Eyesight and hearing

Short sight (myopia) is quite common and a few children have severe myopia (more than -10D). Strabismus (cross eye or squint) may be present. It is recommended that the affected children have an ophthalmological assessment. A few children have severe sensorineural [permanent] hearing loss.

Anaemia

85% of children with ATR-X have a mild anaemia caused by a problem in making one of the components of the red pigment haemoglobin which carries the oxygen in blood. This is called alpha thalassaemia. A special blood test can show if it is present and this is a useful diagnostic test for the condition. The anaemia rarely causes problems and does not require treatment. It is important that children are not given iron for this type of anaemia.

Malignancies

There have been two reports of affected children developing a form of bone cancer but the risk of this is low and routine screening is not recommended. Nevertheless, painful swellings in a bone should be investigated.

Managing ATR-X syndrome

At diagnosis

- Kidney and heart ultrasound scans
- Hearing and eyesight tests if needed
- Consider EEG (test of brain's electrical activity) if seizures are suspected
- Feeding management and thorough assessment if reflux is present

After diagnosis

- Yearly evaluation by a developmental paediatrician
- Early intervention with speech and physical therapy
- Regular eyesight tests
- Regular assessment of oesophageal reflux and constipation
- Regular assessment for curvature of the spine

Families say ...

"His smile lights up a room." Age almost 6 years

Inform Network Support

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Join Unique for family links, information and support

Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org Please help us to help you!

Websites, Facebook groups and other links

ATR-X syndrome website
http://www.imm.ox.ac.uk/atr-x-syndrome-information

The Dutch ATR-x Foundation
www.atrxsyndroom.nl info@atrxsyndroom.nl
Excellent information in Dutch and English
https://www.youtube.com/watch?v=YKLnTvPi4rk

Facebook group for ATR-X syndrome
https://www.facebook.com/groups/163849465337

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

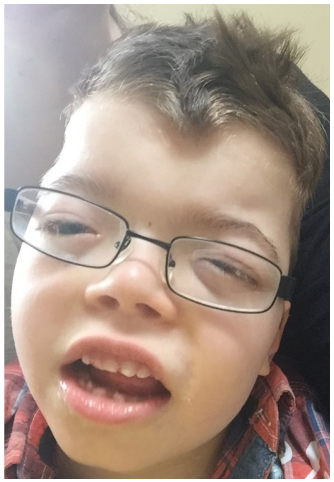
This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. The text was written by Professor Richard Gibbons, FMedSci, FRCP, Professor of Clinical Genetics, University of Oxford, UK, and the guide was compiled by Unique.

2015 Version 1 (PM). 2016 Version 1.1 (PM). 2017 Version 1.2 (AP)/CA)

Rare Chromosome Disorder Support Group: Charity Number 1110661
Registered in England and Wales: Company Number 5460413

Understanding chromosome disorders Unique

ATR-X syndrome



What is ATR-X syndrome and how is it caused?

ATR-X syndrome was first recognised around 1990. ATR-X is short for Alpha thalassaemia mental retardation, X-linked, but today the syndrome is more commonly referred to by its abbreviated name or as X-linked alpha thalassaemia intellectual disability syndrome. It affects boys who have a change in a particular gene, *ATRX*.

The *ATRX* gene is found on the X chromosome. It is on the long arm of the chromosome, in a band known as Xq21.1.

ATR-X syndrome is caused by changes in the DNA (genetic material) in the *ATRX* gene. Genes provide the instructions to make proteins. The ATRX protein works with a partner protein called DAXX and helps maintain the integrity of the genetic material and how it is packaged in the cell. We do not understand yet the precise way that intellectual disability or other features of the ATR-X syndrome are caused, but research is ongoing.

How many people have ATR-X syndrome?

We are continuing to learn about this condition as new cases are identified - around 200 cases have been described in the medical literature. Whereas the first cases were identified because of the constellation of clinical features, with the introduction of new methods for genetic testing, cases where the condition might not have been considered are being identified. This is revealing a small but growing group of children who have a milder version of the syndrome. It is likely that the published cases are at the more severe end of the spectrum.

Can it be cured?

It is not possible to repair the damage in the *ATRX* gene. Treatments can be offered for some of the symptoms such as gastro-oesophageal reflux. Early intervention can optimise children's potential, especially in facilitating communication.

Why did this happen?

The *ATRX* gene lies on the X chromosome and boys inherit their X chromosome from their mother. In most families, the mother carries the same genetic change as their affected son. The mother, however, has two X chromosomes and it appears that she uses the normal version of the *ATRX* gene rather than the one with the change in it and so is unaffected by this change.

In some families the DNA change in *ATRX* occurs out of the blue (de novo). These types of change happen naturally in all species - humans, plants and animals - and are not due to your lifestyle or anything you did.

Can it happen again?

The risk of having another child affected by ATR-X syndrome depends on whether the mother carries the change in the *ATRX* gene that is seen in the affected child. If the mother is a carrier then there is 50% chance of passing it on since she has two X chromosomes, one with the normal copy of *ATRX* and one with the genetic change. If a boy inherits the affected copy of *ATRX* he will be born with ATR-X syndrome. If a daughter inherits the affected gene, she will be an unaffected carrier like her mother. Each family situation is different and a clinical geneticist or genetic counsellor can give you specific advice.

Most common features

- Severe learning difficulties
- Delay in speech and walking
- A particular facial appearance
- Characteristic but mild anaemia

Development

Physical development

Learning to walk is always late, and may never be possible for up to half of the children. Of those who do eventually walk, 25% do so by 3 years, 50% by 6 years, 75% by the age of 9 and some not until their teens.

Speech and learning

A small group of children with changes in the *ATRX* gene are only mildly affected, have good speech and can use a phone or computer.

However, most affected children have no speech. They are dependent on caregivers for most activities of daily living and may only attain partial bowel and bladder control. Nevertheless their performance in other ways may be significantly better and they may for example be able to turn on the television and operate a DVD player.

Behaviour

Children with an *ATRX* change are often considered very affectionate. However, as they get older they may develop aggressive behaviour, possibly associated with their difficulty in communicating. Some children exhibit autistic traits.

Growth

Two children in three with ATR-X syndrome are unusually short. Although they are usually born with a normal sized head, three quarters of them will have a small head as they get older.

Medical concerns

Feeding difficulties

Poor sucking is very common in newborn babies who often require tube feeding. This usually improves with age but occasionally persists and may require a more permanent solution via a percutaneous endoscopic gastrostomy. However, gastro-oesophageal reflux can be a major problem in the first few years and can lead to inflammation of the oesophagus. This needs to be investigated as it may require corrective surgery. Reflux can lead to pneumonia in some children if the food goes down the windpipe.

Dribbling

This affects most children with ATR-X especially when they are young. It is probably best to avoid drugs known as anticholinergics such as hyoscine or glycopyrrolate to treat this as they may exacerbate the sluggish nature of the gut in these children. Alternative approaches include botulinum [Botox] injections into the salivary glands [performed in a specialist centre] and surgery to tie off or re-route some salivary glands.

Other gastro-intestinal problems

Constipation can be a significant problem and reflects the sluggish nature of the gut in this condition. Food refusal associated with severe abdominal pain may indicate a twist in the bowel (volvulus) which needs medical assessment.

Seizures

Around one third of affected children will develop seizures at some time during their lifetime. They usually respond well to therapy.

Genital

80% of children are born with genital abnormalities. These may be mild such as a deficient foreskin or undescended testes but some boys have more severe problems such as micropenis and a few have been raised as girls as the genitalia have a female appearance. Undescended testes may need surgical correction.

Skeletal problems

A number of children have been born with clubfoot/talipes: this usually responds well to splinting and physiotherapy. Since around 30% of children develop curvature of the spine, this needs to be looked for during childhood.

Heart/ kidneys

A small proportion of babies with an *ATRX* change may have heart or kidney problems. In young children heart and kidney screening is therefore recommended. Urinary tract infections may be an early clue to an underlying kidney abnormality.

Sleep disturbance

Some children may benefit from assessment and treatment for sleeping difficulty.