The Dor Yeshorim Story: Community-Based Carrier Screening for Tay-Sachs Disease

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I. INTRODUCTION

The Dor Yeshorim program, like other carrier testing programs for autosomal recessive diseases, is in the practice of helping individuals to prevent the occurrence in their families of serious human genetic diseases. This objective is being accomplished through voluntary testing of large portions of the religious Jewish population, initially in the metropolitan New York area and now worldwide, wherever concentrations of Orthodox Jews live. The Dor Yeshorim program began in 1983 with screening for Tay-Sachs disease, and has developed a novel system, which provides for anonymous testing in an effort to prevent the disease and at the same time avoid the stigma which could be attached to knowledge of an individual’s carrier status. As these issues are being discussed by the genetics community, the Dor Yeshorim program is one that could be studied for new ideas about minimizing the risks associated with finding out about our genetic constitution.

In this chapter we will describe the community characteristics and dynamics, which are the context for the Dor Yeshorim program, as well as the mechanics of the program. The 17-year history and its findings and accomplishments are summarized; some interesting and surprising results are also discussed. Since genetics is fraught with difficult issues, in terms of how and when to use its powerful capabilities, we are likely to come to solutions that our society can accept if we remain open to a wide diversity of ideas. We hope that this discussion of the Dor Yeshorim program can contribute to such solution building. This program serves as a successful model of “genetic compatibility” testing and was designed to meet the special needs of the Orthodox Jewish community.

II. UNDERSTANDING A COMMUNITY AT RISK

Dor Yeshorim, the Committee for Prevention of Jewish Genetic Diseases, began within the context of the Hasidic Jewish community, then expanded to the broader Orthodox Jewish communities of the metropolitan New York area. The program expanded its services in later years to include similar communities across the United States, Canada, Europe, Israel, and Australia (Broide et al., 1993; Burnett et al., 1995). Dor Yeshorim’s success in preventing Tay-Sachs disease in these communities is a direct result of how well the program’s structure fulfills the needs of its served community. Therefore, before describing the history of Dor Yeshorim or the structure of the program, it is important to first appreciate the characteristics and dynamics of these communities.

In 1990 there were 1.6 million Jews living in the metropolitan New York area; of these, 1.1 million lived in New York City. This is a very significant concentration of Jewish people, considering that there are only 5.5 million Jews in
the entire United States; in other words, 1 in 5 American Jews lives within a geographic area of 327 square miles. This physical proximity is a graphic manifestation of the powerful beliefs which especially bind traditional Jewish peoples together. So-called religious or traditional Jews can be thought of as those who adhere to similar practices and beliefs and who can be categorized into two main groups: the Orthodox and Hasidim. The “modern Orthodox” population is approximately three times the size of the traditional community; this community and the potential for approaching its citizens are discussed in the Section VII of this chapter.

A. Orthodox and Hasidic Jews: Preserving a religion and community

The Hasidic community believes very strongly that the only way they will preserve their religious identity is by maintaining the old “Shtetel” (village) ways. Thus, they seek to preserve the traditional means of communication through the Yiddish language, as well as customs and mode of dress, which can be distinguished from the rest of society and even from other Jews. However, in the Orthodox community these distinguishing characteristics are subtle.

In both of these groups, the traditional interpretations of the Torah (Old Testament) and its laws are followed. Although they may use modern technologies (fax machines, computers, cellular phones, etc.), both groups generally do not own televisions, and even radio is discouraged; the media may be viewed as providing immodest and/or immoral messages or images. There is a tremendous effort and concentration on teaching children that some of the ways of the outside society may be detrimental to a “kosher” way of life. Thus, rabbinical leaders, parents, and community leaders screen communications from the outside world.

B. Beliefs about health and medical issues

Members of the observant Jewish community believe that they have a religious obligation to care for their physical well-being. Therefore, seeking help for illness and pursuing preventive measures to guard against illness are widely practiced. They seek help first, and often exclusively within the community, and frequently consult with their rabbi about where to seek medical advice.

Because this community is distrustful, or at least skeptical, about some of the information being generated outside their community, a portion of the literature regarding medical practices and options is not acceptable to them. In particular, standard educational material about genetic diseases is typically viewed as containing biased or value-laden information inasmuch as it may present options such as abortion or other practices prohibited by Biblical law. For these reasons, only information emanating from a community-based organization with the endorsement of its community and rabbinical leaders is able to make an impact on the attitudes of this group toward any medical or public health intervention.
C. Beliefs about procreation

Like many people of various religious or philosophical perspectives, observant Jews view having children as the most fundamental expression of their humanity. The typical Hasidic or Orthodox couple is interested in producing a large family to fulfill the Biblical commandment to “be fruitful and multiply.” Most families have 5 to 10 children. Jewish law does not permit birth control or abortion. However, individuals may seek special dispensation from their rabbi in extreme circumstances on a case-by-case basis. Consideration of this basic value of the absolute sanctity of human life was a founding principle for the Dor Yeshorim screening program.

D. Courtship and marriage: The concern about genetic stigmatization

Since the observant Jew believes in separation of the sexes, social dating and other such customs are unacceptable. There are no social clubs or other means of meeting a potential spouse. The couple usually come from similar backgrounds and values. Most girls marry at around 18, most boys by their early 20s. Although marriages among Hasidim can be considered to be “arranged,” the young couple in question do have choice in the matter, and either one can decline a suggested partner. Within Orthodox circles, dating will occur for the purpose of seeking a marriage partner.

Since the primary purpose of the marriage is to begin a new, hopefully large family, information about the health of each partner and the potential health of future children is of great concern when considering a potential spouse; this would include information about genetic diseases in either family. Today, with almost two decades of experience with the Dor Yeshorim program, it is quite typical for a family to seek genetic counseling upon hearing of genetic disease in the family of a potential partner. Previously, it was more common that a decision would be made not to pursue this “problem family” because of the lack of accurate scientific information in hand. This practice often led community members to “hide” genetic problems for fear that the “marriageability” of their normal children and relatives would be harmed.

E. Summary

Because the Orthodox and Hasidic Jewish communities adhere to strict religious practices, are health conscious, and have strong beliefs about family, any program directed at serving these communities must accommodate these principles and practices. It was in this context of a tightly knit religious community with strong concerns about genetic stigmatization that the Dor Yeshorim screening program was conceived.
III. EARLY EFFORTS AT SCREENING

After the establishment of standard carrier screening programs in the 1970s and 1980s by Dr. Michael Kaback and others, including one in close proximity to the religious Jewish communities (at the Mount Sinai School of Medicine), it became apparent that the Orthodox and Hasidic communities were generally not participating. The birth rate of babies with Tay-Sachs disease began to decline in the 1970s, but this was not true among the children of religious Jews.

To bring preventive carrier testing to this community required the close collaboration of a motivated rabbi, an expert, dedicated physician, and two devoted community members. In 1983, Rabbi Josef Ekstein found himself the father of yet a fourth child with Tay-Sachs disease. He elected to translate this personal tragedy of four children with Tay-Sachs disease into a mission to spare others in his community from experiencing what he realized was preventable. Rabbi Ekstein sought the help and advice of Dr. Robert Desnick, chairman of the Department of Human Genetics at the Mount Sinai School of Medicine, the physician who diagnosed and cared for the fourth of Rabbi Ekstein’s Tay-Sachs children. With Dr. Desnick's expert advice and strong support, Rabbi Ekstein and his colleagues proposed to their community leaders that a screening program be established from within.

However, since traditional screening programs focused on testing individuals who were already married, if not pregnant, the religious communities viewed them as inappropriate for people like themselves who would not consider abortion. Furthermore, there was widespread fear that carriers and their entire families would become stigmatized as undesirable marriage partners. In particular, family members of affected children were vehement in their opposition to testing. Community leaders also became concerned that the open identification of adolescents as carriers could cause them unnecessary stress and anxiety. In 1976, the prominent bioethicist, Dr. Fred Rosner, reviewed a plethora of opinions that had accumulated from medical and Jewish authorities (Rosner, 1976) on the pros and cons of testing young people. Indeed, Rabbi Moses Feinstein, the most notable Jewish scholar on the interpretation of the law for postwar Orthodox Jewry, wrote in 1973 against mass carrier testing of young adults for all these reasons (Feinstein, 1973).

Together with his colleagues, Mr. Elias Horowitz and Mr. Kalman Weiss, Rabbi Ekstein countered these objections to screening with a proposal for a community-based program, which could provide absolute anonymity and confidentiality to those tested. Because these community leaders had the commitment of a leader in the medical genetics community in Dr. Desnick, their proposal had credibility as a true collaboration between medicine and community. The novel structure of the Dor Yeshorim program allowed all young couples considering...
to be protected from the risk of having a child with Tay-Sachs disease, while also protecting the identity of carriers in the community. Indeed, even the members of the Dor Yeshorim staff would not know the identity of carriers in this truly anonymous system. The dedicated vision of Dr. Desnick and the other founders of the Dor Yeshorim program resulted in a slow but meaningful reversal of previous objections to screening. For example, a year after the initiation of the Dor Yeshorim program in 1983, Rabbi Feinstein wrote a public letter supporting the Dor Yeshorim screening program for all Jews, since previous concerns had been addressed by the screening program.

IV. MECHANICS OF THE PREMARITAL, ANONYMOUS SCREENING PROGRAM

As young people in these communities typically marry by age 20, the Dor Yeshorim program is primarily offering testing to high school senior girls and seminary boys (90% of tests obtained through Dor Yeshorim) in order to achieve early premarital screening. Before a screening day, students are introduced to the clinical picture of Tay-Sachs disease and the 1-in-4 risk if two carriers marry. Students also learn that carriers are not themselves ill, and that one carrier in a couple presents no risk for affected children. This and other information is provided in a pamphlet that is given out at school, and the concepts are discussed in the classroom. The parents are encouraged to discuss testing and its merits at home and must sign a consent form for their minor children to be tested. Since the Dor Yeshorim program has been in effect for almost two decades, these young people also may have learned of the program through older siblings. Approximately 90% of students choose to be tested.

On the day of testing, each student who has a signed parental consent form is given an individual consent form and a card printed with a unique identification number. All materials including the blood collection tubes are labeled with the individual’s unique identification number. A random control number is also added to each identification number to provide a quality control measure. Each student who wishes to be tested writes his or her date of birth and family’s countries of origin. The consent form is signed with his or her identification number. From this point forward, each individual and blood sample can only be identified by the anonymous identification number. The card which each students keeps has the phone number of Dor Yeshorim on it as well as his or her preprinted identification number and a reminder to call for compatibility results in the early stages of a potential marriage relationship. Professional, licensed phlebotomists draw blood samples.

When a young couple is considering a “shidduch” (marriage match), they have the opportunity to call Dor Yeshorim, to which they can provide their two
ID numbers and dates of birth and receive a genetic compatibility assessment. The couple is told only whether or not they are compatible; two carriers for Tay-Sachs disease are incompatible. Two noncarriers or one carrier and one noncarrier are compatible. It is not divulged that one member is a carrier, so as to protect the carrier and his or her family from stigmatization. Since the staff at Dor Yeshorim have only the identification numbers and birthdates of the individuals in question, they are also blind as to the identity of carriers. If a couple is “potentially incompatible” (inconclusive by inconclusive or carrier by carrier or inconclusive by carrier), they are counseled regarding the disease, and the 1-in-4 risk with each pregnancy of having an affected child, if both are carriers. Blood samples are redrawn for confirmatory retesting. During retesting they are continuously counseled. If the couple is confirmed as incompatible, they are offered further genetic counseling. The choice about whether or not to pursue the marriage in light of this information is strictly up to the couple. In addition, the couple is reminded that each of them is very likely to be compatible with another individual in another potential partnering.

The Dor Yeshorim program provides hours of counseling to couples who have been found to both be carriers of Tay-Sachs disease or another Jewish genetic disease (e.g., cystic fibrosis, Canavan disease, Fanconi anemia type C), to educate them about their specific risk. Such a couple is keenly focused on this information, which pertains to them in particular; i.e., this is education about themselves. Thus, genetic counseling is efficiently focused on at-risk couples instead of on each individual carrier identified, permitting in-depth counseling and, in part, addressing the problem of the shortage of genetic counselors trained in these issues as well as the high cost of carrier counseling. Dor Yeshorim is committed to spending as much time as necessary with these at-risk couples; they can afford to do so, since the number of such couples is small compared to the number of individual carriers in the population.

A. Quality control and quality assurance

Dor Yeshorim sends blood samples to several quality control laboratories in the United States for DNA testing and/or enzyme assays. Samples are labeled only with the identification number. Results from participating laboratories are entered into a secured computer file by identification number. Entry is performed twice by different data entry personnel. The computer compares the two entries for any discrepancies and does not allow the deposition of nonduplicate data.

The use of several independent laboratories for testing is an important aspect of the quality control measures that are embedded in Dor Yeshorim’s program. Both academic and commercial laboratories have provided or are currently providing testing services to the program. Each laboratory has all the basic elements required for CLIA and other required certifications as general clinical laboratories.
However, selecting a specialty genetics laboratory has required further assessment of the following aspects of laboratory practice: (1) quality control measures appropriate to DNA or enzyme analysis practiced by the laboratory; (2) turnaround time for results back to Dor Yeshorim; (3) qualifications for interpretation of results by the laboratory directors; (4) ability to manage large volumes of samples; and (5) willingness to participate in blind control sampling as part of Dor Yeshorim’s quality control program. A list of the excellent laboratories that have provided testing services to Dor Yeshorim are provided in Section VIII of this chapter.

As mentioned above, Dor Yeshorim includes random control samples in most shipments of samples to each laboratory. Multiple laboratories, using all methods in practice, have analyzed each control sample so that the genotype of the sample is well documented. Indeed, as revealed in Table 23.2, control sampling and confirmatory testing at one time represented approximately 32% of all samples sent for analysis. This large quantity and frequency of control sampling has proven to be of great value in enzyme testing, since the assessment of normal, inconclusive, and carrier quantities of hexosaminidase A activity is so sensitive to minor variations in samples, patient, and assay conditions. Far fewer DNA controls are included in shipments, since mutation analysis is not sensitive to such external factors. Since any discrepant results on control samples are discussed confidentially with the laboratory, this program is typically viewed by the laboratory as a valuable external assessment of reliability and laboratory performance.

B. Goals and guidelines

The Dor Yeshorim program has two goals. The first is to provide a system whereby young men and women of marriageable age can avoid the risk of having a child with Tay-Sachs disease and other recessive diseases that are prevalent among the Ashkenazim (Jews of Eastern European descent). Importantly, the goal of the program is to provide this preventive measure without placing these young people at risk of social stigmatization and discrimination in the community or by insurance carriers or employers as a result of test results. The second goal is to allow young people with a family history of Tay-Sachs disease or other genetic diseases to participate without the fear of being identified and stigmatized.

Dor Yeshorim stresses confidentiality and anonymity very strongly. For couples who are identified to be at risk, it is essential that a confidential environment for obtaining information and assistance be guaranteed. Indeed, since its founding, Dor Yeshorim has seen a regular flow of parents, siblings, and other family members of individuals afflicted with other genetic diseases coming to seek information and help in preventing genetic disease. As Dor Yeshorim has come to represent a reliable mechanism for obtaining compatibility assessments, so has it become a resource for referrals and for research on many of the recessive illnesses found among Jewish peoples (see below).
V. FINDINGS AND ACCOMPLISHMENTS

Since 1983, the Dor Yeshorim program has received and processed blood samples from over 120,000 individuals (Table 23.1). The volume of testing has increased over the years, with almost 12,500 being tested in 2000. Dor Yeshorim added testing for cystic fibrosis to its program in 1993, and for Canavan disease and type C Fanconi anemia in 1995. Dor Yeshorim also facilitates access to testing for other autosomal recessive diseases upon request from families. In addition, Dor Yeshorim has explored through pilot studies the merits of screening for Gaucher disease. These new screening opportunities have provoked the retesting of an additional 18,608 individuals (Table 23.1). This expansion of the Dor Yeshorim program to other recessive disorders is discussed elsewhere (Desnick, in press). The numbers are noteworthy, since the individuals who were retested for these additional diseases did so by special request; this avid reuse of the program seems a significant affirmation of how the community has embraced the screening program.

Dor Yeshorim has had almost 60,000 requests for compatibility assessment from couples, with 7,759 of these in the last year alone (Table 23.1). These queries have resulted in finding 295 potential matches that were confirmed as incompatible for at least one of the disorders for which carrier tests were available.

To date, the program has logged Tay-Sachs carrier status results for 117,302 individuals, plus an additional 55,487 control sample results (Table 23.2). Taken together, some 172,789 tests for Tay-Sachs disease have been performed and cataloged over 17 years. Among the 117,302 tested individuals, 5,416 were found to be carriers by enzyme or DNA analysis. The overall carrier rate of all testing methods was found to be 1:22. The carrier rate from serum testing was approximately 1:20. The rate of inconclusive enzyme analysis results was 1:15.

Since 1992, there have been 39,574 individuals who also received gene-based testing for Tay-Sachs disease by analysis of the three common mutations in the Ashkenazim (see Table 23.3). Of these, 1,718 were found to be carriers of one mutation, a carrier rate of 1:23. This carrier rate, when compared with the 1:22 rate derived from total testing (serum and DNA tests), is consistent with

<table>
<thead>
<tr>
<th>Table 23.1. Summary of Screening Activity at Dor Yeshorim: 1983–2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
</tr>
<tr>
<td>Total individuals tested</td>
</tr>
<tr>
<td>Total retested for additional disease or confirmation</td>
</tr>
<tr>
<td>Total couples called to check compatibility</td>
</tr>
<tr>
<td>Total incompatible; all diseases</td>
</tr>
</tbody>
</table>

a Testing for CF was added in 1993, Canavan disease and Fanconi anemia Type C in 1995.
Ekstein and Katzenstein

Table 23.2. Tay-Sachs Screening; 1983–2000

<table>
<thead>
<tr>
<th></th>
<th>Number of individuals tested</th>
<th>Carriers (rate)</th>
<th>Inconclusives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total individuals sampled</td>
<td>118,689</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total individuals analyzed to date&lt;sup&gt;a&lt;/sup&gt;</td>
<td>117,302</td>
<td>5,416(1:22)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8,036(1:15)</td>
</tr>
<tr>
<td>Carriers and inconclusives by serum, retested by platelet or leukocyte assay</td>
<td>1,227</td>
<td>415</td>
<td>98</td>
</tr>
<tr>
<td>Normal control samples tested</td>
<td>55,487</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total tests</td>
<td>172,789</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incompatible couples</td>
<td>136</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of biochemical/DNA results

<table>
<thead>
<tr>
<th></th>
<th>Number of individuals tested</th>
<th>DNA positive (rate)</th>
<th>DNA negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals tested by DNA and serum</td>
<td>39,574</td>
<td>1,718(1:23)</td>
<td>37,856</td>
</tr>
<tr>
<td>Carriers by serum</td>
<td>2,037</td>
<td>1,602</td>
<td>435&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Inconclusives by serum</td>
<td>4,152</td>
<td>99</td>
<td>4,053</td>
</tr>
<tr>
<td>Negatives by serum</td>
<td>33,385</td>
<td>17&lt;sup&gt;d&lt;/sup&gt;</td>
<td>33,368</td>
</tr>
<tr>
<td>Individuals tested by platelet or leukocytes and DNA</td>
<td>1,047</td>
<td>232</td>
<td>815</td>
</tr>
<tr>
<td>Carriers detected by platelet or leukocyte assay</td>
<td>239</td>
<td>224</td>
<td>15&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Inconclusives by above platelet or leukocyte assay</td>
<td>63</td>
<td>8</td>
<td>55&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Negatives by platelet or leukocyte assay</td>
<td>745</td>
<td>0</td>
<td>745</td>
</tr>
<tr>
<td>Control DNA samples</td>
<td>5,107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total DNA results</td>
<td>44,681</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Serum and DNA together.
<sup>b</sup>By serum, not confirmed.
<sup>c</sup>Three individuals in this category were found to have the common pseudodeficiency gene.
<sup>d</sup>One of the individuals had a bone marrow transplant.
<sup>e</sup>Two individuals in each of these categories were found to have the common pseudodeficiency gene.

Table 23.3. Mutation Analysis of β-Hexosaminidase A Gene<sup>d</sup>

<table>
<thead>
<tr>
<th>Specimens</th>
<th>Number of individuals</th>
<th>Mutation frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total specimens</td>
<td>59,819</td>
<td></td>
</tr>
<tr>
<td>Total mutations detected</td>
<td>2,491</td>
<td></td>
</tr>
<tr>
<td>1,277 insertion</td>
<td>2,202</td>
<td>88.4%</td>
</tr>
<tr>
<td>1,421 splice site</td>
<td>206</td>
<td>8.3%</td>
</tr>
<tr>
<td>G269</td>
<td>79</td>
<td>3.2%</td>
</tr>
<tr>
<td>Other&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4</td>
<td>.2%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Analysis of mutations includes research. Samples.
<sup>b</sup>Includes one convert and three individuals with sephardic lineage.
the observation of 435 individuals who were determined to be carriers by serum testing but who were negative for all three mutations by DNA analysis. It has not been possible to retest all 435 individuals to clear the discrepant results. It is likely that the discrepant results are due to the known false positive rate associated with serum tests.

After six years of parallel Tay-Sachs testing by enzyme and mutation analyses, Dor Yeshorim concluded that mutation analysis offered close to 100% sensitivity and specificity for Ashkenazi Jewish individuals (Bach et al., 2001). DNA testing did not have the drawbacks associated with enzyme analyses, the latter having approximately 15% inconclusives as well as false positives. Of 151 Tay-Sachs disease chromosomes from patients or obligate carriers, all were identified by the analysis of the three Tay-Sachs disease mutations. Blood samples from 478 enzyme positive or inconclusive and DNA negative individuals were analyzed for 10 other Tay-Sachs disease/pseudodeficiency mutations. Five carriers of a pseudodeficiency mutation were found, as well as one carrier of the C509A mutation. Ten of the specimens that were also positive/inconclusive by leukocyte/platelet, and negative for the three common Tay-Sachs disease mutations, were analyzed for the 10 above-mentioned mutations. Two were found to be carriers of pseudodeficiency mutations. The remaining eight patients were analyzed by gene sequencing, and no Tay-Sachs disease mutation was detected.

Since the inception of Dor Yeshorim, over 135 proposed matches were found to be incompatible for Tay-Sachs disease. Based on the 1:23 carrier rate derived from the DNA analysis, one would predict that 222 incompatible couples would be identified. However, since incompatible matches were identified only upon the request of particular individuals at the time of considering a potential partner, there is a lag between when Dor Yeshorim obtains carrier results and when incompatibilities are identified. This lag is 2–3 years, because girls are screened on average 2–3 years prior to the time of peak marriage considerations. As many as 25% of the individuals in the Dor Yeshorim database have not been queried for compatibility due to this lag. Therefore, the observed incompatibility rate is expected to be lower than that theoretically predicted from the total individuals tested.

Currently, the Dor Yeshorim program relies exclusively on DNA results for these individuals of Ashkenazi Jewish descent. Individuals who are not solely of Ashkenazi descent [i.e., Sephardi Jews (Jews of Mediterranean descent) or converts] undergo enzyme and DNA analysis.

Dor Yeshorim has observed that the vast majority of at-risk, incompatible couples did not pursue marriage, based on subsequent queries with different suitors. However, a handful of these couples did proceed with the engagement, after further counseling at Dor Yeshorim and elsewhere.

In 1996, there were no children with Tay-Sachs disease in the special unit for children with inborn errors of metabolism at Kingsbrook Jewish Medical Center in Brooklyn, New York (personal communication, Dr. Larry Schneck).
This hospital has had a special ward devoted to the care of patients with Tay-Sachs disease and other inherited metabolic diseases for the past 40 years. Prior to Tay-Sachs prevention programs and the Dor Yeshorim program, the ward had as many as 16 Tay-Sachs patients and had a waiting list of affected children. The last child, the fifth affected child of a religious family, expired in March 1996. It is now a rare occurrence indeed for a child to be born with Tay-Sachs disease in the community served by the Dor Yeshorim program. Clearly, the Dor Yeshorim program is meeting its primary goal of prevention.

VI. RESEARCH

As the religious Jewish community has been greatly served by the endeavors and successes of the general research community, so has the religious Jewish community endeavored to help further advance work in the area of Jewish recessive genetic diseases. Dor Yeshorim has been able to provide hundreds of trial samples to laboratories wishing to establish testing services, as well as positive and negative control samples for laboratory standards. Furthermore, after the discovery of the β-hexosaminidase A gene, the program provided samples to help establish mutation frequencies for Tay-Sachs disease in this population as part of worldwide survey efforts. Dor Yeshorim also has assisted in the identification and validation of the genes that cause Canavan disease, Gaucher type I disease, and Fanconi anemia—all diseases which occur quite commonly in the Dor Yeshorim catchment population (Desnick, in press). This synergy between prevention of serious diseases and research is a valuable outcome of the firm base of trust and participation that Dor Yeshorim has established in its community. The benefits of such cooperation and mutual assistance cannot be overestimated.

VII. CAN THE DOR YESHORIM MODEL BE APPLIED TO OTHER COMMUNITIES?

The Dor Yeshorim screening program must still reach the much larger modern Orthodox community, since this community has not yet embraced the concept of couple-based screening. However, with education and appropriate methods of practice in the program, we believe that a modified version of the Dor Yeshorim model could be applied successfully in this community.

It is for religious and social reasons that the Dor Yeshorim program is focused on testing premarital young adults. At this point in developing a relationship, genetic factors as well as values, family, and moral character are
considered. In Canada there has also been a pilot program of testing high school students for Tay-Sachs disease and more recently for cystic fibrosis carrier status, with a reportedly positive impact (Zeesman et al., 1984; Scriver, 1993). Furthermore, the current program of couple-based carrier screening in Britain seems to have met with a positive response in that population (Livingstone et al., 1993; Brock, 1996). Studies on the perceived value that American youth might place on genetic compatibility as one important factor to consider when contemplating a potential marriage relationship might be very interesting. After all, many young couples dissolve relationships upon discovering that the partner does not share similar values with regard to child rearing, religion, or career aspirations. What would such young people do with information that they are both carriers of a severe recessive genetic disease, and have a 1-in-4 risk for an affected child? They would have to choose options including having no children vs. risking having a child with a serious untreatable disease vs. terminating a pregnancy. Perhaps these are choices that a potential couple would choose to avoid, just as many now choose to avoid the difficult choices surrounding the blending of dissonant philosophical or religious views.

VIII. ANALYTICAL LABORATORIES

Dor Yeshorim would like to acknowledge the expert services of all the laboratories which have provided Tay-Sachs carrier-testing services for the Dor Yeshorim program: Mount Sinai School of Medicine, New York, NY; Albert Einstein College of Medicine, Bronx, NY; Baylor College of Medicine Kleeberg DNA Laboratory, Houston, TX; University of Pittsburgh, Pittsburgh, PA; Kingsbrook Jewish Medical Center, Brooklyn, NY; New York University, New York, NY; Hadassah Hebrew University Hospital, Jerusalem, Israel; National Hospital, Institute of Neurology, London, England; Thomas Jefferson Hospital, Philadelphia, PA; Scripps Research Laboratory, San Diego, CA; Genzyme Genetics, Framingham, MA.

Acknowledgments

Dor Yeshorim’s success (even survival) has relied heavily on the service and contributions of many people in laboratories, offices, and centers around the world. Rabbi Ekstein and the staff at Dor Yeshorim would like to particularly thank Dr. Robert Desnick, Mr. Elias Horowitz, and Mr. Kalman Weiss for their vision and support in their co-founding and guidance of the Dor Yeshorim program. In addition, Dr. Harold M. Nitowsky’s ongoing commitment to Dor Yeshorim as medical director and general advisor has given the program much-needed knowledge, perspective, and professional guidance. The expertise and work of almost 20 years of Frances Berkowitz, M.S., as our genetic counselor has given the program the ability to reach out to those in difficult times. We are grateful to Karen Greendale, M.A., and The New York State Department of Health for their assistance.
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Dor Yeshorim is also grateful for the advice and assistance of Dr. Barbara Handelin, in particular for help in preparation of this manuscript. Many thanks also are extended to the laboratory directors and coordinators whose dedication to quality and service are very much appreciated: Dr. Christine Eng, Dr. Ruth Kornreich, Dr. Sue Richards, Dr. John Barranger, Dr. Bernice Allito, Dr. Jean DeMarchi, Ms. Guuta Perle, Dr. Edwin Kolodny, Dr. Tomczak, Dr. E. J. Thompson, Ms. Patricia Morris, and Dr. Eugene Grebner. Special thanks especially go to Dr. S. Nikagawa and Profs. Gideon Bach and Dvorah Abeliovich, who on a daily basis provide service and support to Dor Yeshorim. Finally, Dor Yeshorim has been enabled and guided by the office of The New York State Department of Health through the advocacy and diligent efforts of Dr. Ann Willey, Dr. Kenneth Pass, Ms. Katherine Harris, and Dr. Jane Lin Fu and Dr. Margaret Lee of H.H.S. Bureau of Maternal and Child Health.

Rabbi Ekstein is grateful to have received the Robert Wood Johnson Community Health Leadership award for 1996; Dor Yeshorim is very proud to receive such external recognition and support.

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