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THE TAY-SACHS DISEASE SCREENING PROGRAM IN THE U.S. AS A MODEL FOR THE CONTROL OF GENETIC DISEASE: AN HISTORICAL VIEW

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TAY-SACHS DISEASE IS A HEREDITARY disorder of the central nervous system in which symptoms develop within the first six months of life and which end fatally three to four years later. Apparently normal at birth, most children with Tay-Sachs Disease will begin to show definite signs of neurologic deterioration sometime in their first year of life. Once symptoms develop, the course is considered one of inexorable decline. Blindness, seizures, profound mental retardation, and death develop before age five.¹

The disease was first described in 1881 by Dr. Warren Tay, an English physician.² It was more fully described by Dr. Bernard Sachs, a neurologist at Mt. Sinai Hospital in New York City who reported on a pair of affected siblings in 1887, and, more definitively, in 1896.³ Dr. Sachs, a Harvard graduate, named the condition "amaurotic familial idiocy," the name being derived from the Greek term for blindness.⁴

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1. See generally Howard R. Sloan & Donald S. Fredrickson, *GM2 Gnanliosidoses: Tay-Sachs Disease*, in *THE METABOLIC BASIS OF INHERITED DISEASE* 615 (John B. Stanbury et al. eds., 1972).

2. See Warren Tay, *Symmetrical Changes in the Region of the Yellow Spot in Each Eye of an Infant*, *TRANSACTIONS OPHTHALMOLOGICAL SOC'Y U.K.*, Apr. 1881, at 55-56 (describing the physiological effects of Tay-Sachs Disease for the first time).

3. See Bernard Sachs, *On Arrested Cerebral Development, with Special Reference to its Cortical Pathology*, 14 *J. NERVOUS & MENTAL DISEASE* 541, 543-53 (1887); Bernard Sachs, *A Family Form of Idiocy, Generally Fatal, Associated with Early Blindness*, 21 *J. NERVOUS & MENTAL DISEASE* 475-79 (1896) [hereinafter *A Family Form of Idiocy*].

4. *A Family Form of Idiocy*, *supra* note 3, at 475.

Over the next eighty years, Tay-Sachs Disease was recognized as a rare, but recurring disease occurring primarily, but not exclusively, in descendants of Eastern European (Ashkenazi) Jews. Primarily, the disease was found in individuals from Kovno, Suwalik, and certain other provinces in North-eastern Poland which had been included in the Russified "Jewish Pale of Settlement."⁵

As Dr. Howard Markel described in this symposium,⁶ the 1880s saw an epic migration of Jewish families from Russia to cities in North America. These immigrants were first driven by cholera, and then by outbreaks of anti-Semitic violence in Russia and Russian Poland. Over the decade, more than a million people emigrated to New York, Montreal, Boston, and other Atlantic ports. Indeed, it is likely that Dr. Sachs' patients were born to one of these displaced Russian Jewish families.

As the Ashkenazi community grew, so did the number of cases of Tay-Sachs Disease. By the mid-1950s, a ward at the Jewish Hospital for Chronic Diseases in Brooklyn, New York was devoted entirely to the care of children with Tay-Sachs Disease and similar conditions. To aid this work, a group of parents of children with Tay-Sachs Disease formed the National Tay-Sachs and Allied Diseases Association. This Association helped to establish the Isaac Albert Research Institute at the hospital to support research into the cause and treatment of the disease.⁷

By the mid-1960s, Tay-Sachs Disease was recognized as one of several conditions, including Niemann-Pick and Gaucher Diseases, where the absence of a normal degradative enzyme allows the accumulation of cellular waste components which over time intrude on, and eventually destroy, normal organ function. Such "storage diseases," as they came to be known,

5. See generally Arlene L. Fraikor, *An Anthropological Analysis of Tay-Sachs Disease: Genetic Drift Among the Ashkenazim Jews* (1973) (Ph.D. dissertation, University of Colorado) (on file with the University of South Carolina Libraries) (describing the cultural connection between Tay-Sachs disease and Ashkenazim Jews).

6. See generally Howard Markel, *Di Goldine Medina (The Golden Land): Historical Perspectives of Eugenics and the East European (Ashkenazi) Jewish-American Community, 1880-1925*, 7 HEALTH MATRIX 49 (1997).

7. See Judith Saperstein, *The National Tay-Sachs and Allied Diseases Association, Inc.*, in TAY-SACHS DISEASE: SCREENING AND PREVENTION 9, 9-10 (Michael M. Kabach et al. eds., 1977) (discussing the history of the National Tay-Sachs and Allied Diseases Association).

were objects of intense scientific investigation in the 1960s and 1970s.⁸ In 1971, John O'Brien and Shintaro Okada developed an assay for the so-called Tay-Sachs enzyme, Hexosaminidase A (Hex A). Hex A could identify not only affected individuals themselves, each of whose two copies of the Hex A gene had the Tay-Sachs mutation, but also the healthy heterozygous parents who were known as "carriers." Carriers each possess a single copy of the abnormal gene, and as a result had half the normal levels of Hex A.⁹ Because even half-normal enzyme levels are sufficient to allow normal function, it is only when two "carrier" parents have a child who receives the Tay-Sachs gene from each that the disease occurs. Thus, by screening people for the "carrier" condition, and in this way identifying couples at risk for having children with Tay-Sachs Disease, it is theoretically possible to prevent the birth of affected children.

By 1973, the National Tay-Sachs Foundation had a new goal -- to control Tay-Sachs Disease by promoting carrier screening. In 1975, Ms. Judith Saperstein, President of the Foundation, stated the goal in her address to the First International Conference on Tay-Sachs Disease sponsored by the Foundation:

Since the start of this decade, when carrier identification and prenatal diagnosis became a reality, our organization has shifted its emphasis somewhat away from scientific research — which no longer really needs us to the extent it once did, as it now has its own momentum and interest — and more to education, screening, and prevention.¹⁰

Thus, from the very beginning, many people took as axiomatic that screening programs could and would work to prevent Tay-Sachs Disease, and to a great extent, therefore, the

8. See generally Shintaro Okada et al., *Ganglioside GM₂ Storage Diseases: Hexosaminidase Deficiencies in Cultured Fibroblasts*, 23 AM. J. HUM. GENETICS 55, 55-61 (1971).

9. See Shintaro Okada & John S. O'Brien, *Tay-Sachs Disease: Generalized Absence of a Beta-D-N-Acetylhexosaminidase Component*, 165 SCIENCE 698, 698-700 (1969) (presenting results of a study concluding that hexosaminidase assay can be used to diagnose individuals homozygotic for Tay-Sachs disease); John S. O'Brien et al., *Tay-Sachs Disease: Detection of Heterozygotes and Homozygotes by Serum Hexosaminidase Assay*, 283 NEW ENG. J. MED. 15, 15-20 (1970) (explaining the genetic transfer of Tay-Sachs and the early identification of the disease).

10. See Saperstein, *The National Tay-Sachs and Allied Diseases Association, Inc.*, in TAY-SACHS DISEASE: SCREENING AND PREVENTION, *supra* note 7, at 9-10.

problem of Tay-Sachs Disease was now solved. Furthermore, many scientists declared, even before much experience with screening had been accumulated, let alone digested and analyzed, that Tay-Sachs screening was not only a great success in its own right, but also that it could serve as a model for other screening programs for genetic disorders.¹¹

While there is evidence that the Tay-Sachs programs have been effective in educating people about their risks of having children affected by the disease, and perhaps even some evidence suggesting that these programs have led to a decline in the birth rate of children with Tay-Sachs Disease, a careful reading of the historical record suggests that Tay-Sachs screening has not been the unqualified success it has sometimes been described to have been. Moreover, the Tay-Sachs Model may not necessarily be the most appropriate model to use in designing programs for the control of other genetic diseases.

The approach taken to screening for Tay-Sachs Disease carriers was based on three notions: (i) that Tay-Sachs Disease is a rare disease in the general population, occurring in perhaps 1:360,000 births; (ii) that it is perhaps one hundred times more common among Ashkenazi-Jewish families (about 1:3,600 births); and (iii) that the disease could only be controlled by affecting the reproductive decisions of couples at risk for having affected children. Therefore, programs were developed which were primarily aimed at young Ashkenazi-Jewish married couples who had not yet completed their families. The programs were organized on a community by community basis, usually stimulated by academic physicians at a local institution who had professional interests in Tay-Sachs Disease.

Although the programs were often supported by both public and private funds,¹² the programs were nearly always carried out under the auspices of local Jewish community

11. See generally Michael M. Kaback & Robert S. Zeiger, *Heterozygote Detection in Tay-Sachs Disease: A Prototype Community Screening Program for the Prevention of Recessive Genetic Disorders*, in *ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY* 628-30 (Bruno W. Volk & Stanley M. Aronson eds., 1972) (explaining the use of Tay-Sachs screening as a model for other screening programs).

12. See Michael M. Kaback et al., *Tay-Sachs Disease: Heterozygote Screening and Prenatal Diagnosis-U.S. Experience and World Experience*, in *TAY-SACHS DISEASE: SCREENING AND PREVENTION* 16-17 (Michael M. Kaback et al. eds., 1977) (demonstrating the breakdown of funding for Tay-Sachs screening programs).

groups.¹³ These groups were often both financial and social sponsors of the programs as well as important sources of volunteer workers. Jewish women's groups were especially important in the effort.

Most programs spent a considerable amount of time in educational activities, even before the actual screening sessions began. These activities involved not only efforts to acquaint the Jewish community with the nature of Tay-Sachs Disease, but also more "politically" inclined efforts to recruit the support of lay, and more importantly, religious leaders of all the principal sects — Conservative, Reformed, Orthodox, and Hasidic. Such early discussions laid the ground work for the public announcement of the screening campaigns and protected the programs from public controversy over the relation of screening to abortion — an issue on which each of the principal religious groupings took a somewhat different position.

In the first ten years of the screening program, over 100,000 people were screened in the United States, and slightly over 4,000 carriers of the Tay-Sachs gene were identified. World-wide, 124 at-risk couples were identified. Furthermore, through 1976, ninety pregnancies of such couples were monitored, of which twenty-one, which test results identified as affected, were terminated, and sixty-seven unaffected off-spring were born. One unaffected pregnancy "spontaneously" aborted one week after amniocentesis was performed. In addition, in one case an infant was born who had been erroneously diagnosed as unaffected, but who later developed Tay-Sachs Disease.

Despite these generally positive aggregate statistics, specific U.S. programs, as well as certain programs in other countries, were not as successful. Some programs had poor community responses, like the one in Honolulu, where of an estimated 60,000 Jewish residents, only seventy showed up for Tay-Sachs screening, or the British experience in which despite efforts to encourage mass screening among the 400,000 members of the

13. See David V. McQueen, *Social Aspects of Genetic Screening for Tay-Sachs Disease: The Pilot Community Screening Program in Baltimore and Washington*, 22 SOC. BIOLOGY 125, 125-33 (1975) (discussing the role of the Jewish community in the pilot Tay-Sachs Disease screening program).

Jewish community, fewer than 400 persons were tested.¹⁴ Indeed, even for the United States as a whole, only about ten percent of the estimated target population of more than one million, participated in Tay-Sachs screening.

Perhaps a more concerning outcome than the failure to reach appropriate persons for screening, was the screening of less appropriate groups, for example, high school students too young to be planning families and persons whose families were already complete. The Montreal program specifically focused on high school and college students for screening.¹⁵ Unlike most of the U.S. programs in which married persons predominated, in this group only thirty-four percent of those screened were married. Although participation rates were considerably better than those among programs targeting couples (about seventy-five percent), follow-up studies indicated that though knowledge about Tay-Sachs Disease generally rose with participation in screening, among high school students who were identified as "carriers," nearly half felt "worried," or "depressed" by the information shortly after testing, and about one-third still felt "worried" or "depressed" up to seventeen months later.

Perhaps rather than debating the extent to which Tay-Sachs screening programs were successful in the 1970s, a more interesting historical question is why, after the "eugenic" programs of the Nazi state, post-war Jewish communities would be interested in even considering participation in a program which would identify what some would have called a "race-based" genetic "defect" present among Eastern European Jews. This is particularly intriguing because it would lead, albeit selectively, to the abortion of Jewish pregnancies.

Several reasons have been offered for the willingness of so many persons in the Jewish community to participate in Tay-

14. See Charles R. Scriver & Reynold J.M. Gold, *Tay-Sachs Heterozygote Screening: Specificity and Sensitivity*, in TAY-SACHS DISEASE: SCREENING AND PREVENTION, 239-43 (Michael M. Kaback et al. eds., 1977) (stating that screening tests sort out apparently well persons who probably have a [trait] from those who do not).

15. See Carol L. Clow & Charles R. Scriver, *The Adolescent Copes with Genetic Screening: A Study of Tay-Sachs Screening Among High-School Students*, in TAY-SACHS DISEASE: SCREENING AND PREVENTION 381, 381-93 (Michael M. Kaback et al. eds., 1977) (discussing genetic testing of high school students for genetic predisposition to Tay-Sachs Disease).

Sachs screening. Some commentators have suggested that the nature of the disease itself has driven the interest in screening. While this may have been an important motivation in some participants, particularly individuals with a family history of Tay-Sachs Disease, surveys show a large percentage of participants in screening programs to have been essentially uninformed about the nature of Tay-Sachs Disease.¹⁶ Others have suggested that higher educational levels in a community generally translate into greater cooperation with mass screening programs. However, there is little, if any, data which actually examines this idea. Furthermore, the information that is available, principally from work done on participants in the Los Angeles screening program, suggests that other factors, particularly gender, played a much greater role in motivating cooperation.

I would suggest that application of the historian's concept of how a disease is "framed"¹⁷ may be a more fruitful approach to understanding the surprising acceptance of Tay-Sachs screening by the American-Jewish community. From the beginning, this community has been deeply involved in defining the nature and meaning of Tay-Sachs Disease. Jewish physicians had been active in diagnosing and treating cases, and in determining the prevalence of the Tay-Sachs mutation in the Jewish population. Likewise, Jewish medical and philanthropic institutions, and perhaps most importantly, voluntary associations, were centrally involved in developing not only the scientific, but also the social understanding of this condition. This, presumably, has led to a characterization of the birth of a child with Tay-Sachs Disease as a personal and family tragedy, to be avoided if possible, rather than as a fault for which blame should be assigned to the infant's "carrier" parents.

For the scientists involved, rather than a disease of amorphous, even protean characteristics, hard to recognize at first

16. See Fred Massarik et al., *Community-Based Genetic Education, Community Channels, and Knowledge of Tay-Sachs Disease*, in TAY-SACHS DISEASE: SCREENING AND PREVENTION 353, 359 (Michael M. Kaback et al. eds., 1977) (discussing the level of knowledge held by people of different educational training with respect to Tay-Sachs Disease).

17. See generally FRAMING DISEASE: STUDIES IN CULTURAL HISTORY (Charles E. Rosenberg & Janet Golden eds., 1992) (explaining that disease has both social and biological elements).

and always difficult to distinguish from clinically and in some cases biochemically similar conditions, Tay-Sachs Disease has been repeatedly pictured as a highly distinctive condition with an almost stereotyped clinical and pathological appearance. Little attention has been drawn to the need for careful interpretation of what can in many cases be ambiguous or misleading test results, researchers preferring to emphasize the nearly "automatic" nature of the screening test, and insisting on, even when discussing occasional, but tragic errors resulting from its use, its almost absolute reliability.¹⁸

In so far as there were complex religious and moral issues raised by a strategy which depends primarily upon selective abortion to control the prevalence of this dreaded disease, it is important to appreciate that screening has been interpreted as offering "carrier" couples the chance to have unaffected children, and crediting the birth of healthy offspring to these couples as a positive outcome of the programs. By interpreting screening programs in this way, not only is it easier to gain rabbinical support, but it also makes it easier to focus on young married couples as the principal targets of screening because they are the most likely group to want such information.

Lastly, there has been a general acceptance that biochemical, or more recently, gene-based diagnosis of Tay-Sachs Disease is uniformly correlated with a malignant and ultimately fatal clinical course.

Given such a "frame," it no longer seems quite as surprising that Tay-Sachs screening would be widely accepted by the American Jewish community. However, such key characteristics as the tight coupling between diagnosis and clinical outcome, the clear implications for specific action which the identification of "carrier" status has, and the relatively brief and well-defined time span within which persons have to act with regard to this information, all seem to be essential to the programs' successes.

To the extent that other diseases are framed differently, address a very different target audience, or have very different

18. See Kaback & Zeiger, *supra* note 11, at 22-23 (suggesting that Tay-Sachs screening tests, although good, do not produce exact results all the time).

functional characteristics, it would seem that those diseases would be less likely to benefit from many of the factors leading to successes in Tay-Sachs screening. Instead, it seems prudent to consider that any attempt to apply the “lessons” of Tay-Sachs screening needs to be done in a very cautious and highly nuanced way, with much attention to the specific details of the situations being analogized.

I would like to end with a cautionary word of advice originally offered by Albert Einstein with regard to the science of relativity, but which I think can be profitably applied to the task of designing a safe and effective program to use information from BRCA1 testing. It goes something like this:

Everything should be made as simple as possible — but no simpler.

