

Genetic-Metabolic News

One of the primary aims of the genetic counselor is the reduction in the number of children born with either lethal disorders or severe CNS dysfunction (eg. mongolism and midline neural defects). Generally, this goal is accomplished in one of four major ways:

- 1) Where a child's disorder is known to be inherited in a Mendelian fashion, by clearly stating the recurrence risk of 1:2 or 1:4, which is often a deterrent to a parent pair to plan further pregnancies;
- 2) By counseling based on empirically established recurrence risk statistics;
- 3) Where the risk is high, by determining the status of the fetus at 14-16 weeks by aspiration and study of amniotic fluid (amniocentesis)—when the mother is over age 40, or has had a previous child with mongolism, a sex-linked disorder, or one of some fifty metabolic disorders which may be diagnosed by amniotic fluid study, the pregnancy can be terminated before twenty weeks gestation if one of the disorders is detected;
- 4) By ascertainment of parent pairs where both are carriers of an autosomal recessive disorder *before* birth of an involved child so that parents may be advised of the high risk of occurrence of this disorder in their offspring and also be advised of the availability or nonavailability of intrauterine diagnosis by amniocentesis.

At present, two carrier detection programs (for sickle cell anemia and Tay-Sachs disease) have been developed because the following necessary criteria have been met:

- 1) The carrier test is rapid, accurate, and inexpensive within a defined population;
- 2) The frequency of the carrier state is high enough within a defined population to justify the cost of testing;

3) The disorder is a serious health hazard for which there is no definitive cure.

One other disorder, cystic fibrosis (rare in the Black race) meets criteria 2 and 3 but unfortunately, not 1. As soon as an effective carrier test for this disease is developed, however, it will be offered to whites just as today, blacks have available sickle cell testing and Jews, a Tay-Sachs screening test.

The major purpose of this article is to briefly summarize the concept of a Tay-Sachs carrier detection program and to share our experiences in Virginia. This disease, first described by Drs. Tay and Sachs in the 1880's, was classified for over sixty years as a "degenerative disorder" of the central nervous system (CNS).

Approximately five years ago, however, it was shown that the disorder is due to the deficient activity of an enzyme, hexosaminidase A, which catabolizes a normally occurring ganglioside. The accumulation of this sphingolipid causes progressive CNS deterioration in an infant who previously developed normally for the first six-to-nine months of life. Death by the age of four or five is inevitable since no cure is available or imminent.

Over the past few years, an accurate procedure for the quantitation of hexosaminidase A (hex A) activity in serum has been developed which identifies the carriers of this autosomal recessive disorder. Because the Tay-Sachs disease occurs one hundred times as frequently in Ashkenazi Jews (those Jews of Eastern European and Russian ancestry who represent 90% of the United States Jews) as compared to Gentiles and Sephardic Jews, it has become feasible and advisable to use this test to screen this population for the carrier state. Identification of the carrier is important for the following reasons:

- 1) It alerts relatives of carriers (through appropriate genetic counseling) of their very high risk for also being a carrier;
- 2) It allows identification of couples in the childbearing age who may *both* have the abnormal gene and are therefore at a 1:4

risk for having a Tay-Sachs infant. If both members of a parent pair are carriers, three alternatives exist:

- a) limitation of family size;
- b) therapeutic termination of an involved fetus diagnosed by amniocentesis in the 4th month of pregnancy;
- c) artificial insemination from a male known *not* to be a Tay-Sachs carrier—this approach would only be suggested where amniocentesis or termination of pregnancy are not acceptable to the parents.

Over the past twenty months, the Departments of Pediatrics and Pathology at MCV, in cooperation with the Virginia State Health Department and concerned local physicians and volunteers, have organized intensive educational campaigns to outline the rationale of Tay-Sachs carrier testing. These efforts in Richmond, Roanoke, Norfolk-Virginia Beach, Hampton-Newport News, and Fredericksburg, have yielded a voluntary turnout of over 3600 adult Jews at designated testing dates in community centers.

Complete analysis of over 2000 specimens has thus far disclosed a carrier incidence of 1:30. This figure is in close agreement with the 1:28 figure found by the first and largest "outreach" Tay-Sachs screening program—that developed by Dr. Michael Kaback of the Johns Hopkins University Medical Center for the Baltimore-Washington area. Approximately a dozen other large cities have launched similar programs, but none has surpassed the Virginia experience in providing this testing to so many people over so large an area.

Of equal importance to education and testing in such a detection program is the availability of adequate counseling for the carrier. Professional genetic counselors have provided this service for every Tay-Sachs carrier in Virginia, including advice concerning the importance and method of testing at-risk relatives.

The ultimate national goal of such a carrier detection program is to avert the birth of Tay-Sachs children. This could be done most efficiently by testing *only* married Jewish couples in the child-bearing age prior to their planning any children. Because lack of funds and the complexity of the enzyme measurement presently prohibit the wide spread availability of the test, however, this is not feasible in most areas of the country. Logic dictates, therefore, that the best alternative is first

to identify which families (in cities where the test is available) carry the gene abnormality and then to urge testing for high-risk relatives residing in smaller cities where screening is not available. The MCV Tay-Sachs Screening Program has received frozen serum from as distant a city as Niagara Falls, New York, where the relative of a Richmond carrier resided.

For further information regarding the MCV Tay-Sachs Screening Program, contact either Dr. Peter Mamunes or Dr. Seymour Bakerman by writing to Box 187, Medical College of Virginia, Richmond 23298, or by telephoning 804-770-3033.

Sickle cell disease differs from Tay-Sachs disease in many ways. From the standpoint of carrier detection programs, however, the most important differences are that:

- 1) The test is much simpler and blood specimens can be mailed into a central laboratory;
- 2) The carrier rate is considerably higher—approximately 1:12;
- 3) *No prenatal test is available* when both parents are known carriers.

For these reasons, a greater effort of education and testing at an earlier age are indicated.

Much of the screening for sickle cell trait in the state of Virginia is accomplished by the Virginia Sickle Cell Anemia Awareness Program (VaSCAP) of the Medical College of Virginia, and the sickle cell program of the State Health Department. The purposes of these programs are to educate the public, to provide a screening for young people who wish to know whether they carry the recessive trait for sickling, and to provide counseling for those who have been tested.

The VaSCAP program at the Medical College of Virginia tests young people in the child-bearing age, as well as premarital blood samples when the test is desired. A total of 11,000 specimens per year have been screened, many of them from the Richmond metropolitan area. The laboratory of the State Health Department has a capacity for up to 40,000 tests a year and collects samples from all over the state from individuals of any age.

The VaSCAP program at MCV also provides educational services for the school systems in greater Richmond and other outlying areas, as well as educational programs for organizations and health clinics where it is requested. Screening programs

are provided for public schools and colleges in the area, and counseling programs are offered for individuals tested in the program. In addition, the VaSCAP program has provided a series of seminars for public health nurses throughout the state to teach a larger number of individuals the principles of counseling for sickle cell trait.

The offices of the Virginia Sickle Cell Anemia Awareness Program are at 1008 East Clay Street, Richmond, Virginia 23298, and the program is supervised by Mrs. Florence Cooper. The telephone

number is 770-7797. The program of the State Health Department is directed by Dr. Patricia Hunt, Director, Bureau of Child Health, with offices in the Madison Building in Richmond.

Carrier detection programs, such as those above described, have proven that the public will voluntarily present themselves for testing if there is appropriate precedent education and follow-up counseling. Every physician should acquaint himself with these recently available services and join the effort to reduce the incidence of these dreadful disorders.