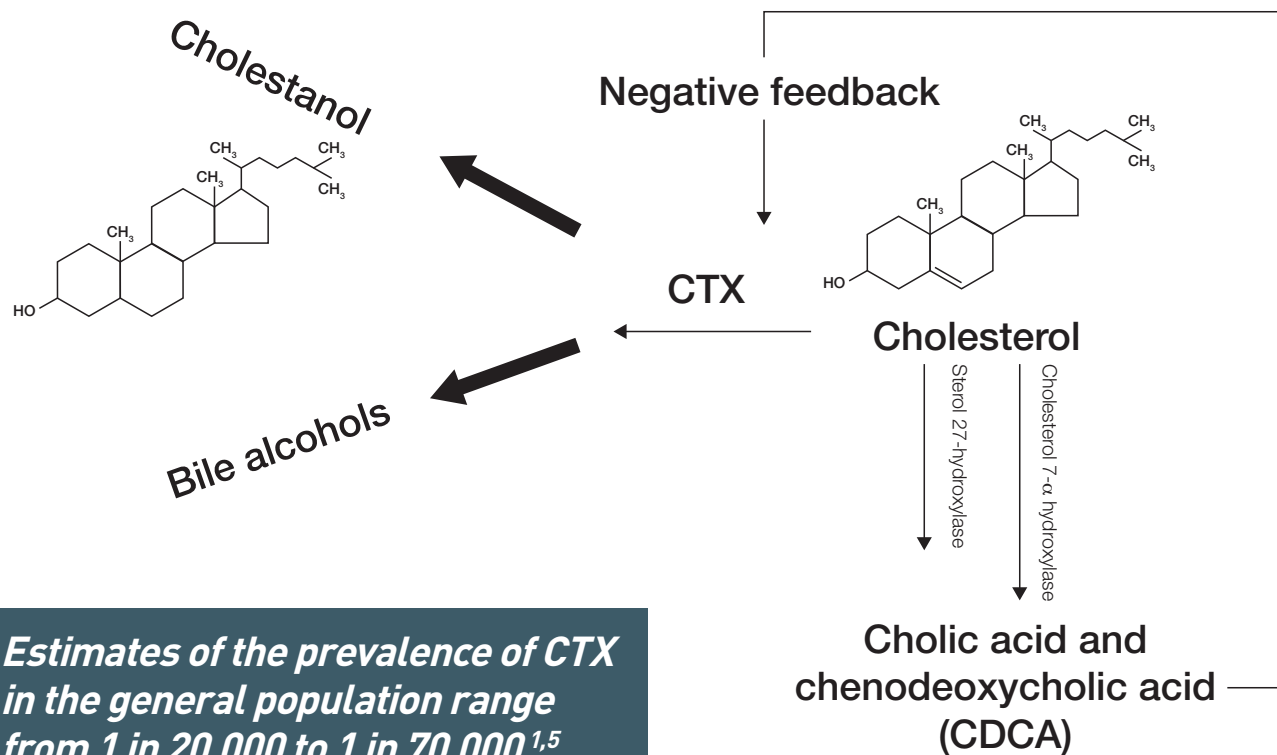


# CEREBROTENDINOUS XANTHOMATOSIS (CTX)

CTX is a rare, autosomal recessive lipid storage disease<sup>1-3</sup>

CTX is caused by mutations of the *CYP27A1* gene, which result in deficiency of sterol-27-hydroxylase.<sup>2,4,5</sup> This enzyme deficiency disrupts the conversion of cholesterol to bile acids.<sup>2,5</sup> This produces a decrease in chenodeoxycholic acid (CDCA) thereby disrupting the feedback regulation on the rate-limiting enzyme, cholesterol 7- $\alpha$ -hydroxylase, in bile acid synthesis.<sup>4,6,7</sup> This results in an accumulation of cholestanol in the central nervous system (CNS), muscle, blood vessels, eyes, and tendons, and an increase in urinary excretion of bile alcohols.<sup>2,5,6</sup>

In CTX, sterol-27-hydroxylase deficiency disrupts cholesterol breakdown<sup>2,6</sup>



*Estimates of the prevalence of CTX in the general population range from 1 in 20,000 to 1 in 70,000.<sup>1,5</sup>*

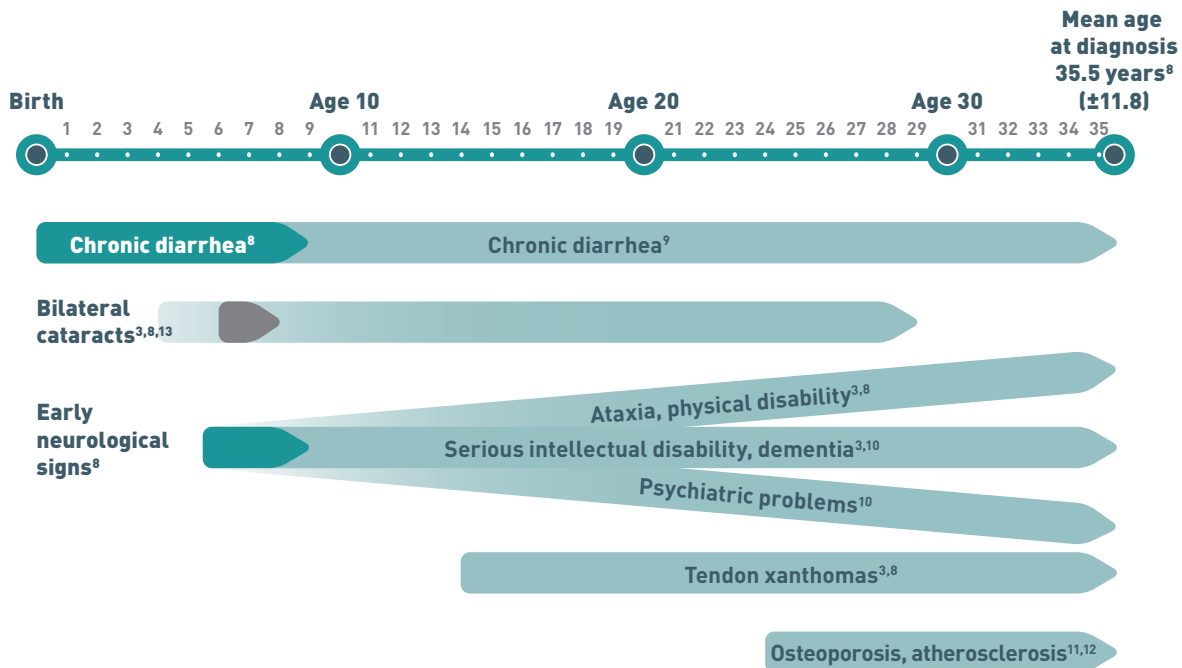
CTX is characterized by a distinct array of hallmark manifestations, though not all occur in every patient<sup>3,8</sup>

Hallmark manifestations have variable onset and severity, which contributes to delayed diagnosis and underdiagnosis.<sup>8</sup> The hallmark manifestations of CTX include infant-onset chronic diarrhea, juvenile-onset bilateral cataracts, tendon xanthomas (particularly of the Achilles tendon), and progressive neurological deterioration.<sup>3,8,9</sup>

Neurological symptoms may include cognitive impairment with learning difficulties that can progress to dementia, spasticity, ataxia, epilepsy, Parkinsonism, and polyneuropathy.<sup>10</sup> Psychiatric manifestations, including personality, affective, and psychotic disorders may also occur, either early in the course of the disease or late, complicating the other neurologic disturbances.<sup>10</sup> Other, later-onset manifestations of CTX may include premature osteoporosis and atherosclerosis.<sup>11,12</sup>

**Retrophin**

# Early diagnosis of CTX can prevent serious physical and intellectual disability<sup>8</sup>



## A published suspicion index can help diagnose CTX patients as early as possible<sup>8</sup>

Indicators	Family history	Systemic	Neurological
Very strong	Sibling with CTX	Tendon xanthomas	
Strong	Consanguineous parents	Juvenile cataract	Ataxia and/or spastic paraparesis
		Childhood-onset chronic diarrhea	Magnetic resonance imaging (MRI) evidence of dentate nuclei signal alterations
		Prolonged unexplained neonatal jaundice or cholestasis	Intellectual disability and/or psychiatric disturbances
Moderate		Early osteoporosis	Epilepsy
			Parkinsonism
			Polyneuropathy

**The primary biochemical test used to diagnose CTX is a blood test for cholestanol. A definitive diagnosis can only be made with molecular analysis of the CYP27A1 gene.<sup>14</sup>**

**References:** 1. Lorincz MT, et al. *Arch Neurol.* 2005;62:1459-1463. 2. Gallus GN, et al. *Neurol Sci.* 2006;27:143-149. 3. Verrips A, et al. *Brain.* 2000;123:908-919. 4. Chiang JYL. *Front Biosci.* 1998;3:176-193. 5. Rafiq M, et al. *Pract Neurol.* 2011;11:296-300. 6. Moghadasian MH. *Clin Invest Med.* 2004;27:42-50. 7. Berginer VM, et al. *N Engl J Med.* 1984;311:1649-1652. 8. Mignarri A, et al. *J Inherit Metab Dis.* 2014;37:421-429. 9. Verrips A, et al. *Arch Neurol.* 2000;57:520-524. 10. Fraidakis MJ. *Transl Psychiatry.* 2013;3:e302. doi:10.1038/tp.2013.76. 11. Berginer VM, et al. *Metabolism.* 1993;42:69-74. 12. Dotti MT, et al. *J Neurol.* 1998;245:723-726. 13. Dotti MT, et al. *J Inherit Metab Dis.* 2001;24:696-706. 14. Federico A, et al. Cerebrotendinous Xanthomatosis. Gene Reviews<sup>®</sup> [internet]. <http://www.ncbi.nlm.nih.gov/books/NBK1409/>. Accessed July 1, 2014.

**Retrophin**