Niemann-Pick disease type C (NPC)

Niemann-Pick disease type C (NPC) is a rare, genetic, neurodegenerative disorder that impairs intracellular cholesterol trafficking, leading to progressive neurological decline and premature death.[1]

NPC is caused by pathogenic variants in the *NPC1* or *NPC2* genes, which encode proteins essential for lysosomal cholesterol transport[1]

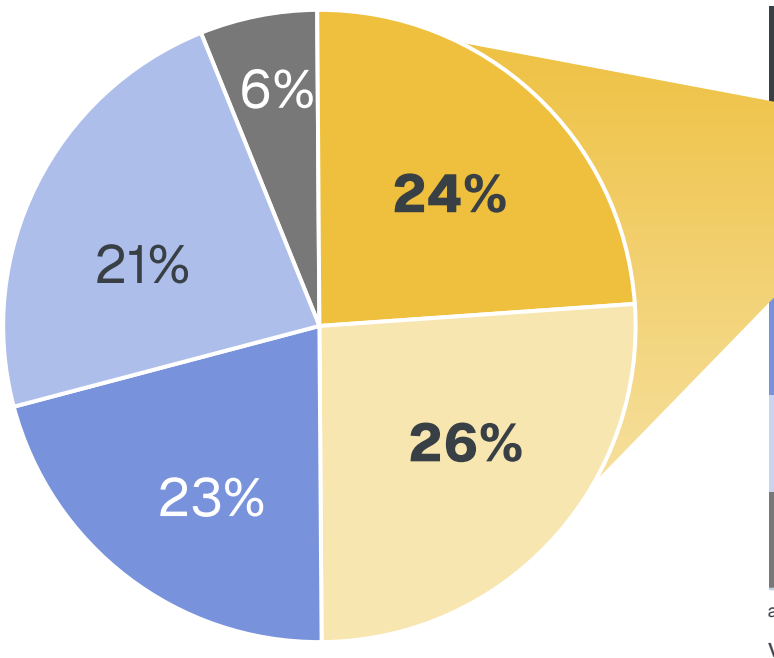
Impaired intracellular cholesterol trafficking results in toxic accumulation of cholesterol in lysosomes and deficiency of cytoplasmic cholesterol needed for normal cellular function[1]

This imbalance leads to neuronal dysfunction, neurodegeneration, progressive neurological decline, and premature mortality[1]

PRESENTATION AND DISEASE COURSE ARE HIGHLY HETEROGENEOUS

Age of neurological symptom onset is the most reliable clinical predictor of disease severity and death, with earlier onset associated with more rapid progression and poorer prognosis. An estimated 50% of individuals diagnosed with NPC have infantile onset (neurological symptom onset before age 6).[1-3]

PREVALENCE AND PROGNOSIS OF NPC CLINICAL SUBTYPES[2]



Clinical subtype[1]	Age of neurological symptom onset[2]	Age of death (mean ± SD)[3]
Early infantile-onset	<2 years	5.6 years (±2.0)
Late infantile-onset	2 to <6 years	13.4 years (±6.7)
Juvenile-onset	6 to 15 years	25.9 years (±8.9)
Adult-onset	>15 years	33.7 years (±6.2)
Other[a]	Not applicable	-

[a]Including individuals with neonatal rapidly fatal NPC, without neurological manifestations, or with visceral symptoms only. Data on mean age of death across this group is not available.

RECOGNIZING THE SIGNS OF INFANTILE-ONSET NPC EARLY ENABLES TIMELY DIAGNOSIS AND INTERVENTION[1,4]

- ☑ Prolonged neonatal cholestatic jaundice
- ☑ Developmental delay or regression
- ☑ Progressive ataxia
- ☑ Isolated splenomegaly ± hepatomegaly
- ☑ Speech delay
- ☑ VSSP/VSGP
- ☑ Hypotonia, delayed motor milestones
- ☑ Clumsiness, frequent falls
- ☑ Gelastic cataplexy

Diagnosis is often delayed. Consider genetic testing in children showing early signs of infantile-onset NPC.[1,4]

ABBREVIATIONS: NPC, Niemann-Pick disease type C; NPC1, NPC intracellular cholesterol transporter 1; NPC2, NPC intracellular cholesterol transporter 2; SD, standard deviation; VSGP, vertical supranuclear gaze palsy; VSSP, vertical supranuclear saccadic palsy.

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