

NTSAD Position Statement

“Standards for Tay-Sachs Carrier Screening”

Background:

Tay-Sachs disease (GM2 gangliosidosis, type 1) is an autosomal recessive neurodegenerative disease caused by deficient activity of the enzyme hexosaminidase A (HexA). The frequency of carriers for Tay-Sachs disease in the general population is approximately 1 in 300. In people of Ashkenazi Jewish and French Canadian descent, the carrier frequency is much higher at about 1 in 30. The carrier frequency is also increased in several other populations, including those of Irish and Cajun descent.

Standard preconception and prenatal care for individuals of these select backgrounds includes offering carrier screening for Tay-Sachs disease as well as other recessively inherited diseases appropriate to one's genetic background. If both parents are found to be carriers prior to conception, the couple can be offered genetic counseling and various reproductive options that allow for the birth of unaffected children. If screening is performed prenatally, couples can be offered prenatal diagnosis (CVS or amniocentesis) to determine whether the fetus is affected with Tay-Sachs disease.

Enzyme Analysis versus DNA screening:

Tay-Sachs carrier screening programs were initially developed in the 1970s to address the high prevalence of Tay-Sachs disease in the Ashkenazi Jewish community. Initial carrier screening was performed by measuring HexA activity in serum or white blood cells via a blood sample. This sensitive technique allowed for inexpensive, reliable, and efficient carrier screening for large numbers of Ashkenazi Jews.

DNA screening for Tay-Sachs disease became available in the 1990s, and screening for at least three mutations has been 92-98% successful in identifying carriers who are of pure Ashkenazi Jewish descent (Bach et al., 2001). DNA testing in the non-Ashkenazi Jewish population using three mutations detects only 20% of carriers (Triggs-Raine et al, 1990) and using a five mutation panel detects only 60% of carriers (Kaback, et al, 1993).

During recent years, specifically from the 1970's to 1990's, Jewish intermarriage rates have increased from 13% to 43% (NJPS, 2000). Therefore, self-identifying “Ashkenazi Jews” currently of reproductive age are less likely than previous generations to be of pure Ashkenazi Jewish background. As the Ashkenazi Jewish population becomes less homogeneous, DNA screening in this population becomes less sensitive.

DNA screening for Tay-Sachs disease can be performed on non-invasive samples such as saliva or buccal swab in addition to blood, and therefore has become popular among those individuals who prefer not to provide a blood sample for enzyme analysis. Although DNA testing is the appropriate screening modality for many other genetic disorders, the decreased sensitivity of DNA screening for Tay-Sachs carrier detection

must be emphasized by medical providers to those individuals choosing not to have enzyme analysis performed.

Conclusion:

As the American population continues to intermarry at a significant rate, leading to a more diverse genetic admixture, enzymatic analysis is recommended as the primary testing modality for identifying carriers for Tay-Sachs disease. DNA testing can and should be used to confirm Tay-Sachs enzyme results, to clarify indeterminate enzyme results, to identify cases of pseudodeficiency, as well as to provide molecular information for reproductive procedures and genetic counseling (Kaback, 1999).

References:

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