Screening for the Tay–Sachs Carrier: A Compromise Program

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A modified program designed to screen for the Tay–Sachs carrier is presented in which testing is limited to one or both partners, as needed, in an Ashkenazi Jewish (Jews of central and eastern Europe ancestry) mating when there is a definite commitment toward having a child, or in the early stages of the pregnancy. Testing of unmarried individuals is discouraged. The approach maximizes individualization of both the medical and laboratory aspects of the program and promotes a positive and beneficial relationship between physician and clinical chemist. There is little involvement of the lay population or clergy, and no special sources of funding are required. Whereas most mass screening programs for the Tay–Sachs carrier have attempted to educate large numbers of the lay public to bring pressure upon the medical community, we have reversed this approach and taken the much easier course of educating small numbers of physicians to better care for their patients. The program has been used successfully in a moderate-size city in which communication lines between laboratory and physician are easily established.

Additional Keyphrases: heritable disorders • screening more efficiently

Screening programs for genetic disorders became fashionable in the early 1960s subsequent to the development of the Guthrie method for detection of phenylketonuria. Since then, many major programs have been established to screen for genetic disorders in the homozygous and (or) heterozygous states (1). Some of these programs have been rather successful, for example, screening for phenylketonuria (2) and hypothyroidism (3). Some have been of lesser significance, such as α1-antitrypsin deficiency screening (4). Some have been of little or uncertain benefit and require some revision in design at the very least, examples being diabetes (5, 6) and sickle cell disease screening (7).

Tay–Sachs disease is the classic example of a genetic disorder that is easily preventable through identification of the carrier state and prenatal diagnosis in pregnancies at risk (8). Strong feelings for (9–13) and against mass screening (14–16) for this disorder have been expressed, and a prudent and studious overview has also been published (17). Hospital-based clinical chemists have frequently been approached by well-meaning individuals and groups to participate in establishing a comprehensive screening program to detect the Tay–Sachs carrier. We present here a modified Tay–Sachs screening program that represents a compromise position, which is capable on the one hand of preventing the disease and on the other of avoiding some of the unfavorable features of mass-screening programs.

The approach resembles that advocated by Kaback et al. (18) but differs in several respects. First, it leans heavily upon community-physician partnership together with a minimum of initiative from and involvement of the lay public. Secondly, it encourages testing early in pregnancy or testing of Ashkenazi Jewish couples definitely committed to having a family. Thirdly, it suggests testing only one of the partners initially, as this will suffice to eliminate the possibility of Tay–Sachs disease about 96% of the time, on a genetic basis. The program thus minimizes the very substantial administrative, organizational, and counseling responsibilities and maximizes individual medical attention by significantly reducing the volume of clients. Finally, it keeps the screening program essentially within the realm of the private practice of medicine with only background support as needed from hospital-based geneticists, physicians specializing in metabolic diseases, and clinical chemists.

The program had been in effect for about four years through personal communication with obstetricians and other physicians and completely without public dissemination of information, but was recently formalized with the following letter to all physicians, which summarizes our attitudes regarding mass screening for this disorder in a moderate-size city such as Akron, OH (population about 300 000). The approach is largely pragmatic, with no attempt to deal with basic philosophical issues, which have been discussed elsewhere (1, 17–19).

Letter to Physicians

The occurrence of Tay–Sachs disease in a defined population (Ashkenazi Jews), the existence of a relatively simple laboratory test (hexosaminidase A) which can identify the disorder in both homozygous and heterozygous (carrier) states, and the availability of prenatal diagnosis make Tay–Sachs disease preventable, provided couples at risk are identified. In this country, the carrier rate is about 1 in 27 in the Ashkenazi Jewish population. Approximately 1 in 900 Jewish couples are at risk. When both mates are carriers, the probability of having a child with Tay–Sachs disease is 25%. About 30–50 children with Tay–Sachs disease are born each year in this country.

Comprehensive mass-screening programs have been carried out in the United States and Canada. Although they differ in some detail, the organizational aspects of these programs are substantial, involving a major publicity effort, enlistment of the medical and religious communities, record-keeping and confidentiality, and instruction and counseling. However, screening of young single individuals would seem to be premature because an individual may not marry, or may marry out of faith (approximately 30–40% intermarriage in this country), or decide not to have children. Furthermore, serious and justifiable concern has been expressed about an adverse psychologic effect of the knowledge that one is a carrier for this disease.

We would like to bring to your attention the details of a program suitable for our community (ca. 1900 Ashkenazic Jewish families), which will accomplish the goal of prevention of Tay–Sachs disease with a minimum of organizational detail and maximization of individual patient care and attention. We are recommending that screening for Tay–Sachs disease in the Jewish community be deferred until marriage or pregnancy. At this stage, one of the partners can be tested for the carrier state, and if a non-carrier status is established (as is the case most of the time), testing of the other partner is unnecessary. If both partners prove to be carriers a potential set-up for Tay–Sachs disease exists and you may wish to refer the family to the Genetics Clinic at Children's Hospital Medical Center of Akron for counseling.

Obviously, it is advantageous to test for heterozygosity as early in pregnancy as possible, and at least prior to 18 weeks pregnancy. Serum hexosaminidase A and white blood cell hexosaminidase A testing are available at Children's Hospital Medical Center of Akron. Serum hexosaminidase A testing should not be used in patients who are pregnant or using birth-control pills or with diabetes mellitus or debilitating illnesses associated with tissue necrosis (hepatitis, pan-
creatitis, etc.). In all these situations, white blood cell hexosaminidase A should be ordered.

In order to succeed, the interest and cooperation of both patients and physicians are required. We are in the process of bringing this information to the attention of the Jewish community so that testing can be requested by patients at the appropriate time. It is also important for physicians, in particular obstetricians, to take an active part in this prevention campaign by identifying and testing their patients.

Results and Discussion

Tay–Sachs disease is such a rare genetic disorder that we have been unable to ascertain a single documented case born in the Akron area during the last 30 years, even though about 1800 Ashkenazi Jewish families live within the immediate area of our hospital with about 60 Jewish births per year. It has been argued that one advantage of the screening experience in young single individuals is a more effective teaching of biology and genetics in high school (11), but the uncertain psychologic impact of the awareness of one’s Tay–Sachs genotype and the availability of many effective alternative approaches to teaching make this argument unconvincing.

The physicians of the community are extremely positive and supportive of the program; indeed, it was furthered by independent physician-to-physician contact emphasizing the importance of the testing program. Thus, medical support was sympathetic and strong and posed no problems. This contrasts with the experience in Canada, where it was found that the physician was a poor advocate of testing. However, this program involved 4000 physicians and 30,000 Ashkenazi Jews (9). In addition, we sent letters to the Jewish Community Center and the rabbis of the three local temples, including a brief note to be published in their bulletins advising Jewish couples planning to have children to identify themselves at the appropriate time to their personal physician so that testing could be undertaken.

Clinical chemists, together with physicians, have a responsibility to design and establish a program that is scientifically sound, minimizes the adverse features inherent in all screening programs, and is tailored to the needs of the particular community in which it is being offered. A program that is quite successful in one city may be entirely inappropriate in another. The psychologic and social hazards of Tay–Sachs screening and the risks and benefits have been dispassionately reviewed (17).

Because screening programs generally do not directly involve the non-specialist physician, his awareness of and interest in these diseases is usually relatively small, particularly if the disease is rare. Our approach clearly reverses this trend. By making the role of the community physicians central and crucial to the success of the program, their expertise in and concern and involvement with genetic diseases are enhanced.

The same is true for the clinical chemist. The reduction in the number of individuals tested provides time to gather the information required to determine whether the serum test or the leukocyte test is appropriate for each patient. A short questionnaire, consisting of yes or no answers, relative to the false-positive factors affecting the serum test, can be easily devised and given to the patient. If the questionnaire is filed with the results, the effectiveness of the program can easily be evaluated, as well as the incidence of the carrier state in the community. Reliable methodology is crucial and requires close scrutiny and attention. The literature should be consulted for the vagaries and vicissitudes of the test (18, 19). Finally, if need be, the clinical chemist can help the physician interpret the results and the proper course to pursue (as outlined in the letter).

Our experience suggests that a primary approach via physician contact and education can be successful, at least within the framework of a community of this size and type (about 7200 births per year in five hospitals, 50 to 55 obstetricians, 40 to 45 pediatricians, and 60 to 75 family practitioners). During the six years that the program has been in effect we have discovered no family in which both members were carriers, and no affected child has been born—not surprising, because with about 60 Ashkenazi–Jewish births per year and no screening program at all, the expectation of a Tay–Sachs birth is about one in 60 years. It was not possible to determine accurately the percentage of pregnancies monitored, owing to incomplete record-keeping in some hospitals, particularly where the religion of the father was not recorded. However, in 1978, even during the informal period of the program, we estimate that about 30% of Jewish pregnancies were tested. After the letters were sent to physicians and the information disseminated to the lay public in synagogue bulletins and the publication at the Jewish Center, we expected a substantially more nearly complete coverage, but our estimates for 1979 showed that coverage remained at 30–35%. Our 1980 yield shows no significant increase. However, the program has been deliberately understated and underpublicized, to avoid flooding of physician’s offices with patients who may be presenting themselves at what we consider to be an inappropriate time and to avoid unnecessary apprehension in the lay community.

It is difficult to compare our results with the experiences obtained elsewhere because the critical data—the percentage of Jewish pregnancies monitored per year—are not easily obtainable. Kaback et al. (20) estimated that the screening programs in Baltimore and Washington elicited a compliance rate of about 50% in Jewish couples planning to have further children, but that figure was based on major assumptions. The Toronto program similarly did not have a reliable data-base to evaluate effectiveness (21). In Cleveland, Ohio, where about 85,000 Jews live, mass-screening programs of the Kaback type during three and one-half years have resulted in 2100 individuals being screened. No couple in which both partners were carriers was detected (personal communication: Dr. Arnold Friedman, Mount Sinai Hospital, Cleveland, OH). A mass-screening program carried out in the mid-Tennessee area, including the cities of Nashville, Knoxville, and Chattanooga, resulted in screening of 8% of the total Jewish population of 7200 individuals in the three cities. Twenty-five carriers, and one couple at risk were identified, but the critical question—the percentage of Jewish births monitored per year—was not addressed (22).

Our program thus compared favorably with the aforementioned studies, but avoids the massive community effort and the unfavorable aspects of the screening experience in other cities. We still believe that essentially total coverage of Jewish pregnancies is attainable in a city of this size and medical structure, and we are now in the process of re-forming the medical community of its responsibility and restating the program in the synagogue and Jewish Center bulletins, but at least another year or so must elapse before we can evaluate the proper admixture of medical and lay involvement for a completely satisfactory program.

References


