How common is CES?

CES is very rare and thought to affect a few hundred people worldwide. However, it is likely that many people are not diagnosed if they have mild or no symptoms. Incidence estimates were made many years ago at between 1:50,000 and 1:150,000.

Why did this happen?

When children are conceived their parents' genetic material is passed on in the egg and sperm that makes a new child. This biological process is not perfect and random, rare changes occur, sometimes genetic material is not distributed properly into egg cells and sperm. CES occurs when one of these changes takes place naturally, it is not due to a parents' lifestyle or anything they did before, during or after pregnancy.

Can it happen again?

The possibility of having another child affected by a rare chromosome disorder depends on the genetic code of the parents. In most families, the genetic change has happened for the first time in their child with CES. This is called a '*de novo*' change. When the parents do not appear to carry the genetic change, the chances of having another child with the same condition are very low (usually less than 1%). It is possible for a parent to test negative for CES following a genetic analysis of their blood sample, but have further children with CES. This is due to germline mosaicism, where the cells of the body do not carry the genetic change but it is found in egg cells or sperm.

If a parent has CES, the chances of passing the syndrome on to a child are much higher at 50%. Each family is different and a clinical geneticist or genetic counsellor can give specific advice for your family.

What is somatic mosaicism

Another feature of CES, for those who have an extra chromosome, is somatic mosaicism, this is when some cells of the body carry the extra chromosome, but others do not. (Somatic cells are the cells from which our bodies are made). This is due to the loss of the extra chromosome as cells divide to make new cells as the body grows and develops. The severity of symptoms may depend on which cells retain the extra DNA and at what stages of development the extra chromosome is lost.

Inform Network Support

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Cat Eye Syndrome International
http://www.cateyesyndrome.info
https://www.facebook.com/cateyesyndromeinternational

Chromosome 22 Central - US Office
http://www.c22c.org

Facebook groups
https://www.facebook.com/groups/5642264660/
https://www.facebook.com/22QFoundation/
https://www.facebook.com/MGH22q11.2Clinic/

Further information
https://rarediseases.org/rare-diseases/cat-eye-syndrome/
https://www.omim.org/entry/115470

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

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 guide was compiled by Unique (AP) and reviewed by Dr Andrea Bartuli, Head of Rare Diseases and Clinical Genetic Unit, Bambino Gesù Children's Hospital, Rome.

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Understanding Chromosome & Gene Disorders

Cat eye syndrome (CES)

rarechromo.org

What is cat eye syndrome (CES)?

CES is a rare chromosome disorder. About half of people with CES have an unusual iris (the coloured part of the eye) that can make the pupil (the black part of the eye) appear elongated, hence the name 'cat eye'.

Over 100 people with CES have been described in the medical literature and symptoms vary greatly in presence and severity. Members of the same family with the same CES causing genetic change can have varying outcomes from no or mild symptoms to moderate or more severe features, as detailed below.

Possible clinical symptoms:

- Malformed rectum (anal atresia) with a fistula (abnormal connection to another 'hollow space' such as the bladder/vagina in girls or urethra/perineum in boys)
- Coloboma of one or both iris' (the coloured part of the eye) that can extend to the middle layer (choroid) and inner membrane (retina). Vision is not affected if only the iris is affected. Coloboma in other layers of the eye may affect vision and can cause blindness.
- Cleft palate (incomplete closure of the roof of the mouth)
- Congenital heart anomalies such as 'totally anomalous pulmonary venous return' (TAPVR), 'tetralogy of Fallot' (TOF) and holes between the heart chambers (atrial or ventricle septal defects)
- Renal anomalies such as an underdeveloped kidney (hypoplasia), stretched/swollen kidneys due to urine build up inside them (hydronephrosis), or absent/extra kidneys
- Eyes can appear to slant downwards slightly towards the ears (down-slanting palpebral fissures), be widely spaced (hypertelorism), have skin folds towards the nose (inner epicanthic folds), be misaligned (strabismus), be small (microphthalmia), have limited horizontal movement (Duane syndrome), have an absent iris (aniridia), have a clouded cornea or lens (cataract), have absent eyelid tissue (eyelid coloboma)
- Ears can be misshapen with a nearby pit (dimple) and/or tag (nodule), very rarely the entire outer ear is reduced to several skin tags and sometimes ear canals do not form properly
- Skeletal features include scoliosis (curvature of the spine), absence/fusion/duplication of certain bones (arm, rib, toes), small jaw bone
- Gastrointestinal malformations and/or hernias
- Cryptorchidism (undescended testis) and/or hypospadias (altered positioning of the opening of the urethra) in males.

Other features have been observed in some people with CES, such as intrauterine growth restriction (IUGR; poor fetal growth during pregnancy), short stature and various abdominal defects. In fact, the symptoms are so varied that anomalies in almost every organ, although rare, have been observed.

Ability to learn

Over half of people diagnosed with CES have normal intellect and others have mild to moderate intellectual disability (ID). Severe ID has also been identified but is very rare.

People with CES have a huge range of symptoms and there is currently not enough knowledge to explain why this happens but may be explained partly by additional undiagnosed genetic changes, particularly for those more severely affected. Another explanation is that in some people with CES, not all cells of the body carry the genetic change (see somatic mosaicism). It is therefore not possible to predict what sort of symptoms, if any, a child with CES will have or will develop.

Management recommendations

Management of CES will depend on the symptoms experienced by each individual and may include:

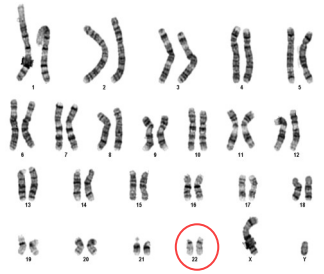
- Surgery for anal atresia and/or other major gastrointestinal malformations
- Cardiac evaluation, complex cardiac anomalies may require medication and/or surgery
- Eyesight (ophthalmology) evaluation
- Hearing evaluation
- Palate evaluation
- Urogenital evaluation
- Abdominal evaluation
- Growth hormone therapy for some children with short stature
- Early intervention with educational support for some children with learning difficulties/disabilities

CES has many names

Cat Eye Syndrome is also known as Schmid-Fraccaro syndrome, partial tetrasomy 22, partial trisomy 22 and invdup(22pter-q11). If you have recently been given a diagnosis you will most likely have also had a genetic test called a microarray or arrayCGH (comparative genomic hybridisation) which may provide more precise details regarding the genetic basis of the CES diagnosis.

What causes cat eye syndrome (CES)?

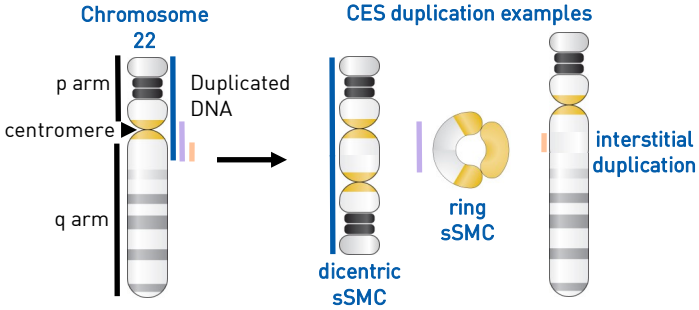
CES is a rare chromosome disorder caused by the presence of duplicated genetic material from one of the body's 46 chromosomes - chromosome 22.



standard set of male chromosomes
chromosome 22 pair is circled in red

Chromosomes usually exist as a set of 23 pairs, numbered 1-22 and a pair of 'sex' chromosomes that establish biological sex. [Males usually have one X and one Y chromosome (XY), and females usually have two X chromosomes (XX)].

In CES, the duplicated DNA commonly exists as an additional chromosome known as a small supernumerary marker chromosome (sSMC). The additional chromosome consist of two mirror copies of a segment of chromosome 22. A sSMC can contain one piece of duplicated chromosome that is shorter than the other so is not always symmetrical. Cells usually have two copies of chromosome 22; the addition of two more copies of part of this chromosome results in four copies of a specific part of chromosome 22 (this is called partial tetrasomy).



Chromosomes have a short 'p' arm and a long 'q' arm that join at the 'centromere' (coloured yellow above). The sSMC found in most people with CES has two centromeres (it is dicentric). A larger section of the q arm of chromosome 22 is duplicated in CES type 2 compared to CES type 1.

Some people have duplications of the same/similar piece of genetic material that has been incorporated into an existing chromosome or forms a small ring chromosome. A single copy of the extra genetic material means a total of three copies are present (this is called partial trisomy).