Dear Colleague:

Thank you for your recent participation in the CME/CE activity, "ExpertPerspectives: The Importance of Early Recognition of Tay-Sachs and Sandhoff Disease."

As you continue to advance the care you provide to these patients, here are the key concepts for you to consider:

- There are 4 recognized phenotypes of GM2-gangliosidosis conditions: 1) infantile; 2) late-infantile; 3) juvenile; and 4) late-onset (or adult), each of which is distinguished by the age of symptom presentation that prompts the patient, patient's caregiver, or clinician to begin a process to seek diagnosis.
- The most prominent symptoms that bring individuals to the clinic for the juvenile and late-onset phenotypes include (1) changes in the patient's ability to ambulate and (2) changes in the patient's ability to speak.
- A key to differentiating Tay-Sachs and Sandhoff disease from each other and other GM2-gangliosidoses is to measure the activity of the enzymes involved, specifically beta-hexosaminidase A and beta-hexosaminidase B. In addition to enzyme activity, molecular diagnostics should be done to determine the specific allele mutations and genotype of the defective gene involved.
- Hematopoietic stem cell transplantation and other therapies are being explored for the treatment of patients with GM2-gangliosidosis conditions, particularly juvenile and late-onset phenotypes. Key mechanisms of action include enzyme replacement, gene modification, pharmacologic chaperones, and substrate reduction. Miglustat and venglustat are substrate reducing therapies in phase 3 clinical trials.

We hope you will be able to participate in other accredited activities we offer. You will find information at www.Annenberg.net.

Regards,
The Annenberg Center Team