emphasis on ambulation and communication) early in the disease to maintenance of quality of life (QoL). The goal of antiepileptic medication is to achieve sufficient seizure control to support function balancing the side effects. Antiepileptic medications may have unique response in patients with CLN2. Carbamazepine and phenytoin should be used with caution. School as well as home environments should be adapted to accommodate physical and cognitive/behavioral impairments as affected children benefit from maintaining social interactions. Physical, occupational and speech therapies are recommended to be initiated early and assessed frequently. Early use of adaptive devices should be considered to support function and independence. Palliative care team engagement is essential to the family soon after diagnosis is made. Appropriate tools to better assess neurobehavior, sleep and pain in this disease are needed.

Conclusions: CLN2 management practices are consistent among experts worldwide. A multidisciplinary approach is critical for optimizing care and QoL of patients and families throughout the disease course. Although gaps in knowledge remain, this effort to identify common management practices represents an initial step towards development of consensus-based management recommendations.

doi:10.1016/j.ymgme.2015.12.432

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The performance characteristics of a 6-plex assay for the detection of six lysosomal diseases and preliminary data for the detection of MPS II, MPS IVA and MPS VI

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We have successfully expanded a MS/MS triplex assay for the detection of Fabry, Pompe, and MPS I disorders to include Gaucher, Niemann-Pick and Krabbe diseases. Several of these assays use improved substrates and internal standards with optimization of buffer conditions. These assays are performing seamlessly within an existing newborn screening laboratory. From the first 32,000 anonymous samples, there were 36 samples with low activity. Each of these samples was genotyped from a 3-mm blood spot, four were identified as being affected with an LD; three samples with Fabry, and one with Gaucher disease. Krabbe was the disorder with the largest number of false positives due to the presence of pseudo-deficiency alleles. The other causes of low enzyme activity were attributed to heterozygosity or variances of unknown significance (VUS). Only nine of the 36 low-activity samples were normal by Sanger sequencing. We are also developing a 3-plex assay for MPS II, MPS IVA and MPS-VI. These sulfatases require a different buffer than the 6-plex and must be assayed separately. They can, however, be combined with the 6-plex assay at the end of their incubation period for a single injection into the MS/MS. Approximately 3,000 samples have been processed by this 3-plex assay and four samples were identified with low activity. One has a nucleotide change consistent with being affected with MPS II, and the three remaining samples were either known pseudo-deficiencies or a VUS. The workflow is designed to use overnight incubation and is programmed to complete 600 samples in 24 hours using a single mass spectrometer.

doi:10.1016/j.ymgme.2015.12.433

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Deletion of sialidase NEU3 causes progressive neurodegeneration in Tay-Sachs mice

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Tay-Sachs disease is a severe lysosomal disorder caused by mutations in the HEXA gene coding for α subunit of lysosomal β-hexosaminidase A which converts GM2 to GM3 ganglioside. HexA-/- mice, depleted of β-hexosaminidase A gene, remains asymptomatic to 1 year of age, owing to the ability of these mice to catabolise stored GM2 ganglioside via sialidase(s) removing sialic acid into glycolipid GA2 which further processed by β-Hexosaminidase B, thereby bypassing the HexA defect. To elucidate whether plasma membrane associated sialidase Neu3 can contribute to GM2 ganglioside degradation, we generated a double deficient mouse model by crossing previously generated HexA-/- mouse model and Neu3-/- mouse model. HexA-/-Neu3-/- mice are healthy at birth but lost weight gradually and died at 4-4.5 months of age. Thin layer chromatography analysis of HexA-/-Neu3-/- mice showed increased GM2 ganglioside level and altered ganglioside pattern in brain as well as liver, kidney and testis. Mass spectrometry analysis confirmed accumulation of GM2 and other gangliosides such as LacCer, GA2 and GM3. Immunohistochemical analysis using anti-GM2 antibodies indicated massive accumulation of GM2 in hippocampus and cortex. Slow movement, ataxia and tremor are among neurological abnormalities. The unexpected severe phenotype of HexA-/- mice appeared to be influence by the status of sialidase Neu3 gene. HexA-/-Neu3-/- mice mimic the fundamental aspects of the neurological abnormalities of Tay-Sachs disease. Our data suggests potential therapy of Tay-Sachs disease based on the upregulation of human sialidase Neu3 by drug treatment.

doi:10.1016/j.ymgme.2015.12.434

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Eye findings in Fabry disease and correlation with disease severity

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Fabry disease (FD) caused by α-galactosidase A (α-gal A) enzyme deficiency is known to have a number of eye manifestations. We performed a cross-sectional cohort study in the National Fabry disease Foundation's Family Conference in Greensboro to evaluate eye findings in 61 males and females with known FD. We analyzed eye findings, disease characteristics and severity, genotype, and gender. All < br/>participants underwent slit-lamp and fundus examination and answered a validated disease severity score survey (MSSI). Eye findings including corneal verticillata, conjunctival and retinal vessel tortuosity, as well as retinal arteriolar narrowing were evaluated and scored. We used descriptive comparisons and linear and logistic regression models to associate disease severity scores and eye findings with demographic and clinical characteristics. We found significantly higher disease severity score with age ($p < 0.001$), individuals undergoing treatment ($p = 0.002$), and individuals who had increased arteriolar narrowing ($p = 0.029$). We also found that increased arteriolar narrowing was significantly associated with frameshift, nonsense, splice-site gene variants ($p = 0.005$), male gender ($p = 0.005$), age ($p = 0.022$), MSSI total score ($p = 0.012$), MSSI neurological score ($p = 0.041$), hypertension ($p = 0.007$), and end stage renal failure ($p = 0.031$). Thus, increased retinal arteriolar