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“ Definitely join... the C22C support group on the web.
There is a lot to learn from other parents and children.

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!

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. The information is believed to be the best available at the time of publication. It was written for *Unique* by Dr Melissa Carter, clinical geneticist and fellow in developmental paediatrics, Bloorview Kids Rehab, Toronto, Canada.
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Emanuel syndrome



“ Your child will bring you joy and pain, just as all children do.
Rejoice in the small achievements.

“ Most of what I have found out about Emanuel syndrome has been
from my internet research.

Why is it called Emanuel syndrome?

Emanuel syndrome is named after Dr Beverly Emanuel, a cytogeneticist in Philadelphia, USA. In 2004, founding members of Chromosome 22 Central, an online parent support group for chromosome 22 disorders, successfully lobbied to have this name applied to the condition caused by having an extra chromosome called 'derivative 22'.

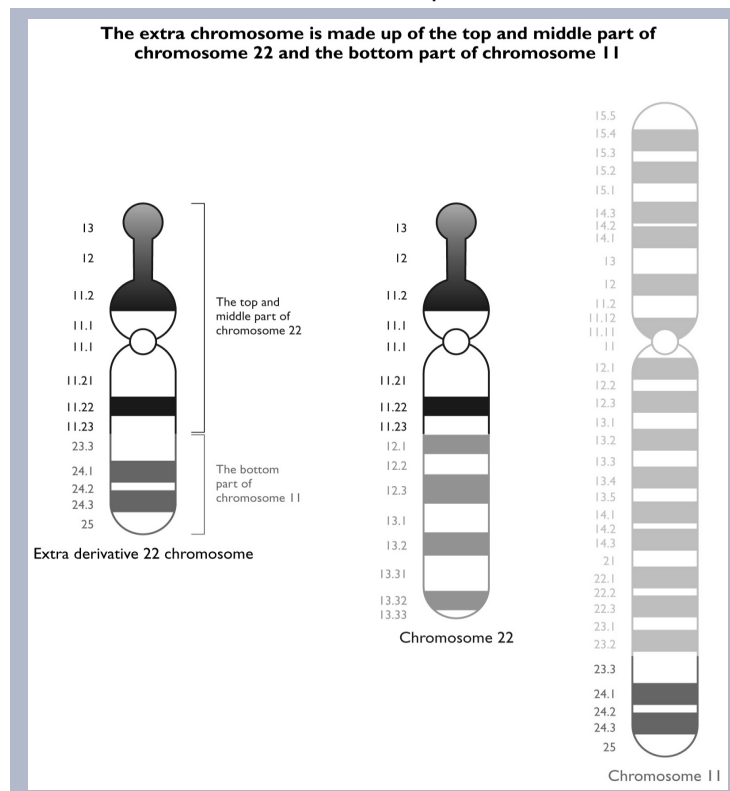
Dr Emanuel is recognised for her laboratory's work on identifying the source of the derivative 22, how it is inherited, and for her association with the parent support group. However, the condition is so rare that many doctors may not have heard of it called by this name.

Other names

In the scientific literature, the name Emanuel syndrome is only starting to be used. Previously it has been referred to as **derivative 22 syndrome**, **derivative 11;22 syndrome** or **partial trisomy 11;22**. These names describe the fact that there are 47, instead of the usual 46, chromosomes present in the cells of the child's body. The very

early literature refers to the condition as **trisomy 22** based on the incorrect assumption that the extra chromosome was a third 22 (hence the name trisomy).

The extra chromosome is made up of the top and middle part of chromosome 22 and the bottom part of chromosome 11 (see diagram, left). This means that there are extra copies of many genes present on both chromosome 22 and 11.



What is the chance I will have another child with Emanuel syndrome in a future pregnancy?

It's difficult to say with certainty what the recurrence risk is for a given couple. We can estimate the risk as follows: if you are female and a carrier of the 11;22 balanced translocation, the risk for *each* pregnancy you have in the future is about six per cent. If you are a male carrier, the risk is lower, about two to five per cent. In the very rare case where neither parent is a carrier, the risk is lower still, probably less than one per cent.

Testing is available to you in each future pregnancy to determine if the unborn baby has Emanuel syndrome. You should let your doctor know that you want prenatal testing as soon as you know you're pregnant.

Who else in our family should be tested?

If you have other children, and they are healthy with no disabilities, generally they do not need to be tested right away, but you should discuss this with your medical geneticist. Once your child is old enough to make decisions about their own health care, if they have not yet been tested they should be made aware that carrier testing is available (again, a blood test) and should be done before starting a family. The chance that they could be a carrier is 50 per cent.

If you are a carrier and have brothers and sisters, let them know that they too can be tested. Assuming that you inherited the translocation from one of your parents, each of your siblings has a 50 per cent chance of being a carrier as well.

If you have a large extended family, your parents may wish to be tested to find out which side of the family the translocation came from. Your aunts, uncles and cousins on the affected side may also wish to know this information.



In this family, the mother is a carrier. The daughter has Emanuel syndrome. The son's chromosomes have not been analysed yet

Reading

The *American Journal of Medical Genetics* volume 149A (2009) contains an important article for people who want more medical detail. [Phenotypic delineation of Emanuel Syndrome \(Supernumerary Derivative 22 Syndrome\): Clinical Features of 63 Individuals](#) by Melissa T Carter *et al* is on pages 1712-1721.

Growth and Puberty



Fourteen years old

Most children with chromosomal imbalances tend to be on the small side compared to other children their age. Their growth is slower in general, and they also tend to eat less and have less muscle mass because of their physical challenges. Puberty seems to proceed as expected in children with Emanuel syndrome, despite their smaller size.

Behaviour

Like all children with physical and intellectual challenges, frustration and anxiety can arise as they struggle to communicate with limited means. However, in general parents of children with Emanuel syndrome comment on how their child is generally happy and sociable, enjoys music and being around people, and has a good sense of humour.

“ She is a happy young lady who is outgoing and loves to be with people. She recognises her Dad and brothers and Grandma and friends of the family and will verbalise and smile at them - *parent of a 20-year-old*

Life expectancy in Emanuel syndrome

There are individuals with Emanuel syndrome currently living who are into their 30s. We don't have information on the average lifespan of an individual with Emanuel syndrome. It really depends on a number of things, most important being the severity of any birth defects. If birth defects are mild or correctable, then the other important factor is the degree of physical disability. Also contributing to premature death are things like severe seizures or a weak immune system, as in any person with severe disabilities.

“ Things have improved so much since our daughters were born, with physiotherapy, OT, education and medical knowledge... I believe the kids born today will be able to do a lot more than our children - *parent of 34-year-old twins*

“ At 26, she is still physically an infant that needs total care - *parent of 26-year-old*

Where does the derivative 22 chromosome come from?

Dr Emanuel's laboratory discovered that the extra chromosome is inherited from one of the parents, most often the mother. This parent is called the [carrier parent](#). The carrier parent has the usual number of chromosomes - 46. However, one of the chromosome 11s and one of the 22s have switched pieces - this is called a translocation. Since no genes are gained or lost, this is called a [balanced translocation](#).



The extra chromosome usually comes from the mother

The 11;22 translocation is unique in that it is one of the only types of balanced translocations that is seen in unrelated people. Most other translocations are unique to a family. Unique also has a guide to the [11;22 translocation](#).

Why does the derivative 22 chromosome usually come from the mother?

We don't know for sure. If you are a man carrying the translocation, you will produce some sperm that have normal chromosomes and some that have the derivative 22. However, the sperm carrying the abnormal chromosome may be less likely to fertilise an egg than the normal sperm. Likewise, women who are carriers of the translocation will produce two types of eggs - those with and without the extra chromosome - but both types seem to be equally likely to be fertilised.

About five per cent of individuals with Emanuel syndrome inherited the extra chromosome from their father; the other 95 per cent inherited it from their mother. It's extremely rare that neither parent is a carrier of the balanced translocation.

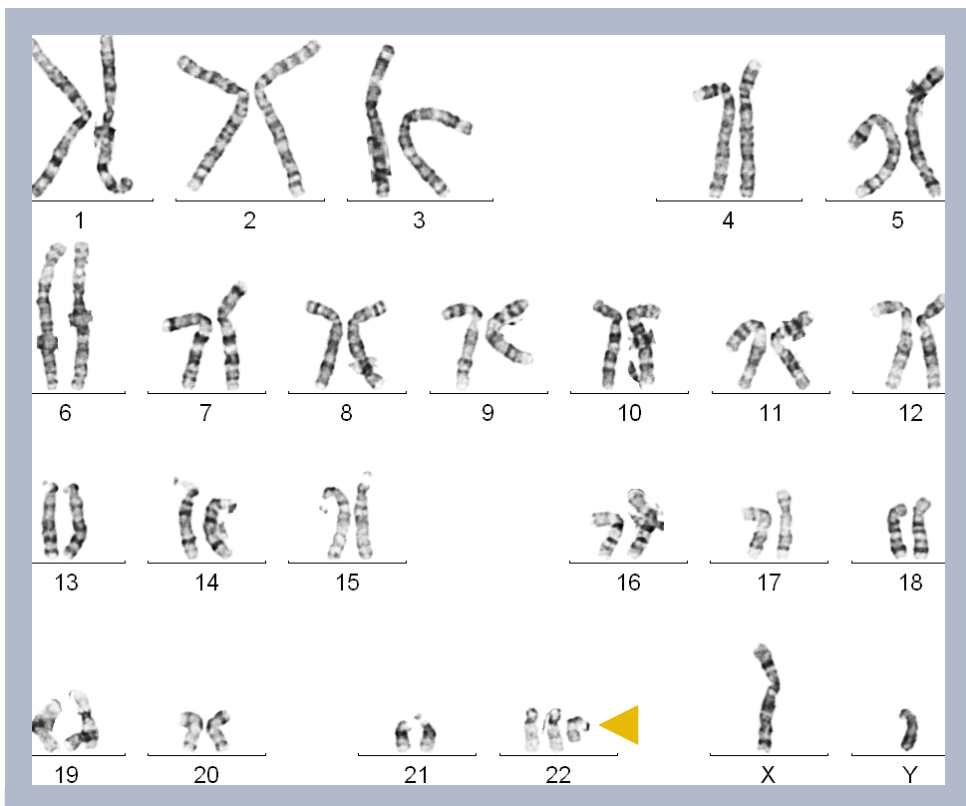
How common is Emanuel syndrome?

The exact incidence is not known. It is quite rare - only about 200 cases have been reported in the literature. However, Unique has 22 members with Emanuel syndrome and there are about 200 present and past members of the online parent support group Chromosome 22 Central with Emanuel syndrome, and likely many more in the non-English speaking world as well.

“ Ask questions and talk to other parents with children like yours. Be as truthful as you can with them, as acceptance of your child's disability will help them as much as you.

Diagnosis

The diagnosis is made with a blood test to analyse the chromosomes. Doctors commonly order a chromosome analysis in babies who have birth defects or delays in their development. Therefore, most children with Emanuel syndrome are diagnosed in infancy (within the first year of life).



The chromosomes of someone (a male) with Emanuel syndrome.
The yellow arrow shows the extra derivative 22 chromosome

In previous generations of your family, there may have been other individuals with Emanuel syndrome. If they died young (which used to be much more common for children with chromosome conditions), they may not have been diagnosed. Or, if they were born prior to the 1980s, they may not have been diagnosed because the technology to look at chromosomes in a blood sample was not available.



Seven months old

“It’s a tough road, but there are many delights along the way.

Seizures

Seizures are common - 48 per cent of parents in the Carter study reported that their child had at least one seizure. Thirty-four per cent indicated that their child was currently taking medication for controlling seizures. The type of seizures is variable. Some have more than one type. There’s no indication from the study that the seizures experienced by children with Emanuel syndrome are any harder to control than in any other child with epilepsy.

Feeding

Feeding can remain problematic beyond infancy, for a variety of reasons. However, this is variable. Some children eat age-appropriate foods, and can finger-feed themselves. Using utensils is a bit trickier for these children due to poor coordination. Most children need specially prepared food (for example, puréed) to be able to swallow safely, as chewing food is a skill that is difficult for them to learn. A minority (19 per cent) are fed via a tube surgically implanted into the stomach through the abdominal wall (G-tube or gastrostomy). The main reasons for this are inability to safely swallow foods without choking or aspirating (inhaling food particles into the lungs), and to give extra calories because of poor weight gain. Sometimes a G-tube is placed only temporarily while weight gain is optimised.

Also complicating feeding is reflux (where stomach acid comes back up into the oesophagus causing pain), which is very common in all children with hypotonia. This tends to get better with age, but sometimes needs to be treated with medication (antacids) or even surgery (fundoplication). Only eight per cent of children in the Carter studies needed surgery to manage their reflux. Constipation is another common problem, so it is important to keep well hydrated and to eat a high-fibre diet. About 30 per cent of children with Emanuel syndrome need to take a daily laxative or stool softener to help them pass stools.



Seven years old

Children and Adolescents with Emanuel syndrome

Motor Development

The floppiness seen in babies with Emanuel syndrome tends to persist but slowly most children gain some control over their muscles. Motor development - the ability to learn how to sit, crawl and walk - is very delayed in most children. Over 70 per cent do learn to walk eventually, but this takes persistence and lots of support. The average age to learn how to walk is five years. Most children with Emanuel syndrome who walk need the support of another person or a walker, but some can walk without support. Most children with Emanuel syndrome, once they grow too big for a stroller, need to have some sort of motorised wheelchair for getting around in the community, even if they have learned to walk, as they tire easily and are unsteady.



“ Keep up daily physiotherapy!

Language Development

Most children with Emanuel syndrome don't learn to talk, although there are certainly exceptions. About 77 per cent are non-verbal, but a few can say single words or learn simple sign language. Parents frequently comment that their child's understanding is much better than their ability to communicate (in other words, receptive language is better than expressive language). Hearing impairment is common as well - almost 75 per cent of children with Emanuel syndrome will have abnormal results on their hearing test. The hearing loss may be mild to moderate, but in some cases (14 per cent) it is severe to profound, requiring hearing aids or cochlear implants. Therefore, it's important to have hearing tested regularly.

“ Don't give up on your child or write them off. Every child has something to give.

Infections

One of the reasons for hearing loss in children with Emanuel syndrome is frequent ear infections. Because they can't tell you that they have an ear infection, it is important to have your doctor check the ears regularly. Most children with Emanuel syndrome end up having tubes placed in the ear drums to drain fluid that can accumulate and lead to infections and hearing problems.

Children with Emanuel syndrome may have other infections, usually chest infections (pneumonia), which can be caused by bacteria or viruses. Like many children with low tone and developmental disabilities, infections that are routine in most children can be more severe and last longer. Sometime hospitalisation is necessary for treatment. Your doctor may check your child's immune system to see if they have adequate antibodies. It's not clear whether children with Emanuel syndrome truly have immune system problems, as no one has specifically investigated this. However, some parents report that their doctor found low levels of antibodies (immunoglobulins) in their child's blood, and therefore put them on a medication called IVIG (which is essentially a transfusion of antibodies). Some parents found it made a difference in the number of infections their child had.

Features of Emanuel syndrome



Seven years old



Twelve years old

A recent study (Carter 2009, *see page 11*) was published in which the researchers surveyed parents of 63 individuals with Emanuel syndrome.

Most of the information in this guide comes from the results of that study, as well as older medical literature.

All children with Emanuel syndrome have some degree of physical and intellectual disability. Like any chromosome disorder, the outcome differs from person to person. However, all of the known individuals with Emanuel syndrome have a moderate to severe level of developmental disability. Having the extra chromosome interferes with how the brain develops, even if the brain looks 'normal' on CT or MRI scan. It also interferes with how the internal organs develop and function, leading to birth defects and health problems.

“ Learn all you can because ultimately you will be the most educated person about your child's needs. You cannot expect specialists to all understand what Emanuel syndrome is.

Main features in infants with Emanuel syndrome

Babies with Emanuel syndrome are usually a bit smaller than average at birth, and grow more slowly. Pregnancy complications and premature delivery are uncommon. If there are pregnancy complications, the most common ones are poor fetal growth (also called intrauterine growth restriction or IUGR) and oligohydramnios (low amniotic fluid). Ultrasounds done routinely during the pregnancy may pick up a heart defect or other birth defect if present. However, over 80 per cent of pregnancies are uneventful.

The doctors in the nursery may notice features in the baby that suggest a possible problem with fetal development - they refer to these as 'dysmorphic features'. Examples of dysmorphic features common in babies with Emanuel syndrome are deep-set eyes, low-set and malformed ears, ear pits or tags, a long upper lip (philtrum), a small chin (micrognathia) and excess skin at the back of the neck. Other things they might notice when examining a newborn with Emanuel syndrome are dislocatable hips, undescended testicles, inguinal hernia(s) (in the groin) and/or a small penis in boys, or a dimple in the skin just above the buttocks (called a sacral dimple). These features may prompt the doctors to order a chromosome test, which reveals the diagnosis.



Seven months old



Four years old

Neurologically, babies with Emanuel syndrome are 'floppy' or hypotonic, which results from the inability of the brain to properly control muscle tone. Hypotonic infants can run into problems with breathing and feeding during the first few months of life. Breathing usually improves, but feeding can remain an issue due to poor motor coordination. The brain doesn't grow well in individuals with Emanuel syndrome, so the head is usually smaller than expected for age (microcephaly). Other differences in the formation of the brain are possible. The most serious is hydrocephalus, which is reported in about 10 per cent of cases. Hydrocephalus is an abnormal increase in the amount of the natural cerebrospinal fluid inside the ventricles of the brain.

If hydrocephalus is present, surgery may be required to relieve the pressure on the brain. Most other brain differences reported in children with Emanuel syndrome are seen on MRI or CT scan of the head, but nothing can be done about them - it's just the way the brain developed.

"She will do something one day and not the next... her skills can be very inconsistent at times - parent of 4-year-old"



Seven years old

types of heart defects - ventricular septal defect (VSD), atrial septal defect (ASD), and patent ductus arteriosus (PDA) - often correct on their own with time. A VSD is a hole in the wall between the two pumping chambers of the heart; an ASD is a hole in the muscular wall between the two filling parts of the heart; PDA is a channel between the aorta and the pulmonary artery that takes blood to the lungs and usually closes shortly after birth but instead stays open. This means that the lungs receive more blood than they should and the heart has to work too hard. A PDA can be closed using minimally invasive surgery by inserting a coil via an artery in the thigh. Tissue grows around the coil, closing the gap.

Malformations of the kidneys are often found on ultrasound in infants with Emanuel syndrome: the kidneys can be smaller than usual, or one kidney could be missing. Generally speaking though, these differences do not affect how well the kidney works.

"He is happy, loving and generally healthy - he has exceeded prognosis at diagnosis - parent of 10-year-old"



Three years old

If the baby has a cleft palate (a split in the roof of the mouth), this can further complicate feeding problems. More than half of babies with Emanuel syndrome are born with a cleft palate. This can be very mild (called a 'submucous cleft') or severe enough to require surgery.

Other common birth defects are malformations of the heart and blood vessels, kidneys, and intestines. Heart defects are present in almost 60 per cent of babies with Emanuel syndrome. However, only about half of these have a heart defect serious enough to require surgery. The most common