

## What causes Chitayat syndrome?

Chitayat syndrome occurs when one copy of the *ERF* gene sequence is altered slightly and its function is altered. The other copy of the *ERF* gene is unaffected and so can carry out its usual function. Chitayat syndrome is **autosomal dominant**, since the change occurred on an autosome (any of the chromosomes 1-22) and symptoms are apparent when only one copy of the gene is altered (dominant).

Other variants have been identified within the *ERF* gene that cause other symptoms such as complex craniosynostosis (when an infant's skull growth is altered by premature bone formation and fusion). Chitayat syndrome however is caused by a very specific and tiny change to the *ERF* gene sequence. It is a recurrent change that is exactly the same in all five diagnoses to date. A genetic test result explaining the sequence change will look something like this:

c.266A→G p.(Tyr89Cys) missense variant

**c** stands for complementary (this means the information was obtained from a cDNA sequence)

**266** denotes the exact position of the genetic change  
**A→G** means that a base change has been made, (the base **Adenine** has been replaced by **Guanine**)

**p** stands for **protein**

**Tyr89Cys** means the DNA sequence change has caused an amino acid change in the protein sequence, amino acid no **89** has been changed from a **Tyrosine** to a **Cysteine**. (amino acids are the 'building blocks' of proteins).

**Missense** means that the DNA sequence change no longer provides the correct code for the appropriate amino acid to be added at this point during protein formation. A protein is still made but it doesn't function as expected.

**Variant** denotes a variation in DNA sequence

The *ERF* gene has multiple roles in the genetic control of our development and functioning. The *ERF* protein binds to DNA, and represses the activity of other genes. Not all functions are fully understood but knowledge in these areas will progress as research continues. This gene is known to be active in the many different tissues of the human body.

## Families say ...

“ From birth feeding was an issue being fed via an NG every 4hours as breathing and feeding was difficult for her, but as soon as she was ready at 14mths she was taking fluids independently. ” - Age 9 years

“ His biggest struggle has been with recurrent respiratory infections and pneumonia. For years, every cold would turn into pneumonia. We work closely with his pulmonary team to ensure prevention is maximized. ”  
- Age 19 years

“ Delay in walking was supported via a walking frame at 19mths and fully mobile independently at 20mths. She has been dancing since the age of 2½ years which has helped with her mobility and posture. ” - Age 9 years

“ He was quite delayed with gross motor skills; he didn't walk until he was 2 1/2. However, he started talking at 9 months old! ” - Age 19 years

## Inform Network Support

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### Facebook groups:

<https://www.facebook.com/chitayatsyndrome/>  
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This 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. This leaflet was written by Unique (AP) and reviewed by Dr Meena Balasubramanian MBBS, DCH, FRCPCH, MD, Consultant Clinical Geneticist, Sheffield Clinical Genetics Service.  
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Understanding Chromosome & Gene Disorders

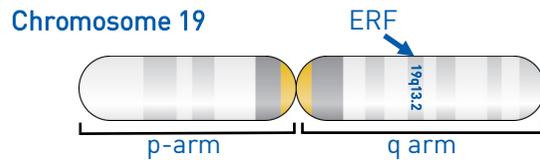
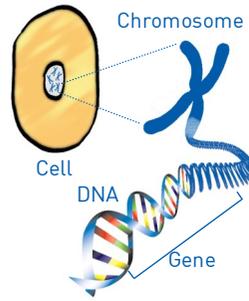
# Chitayat syndrome (ERF variant)



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## What is Chitayat syndrome?

**Chitayat** syndrome is a genetic condition caused by a specific change (known as a variant) of a gene called **ERF** (ERF is an abbreviation of the gene's full name, **ETS2 repressor factor**, which is a description of one of its functions). The ERF gene is located on the long 'q' arm of chromosome 19 in a region called 19q13.2.



Children with Chitayat syndrome may often experience respiratory distress at birth and have noticeable changes to their fingers and toes as well as having a sunken chest. An excessive accumulation of amniotic fluid (the protective liquid that surrounds a fetus) during pregnancy of a baby with Chitayat syndrome has been observed in all mothers to date. This is known as polyhydramnios.

Chitayat syndrome affects boys and girls, and there are both mildly and more significantly affected individuals of both sexes.

### Common features

- Respiratory distress due to weak cartilage in bronchial tube walls (bronchomalacia)
- Sunken/funnel chest (pectus excavatum)
- Shortened index fingers with an extra bone or bone growth at the base (hyperphalangism)
- Bunion (hallux valgus)
- Distinctive facial appearance

### Management recommendations

- Ventilation at birth
- Oxygen supplementation during infancy
- Surgical correction of fingers, toes or chest
- Chronic respiratory infections likely

## Medical concerns

The medical concerns experienced by children with Chitayat syndrome are currently quite consistent.

### ■ Respiratory distress

Shortly after birth, new-borns experience respiratory distress that requires assisted ventilation and possible relocation to an intensive care unit. This is because the walls of the bronchial tubes (and possibly tracheal tubes) are weak due to absent or immature cartilage surrounding the air passages. This is known as bronchiomalacia/tracheomalacia. Children may need continued oxygen supplementation for some time after leaving the hospital and may experience recurrent severe respiratory infections throughout childhood.

### ■ Sunken (funnel) chest

Children appear to have a sunken chest (pectus excavatum) which is due to an abnormality of the cartilage that connects the ribs to the breastbone (sternum). This can lead to shortness of breath during teenage years or adulthood, surgery may be required if the chest shape change is severe.

### ■ Index finger

An unusual index finger is apparent that is slightly shorter and may be angled differently. This is due to an extra bone(s) (or bone growth) (called hyperphalangism) at the knuckle that causes the finger positioning to alter (this is known as ulnar deviation). Other fingers may also appear bent or short.

### ■ Bunions

Bunions is the common term used to describe big toes that are angled towards the neighbouring toes, this is known as hallux valgus in medical terminology. It can arise over time for different reasons, but those with Chitayat syndrome are born with it. The joint that connects the big toe to the foot is altered which causes the big toes to assume an altered positioning.

### Facial appearance

Various minor and possibly distinctive facial appearances have been reported in children with Chitayat syndrome such as: prominent and wideset eyes (hypertelorism), depressed nasal bridge, short region between the tip of the nose and the upper lip (columella), an upturned nose, full lips and high arched eyebrows.

## Development, learning and speech

With only five people reported to date, it is difficult to assess the frequency of developmental delays but they are not expected to be a common feature of Chitayat syndrome. Two children were reported as having developmental delay with motor skills and speech and language being mildly or severely affected (which could be due to severe respiratory complications). However, it remains to be seen whether intellectual abilities will be affected in other children given this diagnosis.

## How common is Chitayat syndrome?

Chitayat syndrome is extremely rare, only 5 people have been reported in the medical literature to date (2019), ranging in age from five to 40 years. We are aware of other children who have been diagnosed with Chitayat syndrome, and have very similar features as described here, but they have not as yet been reported in the medical literature.

## Why did this happen?

When children are conceived their parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random, rare changes occur. This happens naturally in everyone but is only noticeable when an important gene is altered. Chitayat syndrome occurs when one of these random changes affects the *ERF* gene. Such changes are not due to lifestyle factors or anything a parent did prior to, during or after pregnancy.

## Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. In most families, this genetic change has happened for the first time in the child with the *ERF* variant. This is called '*de novo*'. When a genetic test of the parents blood sample does not identify them as carrying this variant, the chances of having another child with the same condition are very low. Very rarely, a parent may be identified as having **germline mosaicism**, which means the genetic change can be present in the egg or sperm but is not detected in a standard blood test. Each family situation is different and a clinical geneticist or genetic counsellor can offer family specific advice.