Guidelines have been published for the general medical management of people with NPC [6]. It is essential that physicians take a comprehensive approach to managing NPC, since patients are most likely to benefit when disease-modifying therapy is combined with meticulous general medical care and symptom management.

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IDENTIFYING NP-C EARLY IN PAEDIATRIC PATIENTS

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Niemann-Pick disease, type C (NP-C) is an autosomal recessive, progressive and ultimately fatal, neurovisceral lysosomal storage disorder involving the accumulation of unesterified cholesterol and glycolipids. Two genes (*NPC1* and *NPC2*) are involved in its pathogenesis. The estimated incidence of NP-C is 1:150,000 live births; however, the true incidence is probably significantly higher, as there is ample evidence that many patients remain undiagnosed.

Clinical presentation in NP-C is extremely heterogenous, often resulting in misdiagnosis. The first signs and symptoms may occur from the prenatal period; through to childhood and late adulthood. The absence of a simple diagnostic test for NP-C precludes the inclusion of the disease in general metabolic screening panels.

The following signs and symptoms should lead

to inclusion of NP-C in a differential diagnosis in paediatric patients: prolonged unexplained neonatal jaundice; hepatosplenomegaly or isolated splenomegaly; and neurological signs including vertical supranuclear gaze palsy, ataxia and/or dystonia, seizures and/or cataplexia, and early and progressive dementia.

At present, definitive diagnosis depends on demonstrating impaired cholesterol transport and homeostasis in cultured skin fibroblasts followed by genetic testing for mutations in *NPC1* and *NPC2*. A simple diagnostic tool based on a scoring system for various visceral, neurological and psychiatric signs and symptoms is currently being developed to facilitate decision-making regarding the need for diagnostic biochemical or genetic studies for NP-C.

With the recent approval of miglustat (Zavesca®) as disease-modifying therapy for NP-C, treatment can now be aimed toward stabilising neurological disease. Early diagnosis of NPC has, thus, become even more important.

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DIFFERENTIAL DIAGNOSIS IN PATIENTS WITH DEVELOPMENTAL DELAY: FOCUS ON INBORN ERRORS OF METABOLISM

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Developmental delay (DD) is common in paediatric practice and is present in 5-10% of children. Detailed evaluation can yield a definitive diagnosis in more than half of these cases and a substantial proportion of these are caused by chromosomal abnormalities and defects in the genes important for embryo development.

An inborn error of metabolism (IEM) can be identified in approximately 1% of patients with DD, but although a diagnosis of IEM is rare, accurate identification could make a big difference to the prognosis for the affected child, as well as counselling of the family and management of siblings. A diagnosis of IEM is more likely in the presence of additional abnormalities and developmental regression. The incidence of IEMs and the frequency of individual disorders vary depending on ethnicity.

IEMs can present at any age, but earlier diagnosis increases the chance of an improved prognosis, particularly in cases where treatments are available.