How common is WITKOS?

WITKOS is very rare. Currently (2020) less than 50 children with a WITKOS diagnosis have been reported in the medical literature. It is expected that more children will be diagnosed with this condition as awareness increases and genetic testing becomes more routine.

Why did this happen?

When children are conceived, the genetic material is copied in the egg and sperm that make a new child. The biological copying method is not perfect, and random rare changes occur in the genetic code of children that are not seen in the DNA of their parents. This happens naturally and is not due to any lifestyle, dietary or environmental factors. No one is to blame and nobody is at fault. Such changes happen to everyone but it's only when a change affects an important gene that health and/or development are affected.

In most children diagnosed with WITKOS so far, the change in the *SIN3A* gene occurred by chance in that child (this is known as *de novo*) and was not found in their parents. A few children are known to have inherited a pathogenic variant of the *SIN3A* gene form a mildly affected parent.

Can it happen again?

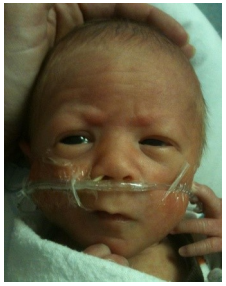
The risk of having another child affected by a rare gene disorder depends on the genetic code of the parents. If the change in the *SIN3A* gene has been shown to be *de novo*, that means neither parent was found to carry it, the chance of having another child with WITKOS is low (less than 1%). If a parent is found to carry the genetic variant, the chances of having another child with WITKOS is 50% for each pregnancy. A clinical geneticist can give you specific advice for your family.

Can it be cured?

WITKOS cannot be cured at the present time however, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.

Families say .....s

"The future is unclear with the nature of the disease, but my goal as his mother is to be his #1 advocate."
~ Age 8 years.



Inform Network Support

Rare Chromosome Disorder Support Group,
The Stables, Station Road West,
Oxted, Surrey. RH8 9EE. UK.
Tel +44(0)1883 723356
info@rarechromo.org
www.rarechromo.org

Websites, Facebook groups and other links:

https://www.facebook.com/groups/1875285455899640
https://youtu.be/o1i1gfsTDas

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/donate Please help us to help you!

Version 1 (AP) 2020

Rare Chromosome Disorder Support Group
Registered in England and Wales

Charity Number 1110661
Company Number 5460413

Understanding Chromosome & Gene Disorders

Witteveen-Kolk syndrome WITKOS (*SIN3A* gene variants)

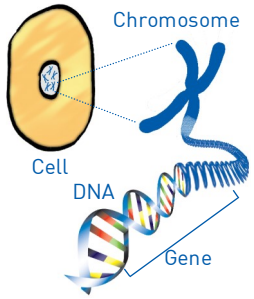
rarechromo.org

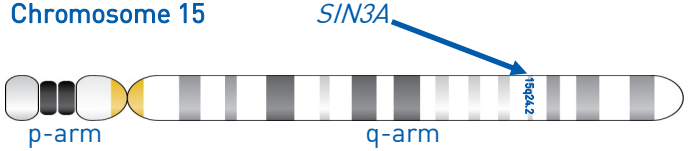
What is Witteveen-Kolk syndrome?

Witteveen-Kolk syndrome, abbreviated to WITKOS, is a rare genetic condition that causes developmental delay and can affect a child's learning abilities and behaviour. As is common with genetic conditions, each person is affected differently. A few children with WITKOS experience seizures, but otherwise, no serious medical concerns have been identified.

What causes Witteveen-Kolk syndrome?

Witteveen-Kolk syndrome is caused by specific changes (known as pathogenic variants) to, or a deletion of, a gene called *SIN3A* (*SIN3A* is an abbreviation of the gene's full name, switch-insensitive 3 transcription regulator family member A). The *SIN3A* gene is located on the long 'q' arm of chromosome 15 in a region called 15q24.2 (see below).





We have two copies of chromosome 15 in our cells, so we also have two copies of the *SIN3A* gene.

WITKOS occurs when only one copy of the SIN3A gene is affected, this is known as autosomal dominant since the change occurred on an autosome (any of the chromosomes numbered 1-22) and features are apparent when only one copy of the gene is altered (this is known as dominant).

The *SIN3A* gene sequence is used to make the SIN3A protein. This protein is part of an important group of proteins that control the activity of other genes. SIN3A has a specific pattern of activity in different parts of the brain, especially during development, so changes to its function may cause neurological difficulties such as those associated with learning and behaviour.

WITKOS features

Most children with WITKOS have:

- Developmental delay
- Learning difficulties/disorders or intellectual disability (ID)

Other possible features include:

- Speech and language delay
- Feeding difficulties in the first few months
- Weak muscle tone (hypotonia)
- Small head size (microcephaly)
- Brain anomaly identified by MRI
- Seizures and epilepsy
- Eye anomaly
- Hearing impairment

Medical concerns

Hypotonia

Almost half of the children reported so far have been found to have weak muscle tone (hypotonia).

Head circumference

About half of the children with WITKOS described so far have a smaller than usual head circumference.

Brain anomaly

Not many children diagnosed with WITKOS have had a brain MRI (2020), but of the few who have, unusual results were found in most.

Seizures

Some children with WITKOS are known to experience seizures or have had a seizure but there is currently very little information regarding seizure activity.

Eye anomaly

Eye anomalies have been reported in a few children with WITKOS but each child has a different condition, no consistent eye anomaly has been identified.

Hearing

Hearing loss has been reported in a few children, one has sensorineural hearing loss, two have conductive hearing loss and two have mixed hearing loss.

Facial features

Some, but not all, children appear to have a few shared facial features such as a broad, tall forehead; small mouth, thin upper lip with pointed chin and eyes that slant downwards slightly.

Development

Physical Development

Developmental delay of motor function, for example walking, has been reported in over half of the children diagnosed with WITKOS so far (2020).

Intellectual Development and Learning

Children with WITKOS usually have some level of learning difficulty or intellectual disability, although some children have an intelligence test score within the expected range. Unusually, verbal intelligence test scores are higher than other performance test scores.

Speech and language

Some form of language developmental delay has been reported in over half of the children diagnosed with WITKOS to date (2020).

Behaviour

About a third of children with WITKOS have been diagnosed with a neurodevelopmental disorder or difficulty. ASD (autism spectrum disorder), ADHD (attention deficit hyperactivity disorder), OCD (obsessive compulsive disorder), anxiety, aggressive behaviour, depression, psychosis and schizoaffective disorder are among the diagnoses.

Feeding

Feeding can be problematic for some children with WITKOS. About half of the children reported so far have had feeding difficulties. At least two children needed nasogastric (NG) tube feeding (when a tube is passed through the nostril directly to the stomach to administer feeds).

Weight

Almost a third of children with WITKOS assessed so far are thought to be underweight.

Height

Some children with WITKOS, less than a third reported so far, have short stature.

Management recommendations:

Children with WITKOS should be under the care of a multidisciplinary team including a geneticist, paediatrician, neuropaediatrician/neurologist and an epilepsy specialist if needed. Children may benefit from speech and language therapy as well as periodic evaluations by a developmental specialist.