learn NPC

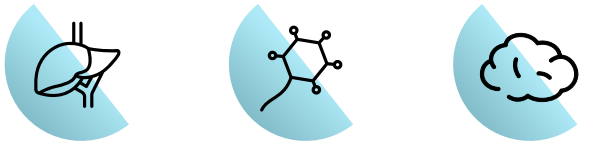
Niemann-Pick disease type C (NPC) can present like many different diseases, so accurate diagnosis and early intervention are critical.[1,2]

NPC presentation and progression are heterogeneous—making timely diagnosis crucial[1-3]

NPC is an ultra-rare, relentlessly progressive, inherited disease, and its variable symptom presentation makes it difficult to diagnose[1-3]

NPC is a lysosomal storage disease (LSD) caused by mutations in either the *NPC1* or *NPC2* genes, with an estimated prevalence of 1 in 1,000,000 individuals in the United States. NPC is progressive, irreversible, and ultimately fatal.[3,4]

Symptoms are[2]:



Visceral **Neurological** **Psychiatric**

> ***Early recognition and diagnosis can be pivotal, as this may allow more time to access appropriate treatment.[1,2]***

Recognizing symptom patterns is key to timely diagnosis[1]

Patients with NPC can present with many different symptoms – and combinations of symptoms – at different ages as the disease progresses and prognosis worsens. Disease progression can be **rapid or slow, making symptom recognition more difficult.**[1-3]

Childhood NPC frequently impacts visceral organs[1,2]	
Neonatal (<2 months)	Most commonly presents as cholestatic jaundice and hepatosplenomegaly
Early-infantile (2 months - <2 years)	Commonly characterized by developmental milestone delay and hepatosplenomegaly
Late-infantile (2 - <6 years)	Commonly characterized by disturbed gait or clumsiness and vertical supranuclear saccade palsy
Juvenile (6 - 15 years)	Most commonly presents as cognitive impairment, coordination problems, seizures, and vertical supranuclear saccade palsy
NPC progression in adults is mostly cognitive[1]	
Adolescent/adult (>15 years)	Commonly presents with cognitive impairment and psychiatric illness, and vertical supranuclear saccade palsy

Symptoms can appear at any age with some features more often seen in younger patients; but in many adults with NPC, childhood development will have been completely normal. In some individuals there may have been a long history of slowly progressing symptoms before the diagnosis is made. Compared to pre-adolescent onset patients (<15 years), adolescent (>15 years) and adult-onset patients may be even more challenging to diagnose.[1,2]

Some NPC symptoms are consistent with other more common diseases making identification difficult[1,2,5]

NPC symptom categories:

Symptoms:	Ambulation	Fine motor skills	Speech	Memory
Ataxia	●	●		
Cataplexy	●	●	●	
Dementia				●
Dysarthria			●	
Dystonia	●	●		
Hypotonia	●	●		
Psychosis			●	●

For illustrative purposes only.

NPC's variable symptom presentation makes diagnosis challenging[1,2]

NPC may be hard to diagnose due to the **heterogeneity of symptom presentation** and because individual symptoms **overlap with other common diseases**. This makes identification difficult resulting in delayed diagnosis or misdiagnosis.[1-3]

To diagnose as early as possible, **collaborating with a multidisciplinary team** including a referring physician, treatment specialists, and treatment supporting physicians is essential.[1]

> ***As a genetic disease characterized by neurodegeneration, NPC can cause many combinations of symptoms.[5]***

More common conditions like Alzheimer's Disease, Parkinson's Disease, and Schizophrenia have similar symptoms to NPC, which can make NPC difficult to identify.[5]

Treatment options are available

Disease-modifying therapies can slow the progression of NPC across symptom domains of ambulation, speech, swallow, and fine motor skills.[1,6,7]

Learn about a treatment option or request a rep.

Testing options on the path to diagnosis

In an unpredictable, irreversible, and degenerative disease such as NPC, timely diagnosis is imperative.[1,3] **Testing is readily available and may be available for no charge to eligible patients**.

Types of tests:

Blood test

Considered first step to NPC diagnosis. Biomarkers currently analyzed include oxysterols, lysosphingolipids (primarily lysosphingomyelin-509), and bile acids.[1]

Genetic test

Gene panels for some of the symptoms of NPC include screenings for mutations in *NPC1* or *NPC2*. Single gene sequencing should be conducted in cases with a high clinical suspicion of NPC.[1]

Skin biopsy

Filipin test* of skin sample on cultured fibroblasts to look for unesterified cholesterol accumulation within the lysosomes.[1]

*No longer standard and only used as confirmatory evidence following inconclusive genetic testing.

In addition, a medical history and clinical examination can aid in proper diagnosis. NPC is not curable, but **management with available treatments is possible**.[1,3]

Learn more about sponsored genetic testing

Genetic testing can help in determining diagnosis. Genetic counselors are available if needed to assist.

Start here for more information about sponsored genetic testing.

References: 1. Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C: *Orphanet J Rare Dis.* 2018;13(1):50. doi:10.1186/s13023-018-0785-7 **2.** Vanier MT. Niemann-Pick disease Type C. *Orphanet J Rare Dis.* 2010;5(16):1-18. doi:10.1186/1750-1172-5-16 **3.** Mengel E, Patterson MC, Gissen P, et al. Impacts and burden of Niemann pick type-C: a patient and caregiver perspective. *Orphanet J Rare Dis.* 2021;16(1):493. doi:10.1186/s13023-021-02105-8 **4.** Burton BK, Ellis AG, Orr B, et al. Estimating the prevalence of Niemann-Pick disease type C (NPC) in the United States. *Mol Genet Metab.* 2021;134(1-2):182-187. doi:10.1016/j.ymgme.2021.06.011 **5.** Patterson MC, Hendriksz CJ, Walterfang M, et al; NP-C Guidelines Working Group. Recommendations for the diagnosis and management of Niemann-Pick disease type C: an update. *Mol Genet Metab.* 2012;106(3):330-344. doi: 10.1016/j.ymgme.2012.03.012 **6.** Cortina-Borja M, te Vruchte D, Mengel E, et al. Annual severity increment score as a tool for stratifying patients with Niemann-Pick disease type C and for recruitment to clinical trials. *Orphanet Rare J Dis.* 2018;16;13(1):143. doi:10.1186/s13023-018-0880-9 **7.** Patterson MC, Lloyd-Price L, Guldberg C, et al. Validation of the 5-domain Niemann-Pick type C Clinical Severity Scale. *Orphanet J Rare Dis.* 2021;16:79. doi.10.1086/s13023-021-01719-2

Get more information for timely and accurate diagnosis of NPC at **learnNPC.com**.

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