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A Twin Register for Eye Studies and Need for Collaboration

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This twin register was organized as a resource for studies on the eye. It has been possible to share this resource with other disciplines through effective collaboration. Conversely, only through the assistance of other investigators who are working with twins, will it be practical to undertake certain studies which are important in ophthalmology. The purpose of this presentation is to convey a description of our register and some of its limitations, and to specify the need for collaboration with others.

The original purpose in assembling this register was to identify a group of twins readily available for multiple clinical examinations. Since the first examining facility was to be located near the National Institutes of Health, practical considerations required that twin residence be limited to the metropolitan Washington, D. C. area. Twins of all ages were included in the register, since proposed investigations pertained to different age categories. No effort was made to select twins through randomization procedures; all twins who were identified were invited to membership in the register. A variety of methods were used to locate twins, including contact with schools and clubs, but the largest proportion of registrants were recommended by other twins.

Twins were offered a thorough eye examination, along with the solicitation of their interest in participating in future research activities. The clinical examination was offered for the following reasons:

1) To encourage informed interest in proposed future investigations by acquainting the twins with our facility and purpose;

2) To perform base-line observations, so as to identify and enumerate ocular characteristics as an aid in selecting subsets of twins for future studies;

3) To obtain data for possible estimates of heritability of selected ocular characteristics.

A list of components of the initial screening examination is given in Tab. I. Typing for all listed blood groups, with the exception of Xg^a, was performed by Mr. Webster C. Leyshon, Human Genetics Branch, NIDR, Bethesda, Md. Typing for the latter group was performed by Dr. J. D. Mann, Butterworth Hospital, Grand Rapids, Mich. Components of the initial history are given in Tab. II.

A grouping of active registrants according to age and zygosity is given in Tab. III. At the end of July 1969, there were a total of 659 twin pairs in the active register; 352 were MZ and 307 DZ. About 500 of the twins included in Tab. III have now been examined.

Tab. I. Twin Register for Eye Examinations - Components of initial screening examination

A. *Ophthalmic Examination*

Visual acuity – corrected and uncorrected
Refraction – cycloplegic under age 35
External examination – including color photographs
Pupils and iris – including reflexes, interpupillary distance and iris photographs
Motility – versions and phoria at distance and near, by Maddox rod and cover test
Fusion – Worth and Wirt tests
Ocular tensions – by applanation and Schiotz tonometry
Fundus examination – cycloplegic with photographs
Keratometry
Slit lamp examination
Ocular dominance – distance and near

B. *Nonophthalmic Components*

Anthropometric measurements – height, weight, fingerprints
Hand dominance
Facial photographs
Blood grouping – ABO, MNSsU, P, Rh, Kell, Lewis, Duffy, Kidd, Xg^a, (Diego)

Tab. II. Twin Register for Eye Examinations - Components of initial history

Census data: address, age, birthplace, race, nationality
Prenatal history: length of pregnancy, terminated pregnancies, live births
Perinatal history: birth order, oxygen history
Presumed zygosity
Eye history: past disease, injury, allergy
Medical history: hospital admissions, hypertension, diabetes
Habitation with cotwin: age at separation
Family history: census data on parents, sibs, offspring, other twins
Identification of family physician

A clinical history has been obtained on nearly all. Examinations have been offered with preference to the older MZ and like sex DZ twins, in order to satisfy the immediate needs of our first investigations.

Activity of the Twin Register for Eye Examinations has been limited to the Washington area; however, the register has an agreement with the Division of Direct Health Services of the US Public Health Service for use of their clinical facilities, where appropriate. Examination of twins residing in the nearby Baltimore area is planned in the near future.

Clearly, ascertainment of twins in the manner described for this register is subject to statistical bias. Since approximately 53% of twins in the active register are MZ, it is not likely that ascertainment was independent of zygosity. Furthermore, since

these twins had previous knowledge of the proposed eye examinations, it is reasonable to anticipate bias with respect to ocular abnormalities. Accordingly, the register may not be well suited for study on the inheritance of abnormalities which are known to the subject. Proposed studies of inheritance using this twin population are limited to characteristics of ocular function and morphology of which the twin is unaware. One such investigation now in progress pertains to the inheritance of a glaucoma-like effect produced by the topical application of corticosteroid eye drops. This study was described earlier in the symposium (Reuling and Schwartz, 1969).

Use of this registry will not be limited to estimates of heritability. Other methods of applying twin studies may hold greater promise for the recovery of clinically use-

Tab. III. Twins in active register through July 1969 - All active twins by zygosity and age

Age	MZ	DZ			Total
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0-4	15	6	10	16	31
5-9	82	36	29	65	147
10-14	80	42	35	77	157
15-19	73	48	32	80	153
20-24	28	13	11	24	52
25-29	12	10	6	16	28
30-34	13	3	3	4	17
35-39	10	1	1	2	12
40-44	6	4	2	6	12
45-49	14	6	4	10	24
50-54	3	1	3	4	7
55-59	6	2	0	2	8
60-64	5	0	0	0	5
65-69	4	1	0	1	5
70-	1	0	0	0	1
Total	352	173	134	307	659

ful information in ophthalmology (Schwartz, 1968). Included are case-control studies, epidemiologic investigations and studies of the early natural history of chronic affections. Because of the relatively low incidence of many important blinding disorders, the categories of investigation just mentioned would be aided greatly through carefully planned collaboration. It may be of interest to cite a few specific needs for collaborative activity.

Diabetic retinopathy is among the leading causes of blindness (Statistics for 1966 on blindness in the model reporting area) and its incidence may be increasing (Winter, 1960). The natural course of this ocular complication of diabetes is extremely

variable, and we lack basic knowledge of factors which contribute to its development and progression. The relative role of hereditary and environmental factors, for example, is unknown. In theory, estimation of heritability by the twin study method should be applicable to this question. Ascertainment of adequate numbers of diabetic MZ and DZ cotwins with retinopathy in the twinship, however, seems unlikely. Still, through wide collaboration, it may be possible to ascertain a population of diabetic MZ twinships, either concordant or discordant for retinopathy. Epidemiologic study of such a population would provide the possibility of identifying environmental factors related to the development or progression of this blinding disorder. On the other hand, collaborative study of just that MZ population which is concordant for retinopathy could provide the opportunity for needed evaluation of specific treatments. Initial requirements for collaboration in this area would include a pooling of ophthalmoscopic data obtained from ongoing studies among diabetic twins. It would also be of value to identify and examine twinships found incidental to international prevalence surveys on diabetes.

Chronic simple glaucoma is another of the world's most common blinding disorders. The role of inheritance is also unsettled with regard to this disease. The logistics problems in studying glaucoma among twins are similar to those for diabetic retinopathy. The problem of case ascertainment, however, may be somewhat more manageable, since glaucoma is variously described to occur in approximately 2% of persons over age 40 (Simmons, 1959). Of particular interest to the fields of ophthalmology and public health is the further elucidation of the early natural history and early parameters of chronic simple glaucoma. Careful prospective study of non-affected members of discordant MZ twinships may provide a realistic method of defining the earliest clinical changes or clinical predictors of glaucoma. International cooperation in identifying affected twinships seems worthy of practical consideration. Screening for glaucoma is a relatively straightforward clinical procedure and might be included in the examination of adult twin populations under study for other purposes. Depending on the numbers and statistical randomization of affected twinships, it may also be possible, through such collaborative effort, to gain an estimate of heritability of chronic simple glaucoma.

Although it is usually not a blinding disorder, myopia is the most prevalent cause of visual disability in the world today. Twin heritability studies on myopia, including measurement of the components of refraction, have been undertaken among British populations by Sorsby et al (1962) and Sorsby and Fraser (1964), and among Japanese populations by Nakajima et al (1966). Although findings are not in complete accord, there is general agreement that inheritance plays a significant role in the etiology of this disorder. It may be possible to undertake international comparisons of the patterns of heritability for myopia. A prerequisite would be collaboration among investigators to establish equivalent protocols for case ascertainment and clinical measurement in order to enhance the recovery of comparable information.

Of perhaps greater immediate need is an evaluation of the effectiveness of measures presently used to modify the expression of myopia, i. e., an evaluation of

therapeutic methods employed to retard the progression of this disorder. Cycloplegic drugs, bifocal spectacles, contact lenses and other treatments are currently employed. An excellent method of evaluating such treatment would be prospective case-control study of populations of young MZ twins who are initially similarly myopic. Our register is preparing to undertake such a study. However, myopic MZ twins are presently available in numbers sufficient for the study of only one method of treatment. Cooperation of other investigators in identifying such twinships and/or the collaborative development of a common protocol would be highly useful in this area. Young myopic twins might be identified in ongoing nonophthalmic studies by the simple testing of visual acuity. The diagnosis is readily verified by an ocular refraction.

Time prevents the mention of further collaborative needs or more detailed discussion of those cited. It will be helpful if the present symposium serves to encourage further development of common investigative interests.

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