# Cerebrotendinous Xanthomatosis (CTX)

## What is CTX?

**CTX is a type of leukodystrophy.**

Leukodystrophies are a group of genetic conditions that mainly affect the white matter of the brain and spinal cord. The white matter is the wiring network of the brain that connects different brain regions and links the brain to the spinal cord and rest of the body.

CTX is characterized by abnormal storage of fats (lipids) in the brain and the connective tissue called tendons. This abnormal accumulation is stored in form of fatty yellow nodules called xanthomas. The xanthomas in the brain accumulate in the myelin (fatty covering on the nerve cells) resulting in myelin destruction that causes impaired signal transmission.

## What are the symptoms of CTX?

**Most symptoms arise during early adulthood.**

**Non-neurological symptoms observed during childhood are:**

- Clouding of the lenses of the eyes (cataracts).
- Chronic diarrhea.
- Jaundice like appearance due to reduced production of liver enzymes (Cholestasis).
- Progressive brittle bones that are prone to fractures (Osteoporosis).

**As children grow older and there is an increased accumulation of fats resulting in various neurological symptoms such as:**

- Recurrent seizures (epilepsy).
- Impaired speech (dysarthria).
- Loss of sensation in the arms and legs (peripheral neuropathy).
- Decline in intellectual function (dementia).
- Joint contractures and mobility issues.
- Movement disorders.

A common clinical presentation includes xanthomas in the tendons, elbow, knees, and the Achilles tendon of the foot.

## What causes CTX?

CTX is caused by gene changes in the *CYP27A1* gene. Changes in this gene leads to abnormal or nonfunctional sterol 27-hydroxylase, resulting in impaired digestion of fats. As a result, certain alternate pathways lead to the formation of a cholesterol like molecule called cholestanol and increased levels of bile acids. This cholestenol and the undigested lipids contribute towards formation of xanthomas.

## How is CTX diagnosed?

There are other conditions that results in a clinical picture similar to CTX, but certain biochemical findings might help establish the diagnosis:

- High plasma and tissue cholestanol concentration.
- Normal-to-low plasma cholesterol concentration.
- Decreased chenodeoxycholic acid.
- Neuroimaging (MRI-Brain) and electroencephalogram (EEG).
- Variants in the *CYPA27* gene, helps confirm the diagnosis.

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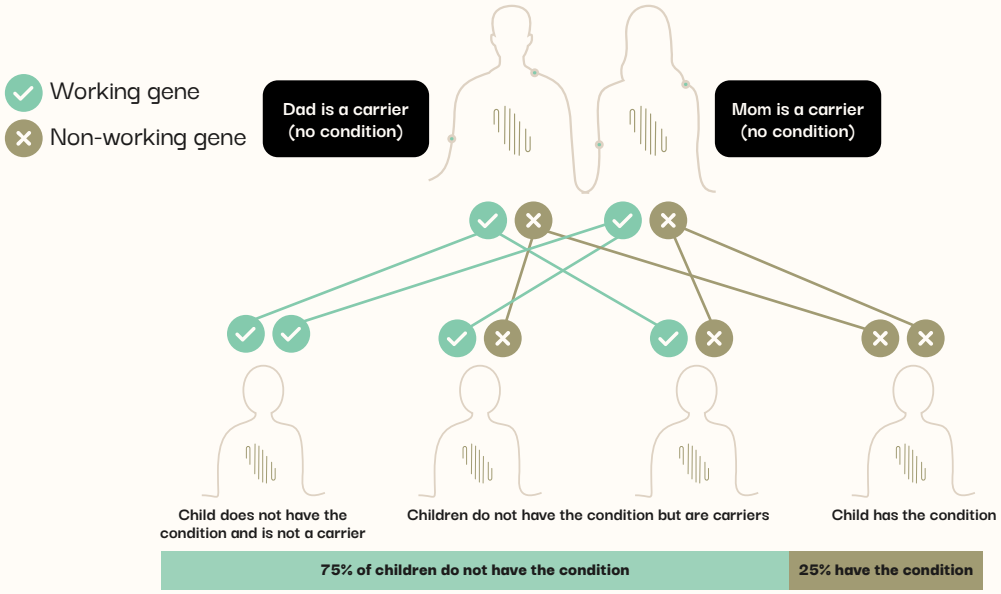
## How is CTX inherited?

CTX is inherited in an autosomal recessive pattern. This is where two altered copies of the gene causes CTX. Each parent passes on one copy of the altered gene change. This means that in each of the subsequent pregnancies the couple has a 1 in 4 chance of having an affected child. This also means that siblings of the parents and the affected child can also be carriers.

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## Can CTX be treated?

The current standard of care is oral administration of Chenodeoxycholic acid. This helps restore normal sterol, bile activity and cholesterol levels. It is also postulated that if it is administered during early stages, disease progression can be controlled.

## Support and resources:

- **Leukodystrophy Australia** leuko.org.au
- **Mission Massimo Foundation** missionmassimo.com
- **United Leukodystrophy Foundation** ulf.org/leukodystrophies/adrenoleukodystrophy
- **Hunter's Hope** huntershope.org/familycare/leukodystrophies/adrenoleukodystrophy

## Research:

- **Australian Leukodystrophy Clinical and Research Program** leukonet.org.au
- **Clinical trials** clinicaltrials.gov/ct2/results?cond=%22x-linked+adrenoleukodystrophy%22
- **Global Leukodystrophy Initiative** theglia.org

## References:


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- medlineplus.gov/genetics/condition/cerebrotendinous-xanthomatosis/#resources
- Salen, G., & Steiner, R. D. (2017). Epidemiology, diagnosis, and treatment of cerebrotendinous xanthomatosis (CTX). Journal of Inherited Metabolic Disease, 40(6), 771–781. doi.org/10.1007/s10545-017-0093-8