partners, the significance of genetic factors in longevity was demonstrated by the finding that the average intra-pair difference of monozygotic pairs (36.9 months) is only about one-half that of dizygotic pairs (78.3 months). This inter-group difference is expected to increase with the progress of the study."

These "Twin Family Studies" are of interest and value both to the geneticist and to the epidemiologist. As the concept of epidemiology broadens and the field of work is extended so as to include more of the chronic diseases, this method of study may prove most useful.

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REAPPRAISING OUR IMMIGRATION POLICY¹

IN VIEW of the public concern over the problems of displaced persons and in view of the current discussions of the wisdom and adequacy of the Displaced Persons Act of 1948, the March, 1949, issue of *The Annals* was devoted to the general topic "Reappraising Our Immigration Policy." Dr. Hugh Carter served as editor of this volume and most of the contributors of the twenty-one articles are easily recognized as authorities in their respective fields.

¹ Carter, Hugh (ed.): Reappraising Our Immigration Policy. *The Annals of the American Academy of Political and Social Science*, Philadelphia, March, 1949, Volume 262.