

## Introduction

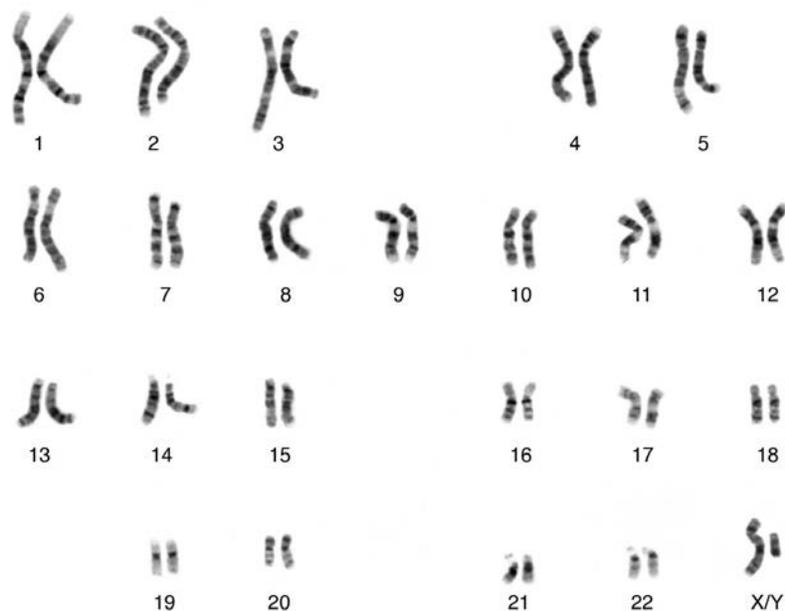
The goal of this page is to describe the major features of Tetrasomy 18p. This information was obtained from a thorough review of the literature as well as from the data of the Chromosome 18 Clinical Research Center. This information may help you and your healthcare team make decisions about how to care for a person with Tetrasomy 18p.

As you read through this article, remember that no two people with Tetrasomy 18p are exactly alike, even though the underlying genetic change is the same. One person may have different medical and developmental concerns from another person with Tetrasomy 18p. Also, remember that no one with Tetrasomy 18p will have all of these features. In addition, people with Tetrasomy 18p share many features with their family members. They will also have their own unique skills and abilities which you will not find in the following list.

Research is critical. As we learn more about Tetrasomy 18p, we also learn more about how to best treat it. This will improve the health and development of people with Tetrasomy 18p.

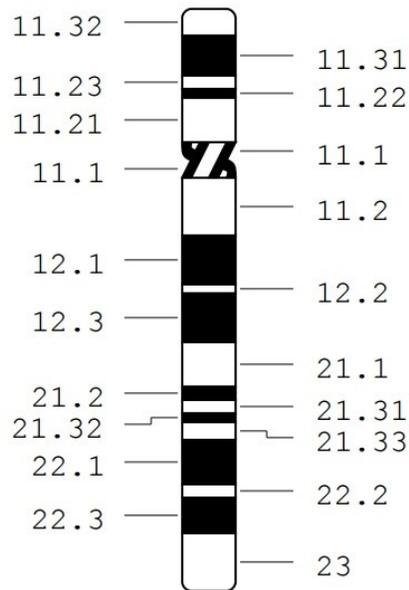
## Genetic Basis

In order to understand the genetic basis of Tetrasomy 18p, it is important to know about the structure of chromosome 18. Every chromosome, including chromosome 18, has a characteristic black and white banding pattern and a constriction (called a centromere) in a characteristic location somewhere along its length. These two things, the banding pattern and the centromere, make each chromosome recognizable to a trained eye.



As you can see, the centromere of each chromosome is not exactly in the middle of the chromosome. This makes the chromosome appear as if it had two distinct segments of unequal length. These segments are called arms. The shorter arm (called "p" for petit) is always shown on top. The longer arm is called the "q" arm and is shown below the p arm.

The bands on each chromosome arm divide it up into regions. The regions are numbered starting at the centromere and progressing to the end of the chromosome arm. Below is a diagram that shows how the bands of chromosome 18 are labeled.



Typically people have 46 chromosomes in every cell of the body. Individuals with Tetrasomy 18p have 47 chromosomes instead of 46. The extra chromosome, also called an “isochromosome” is made up of two additional copies of the short arm of chromosome 18. Therefore, there are a total of four copies of the short arm (the p arm) of chromosome 18. This is why the condition is called Tetrasomy 18p. The prefix “tetra” simply means “four”.

You may also see the term “isochromosome 18p” used to describe this condition. The term “isochromosome” refers to the extra chromosome that is made up of two copies of 18p.

So far, we have talked about the structure of chromosomes. However, we have not discussed their content. Just as the page numbers of the book are meaningful because they describe the location of the words written on them, chromosome bands and base pairs are important because they describe the location of the genes. The genes are aligned along the length of the chromosome. Genes are the instructions for all the activities necessary for life. They give the body instructions for how to grow and develop. They are the words on the page.

Because we have two copies of each chromosome (one from mom and one from dad), we also have two copies of each gene: one on each chromosome copy. When a piece of a chromosome is duplicated, the genes in that part of the chromosome are duplicated as well. Because people with Tetrasomy 18p have four copies of 18p, they also have four copies of each of the genes in that region. The change in the number of genes leads to the medical and developmental concerns associated with Tetrasomy 18p.

For a more in-depth discussion about genetic concepts, we invite you to review a series of podcasts designed and narrated by Dr. Jannine Cody, Director of the Chromosome 18 Clinical Research Center.

## Diagnosis

There are several different reasons that your family’s physicians might suspect that there is an underlying chromosome change present. Some of the more common reasons include:

- Child missing developmental milestones
- Presence of birth defects
- Minor differences in facial features
- A family history of a chromosome condition

Although Tetrasomy 18p can be diagnosed prenatally by chorionic villus sampling (CVS) or amniocentesis, it is most frequently diagnosed during infancy or early childhood. There are two tests that are commonly performed to identify a deletion on Tetrasomy 18p. Both of these tests can be performed on a blood sample.

### ***Routine Chromosome Analysis***

In this test, white blood cells are grown in the lab. The chromosomes are stained and examined under a microscope by a qualified cytogeneticist. This individual is trained in recognizing extra and missing pieces of chromosomes, as well as other rearrangements, such as translocations and inversions. Results from a chromosome analysis will indicate the number of chromosomes, whether the person is a male or a female, and which part of the chromosome is changed. The chromosome result of a person with Tetrasomy 18p might look something like this:

**47,XX,+i(18)(p10)**

This result tells us that there are 47 chromosomes instead of the expected 46. This person is also a female, as indicated by the two copies of the X chromosome. The “i” stands for isochromosome, which is composed of material from chromosome 18. The “p10” tells us that the isochromosome is made of chromosome material that starts at the centromere (p10) and extends to the tip of p arm.

### ***Microarray Analysis***

A microarray analysis is similar to a routine chromosome analysis in that it determines if there is extra or missing pieces of a chromosome. It can detect chromosome deletions and duplications that are not visible under a microscope. A microarray result of a person with Tetrasomy 18p might look something like this:

**arr 18pterp11.21(136,226-15,198,990)x4**

This result tells us that there is a change in the region extending from the tip of chromosome 18p to base pair 15,198,990, which is essentially the centromere. The “x4” at the end tells us that there are actually four copies of that region, which is consistent with a diagnosis of Tetrasomy 18p.

## **Characteristics of Tetrasomy 18p**

### ***Problems in the Newborn Period***

Newborns with Tetrasomy 18p often have problems at birth or shortly thereafter. The most common problem is nursing/feeding difficulties. Infants may have problems latching onto the breast or bottle. They may also have problems coordinating the suck-swallow motion that is required to nurse. Some infants may vomit frequently after eating. In some cases, a referral to an occupational or physical therapist may be recommended. In more serious cases, a feeding tube may be required. Supplementing their diet with a high-calorie formula may also be recommended to help the infant gain weight.

Infants with Tetrasomy 18p may have other problems. Jaundice is a build-up of bilirubin in the baby’s blood, leading to a yellowish color of the skin and eyes. Occasionally, this resolves on its own. However, many infants with Tetrasomy 18p require treatment for jaundice. Treatment is usually very easy. Typically, the baby is simply placed under a light. This helps break down the extra bilirubin in the baby’s blood.

Some infants with Tetrasomy 18p have breathing problems shortly after birth. To assist with the baby’s breathing, doctors may have to provide extra oxygen. This may be done by putting a tube into the baby’s nose.

## *Neurological Changes*

People with Tetrasomy 18p usually have some changes in their muscle tone. They may have increased or decreased muscle tone. This is called hypertonia and hypotonia, respectively. Changes in muscle tone can lead to other difficulties. For example, infants with low muscle tone may have difficulty eating because the muscles surrounding the mouth are weak. Children with high muscle tone may also have spasticity. This means that there are uncontrolled muscle spasms when the muscle is stretched by someone else. Changes in muscle tone and spasticity may also lead to delays in meeting developmental milestones, such as sitting without support and walking. Physical, occupational, and speech therapy may improve some of these problems.

Seizures also happen more often in people with Tetrasomy 18p than in people without Tetrasomy 18p. If seizures are suspected, a doctor may request an electroencephalogram (EEG). They may also refer the patient to a neurologist to help manage the seizures.

Spina bifida has been reported in a small number of people with Tetrasomy 18p. Spina bifida, also known as myelomeningocele, is a type of birth defect. It is an opening in the spinal cord that occurs early in the first trimester of pregnancy. This can lead to paralysis of the legs, problems with the kidneys and urinary system, and hydrocephalus (extra fluid in the brain). Spina bifida is usually treated by a team of specialists, including neurosurgeons, therapists, and urologists. To find a spina bifida clinic in your area, visit the [Spina Bifida Association](#) website.

## *MRI Changes*

Some people with Tetrasomy 18p have changes in the structure of their brain that can only be detected with an MRI. For example, several people have been identified with a thin corpus callosum. The corpus callosum is the bundle of nerves that connect the right and the left sides of the brain. Other people have been diagnosed with “enlarged lateral ventricles”. This simply means that the spaces that contain the cerebrospinal fluid in the brain are larger than expected.

## *Eyes and Vision*

Eye problems are common in people with Tetrasomy 18p. The eyes may be misaligned (strabismus). People with Tetrasomy 18p may also have problems with their vision. They may be near-sighted, far-sighted, or have astigmatism.

Because vision problems are possible, people with Tetrasomy 18p should have regular eye exams.

## *Ear Infections*

Recurrent ear infections are common in babies and toddlers with Tetrasomy 18p. They occur in approximately 50% of individuals. Untreated ear infections may lead to hearing problems. Therefore, it is important to identify and treat ear infections. Most of the time, medicine is prescribed to treat the ear infection. Some children may require surgery to insert tubes in the ears to reduce the number of ear infections.

## *Hearing*

Although hearing loss does occur in some people with Tetrasomy 18p, the majority do not have any hearing problems. It appears that those that do have hearing loss typically have a mild to moderate hearing loss.

Although hearing loss is not very common in people with Tetrasomy 18p, it is still important to screen them for any potential hearing problems. This will help find and treat hearing loss early.

### *Palatal Abnormalities*

The palate is the roof of the mouth. Many people with Tetrasomy 18p have changes in the shape of their palate. For example, the palate may be highly arched and/or narrow. In some cases, these changes may lead to some difficulties with speech. It is important to understand that this is not the same thing as a cleft palate, in which the palate does not completely close.

If a physician feels that a change in the palate may lead to speech problems, he or she may refer a patient to an ENT (a doctor who specializes in problems of the ears, nose, and throat).

### *Heart*

Approximately 30% of people with Tetrasomy 18p have some type of heart defect. Many of the heart defects are “septal defects”, meaning that there is a hole in between the two sides of the heart. In some cases, these defects close without any intervention. However, in some cases, surgery is necessary.

Because heart defects are more common in babies with Tetrasomy 18p, they may have an ultrasound of the heart (echocardiogram) to rule out such defects.

### *Gastrointestinal Changes*

Gastrointestinal problems are fairly common in people with Tetrasomy 18p. The most common concern is constipation. Reflux also occurs somewhat frequently. Structural malformations of the gastrointestinal system are not very common. However, pyloric stenosis and hernias have been reported. Pyloric stenosis is a closure or narrowing of the place where the stomach contents enter the intestines. A hernia occurs when some organs, often the intestines, push outside of the abdomen.

If there is a concern for gastrointestinal problems, a referral to a gastroenterologist is appropriate.

### *Genitourinary Changes*

Males with Tetrasomy 18p may have some changes in the genital region. The testicles may not be fully descended (cryptorchidism). The opening of the urethra may not be at the end of the penis (hypospadias). In some cases, surgery may be required to correct these concerns.

Some people have vesicoureteral reflux. This occurs when urine flows from the bladder up towards the kidneys. This can lead to recurrent urinary tract infections. However, structural changes in the kidneys occur in a small number of males and females with Tetrasomy 18p. A doctor may order an abdominal ultrasound to rule out structural changes in the kidney.

### *Orthopedic Changes*

Some people with Tetrasomy 18p may have minor changes in their hands and feet. For example, they may have narrow feet, or they may have fingers and toes that are partially fused. They may have camptodactyly. Camptodactyly occurs when fingers are in a permanently “flexed” position. However, these issues seldom require medical intervention.

People with Tetrasomy 18p may have scoliosis or kyphosis. This simply means that they have an abnormal curvature of the spine. Flat feet are another common orthopedic concern.

People with foot or spinal changes may see an orthopedic specialist. Braces and inserts, surgery, and therapy may help in addressing orthopedic concerns.

There has been some evidence suggesting that people (including children) with Tetrasomy 18p have decreased bone mineral density, meaning that they may be more susceptible to bone fractures. A DEXA scan (bone scan that determines bone mineral density) may be considered to establish a baseline. Families may also wish to speak with their physician about calcium and vitamin D supplementation. Much research remains to be done to understand whether and how bones are affected in individuals with Tetrasomy 18p.

### *Allergy and Immunology*

In recent years, several individuals have been diagnosed with eosinophilic esophagitis (EoE). EoE is an inflammatory disease that affects the tube that connects the mouth to the stomach (the esophagus). Some symptoms include feeding difficulties and failure to thrive, reflux that doesn't respond to therapy; difficulty swallowing, nausea, and vomiting. For more information about EoE, visit the American Partnership for Eosinophilic Disorders.

If there is a concern for EoE, a gastroenterologist can help make a diagnosis and discuss treatment and management options.

### *Growth*

Children and adults may have changes in their growth patterns. Children with Tetrasomy 18p may be small for their age. In a minority of cases, this is due to growth hormone deficiency. Treatment with growth hormone helps normalize growth and may improve a child's development.

If there is a concern regarding growth, a person can see a pediatric endocrinologist to rule out growth hormone deficiency. Drs. Jannine Cody and Daniel Hale have written an article for the Chromosome 18 Registry & Research Society about growth hormone deficiency in children with chromosome 18 abnormalities.

- [Growth Hormone Deficiency and Chromosome 18 Abnormalities, Chromosome 18 Communique, Spring 1999.](#)

In addition to short stature, many people with Tetrasomy 18p have microcephaly, or a head size that falls below the 3rd percentile.

### *Bone Issues*

There has been some evidence suggesting that people with Tetrasomy 18p have decreased bone mineral density, meaning that they may be more susceptible to bone fractures. A DEXA scan (bone scan that determines bone mineral density) may be considered to establish a baseline. Families may also wish to speak with their physician about calcium and vitamin D supplementation. Much research remains to be done to understand whether and how bones are affected in individuals with Tetrasomy 18p.

### *Facial Features*

People with Tetrasomy 18p may have facial features that are slightly different from other family members. These changes do not affect a child's health or development. They are simply small differences that might be noted by a doctor.

They may have changes in the structure or the placement of the ears. They may have a small mouth, and the area above the upper lip may be smooth. The upper lip may be thin. Their chin may be either larger or smaller than other children's chins.

Although people with Tetrasomy 18p may have facial features in common with one another, it is important to remember that they also have features in common with their family members.

### *Lifespan*

When a child is diagnosed with Tetrasomy 18p, one of the family's first questions is often, "What does this mean for my child's lifespan?" The Chromosome 18 Clinical Research Center has published data regarding life expectancy in people with Tetrasomy 18p. There are 56 individuals with Tetrasomy 18p in the study. In this group, there has been at least one instance of premature death in a person with Tetrasomy 18p. A thirteen year old girl passed away unexpectedly due to sudden heart arrest following a day-long history of nausea, vomiting and lethargy. The direct cause of her sudden deterioration is unknown. She had a history of severe and untreated constipation as well as possible seizures which may have contributed to her death.

### **Development and Behavior:**

Individuals with Tetrasomy 18p frequently have developmental and behavioral concerns in addition to the medical issues discuss above.

Learn more about developmental and behavioral concerns in people with Tetrasomy 18p.

### **Mosaicism**

The term "mosaicism" describes a situation in which different cells in the same individual have different numbers or arrangements of chromosomes. It is called "mosaicism" because, in a way, the cells of the body are similar to the tiles of a mosaic. In a mosaic piece of art, each tile is different. They have different shapes and colors. The tiles are fitted together to make a whole picture.

If a person has mosaicism, their cells are like the tiles of a mosaic. Taken together, the different tiles of the mosaic form the whole picture, similar to the way the cells form the whole body. Just as the tiles of a mosaic have different shapes and colors, the cells of the body have different numbers or arrangements of chromosomes. For example, if an individual has mosaic Tetrasomy 18p, this means that some of the cells have Tetrasomy 18p while other cells do not.

In general, individuals with mosaicism have similar medical and developmental concerns to those with a non-mosaic form of the same chromosome condition. For example, an individual with mosaic Tetrasomy 18p may have many of the same features as someone with non-mosaic Tetrasomy 18p. However, because individuals with mosaicism have fewer cells carrying the chromosome change, they tend to be less severely affected. It is very important to understand that this is not always the case.

Unfortunately, it is impossible to predict exactly how mosaicism will affect an individual at this point in time. This is because we cannot know precisely which cells carry the chromosome change and which cells do not.

## Care of an Individual with Tetrasomy 18p

Based on our current understanding of Tetrasomy 18p, there are several evaluations that we would suggest families consider for anyone recently diagnosed with Tetrasomy 18p. It is important to work with your team of physicians to determine which of these evaluations are appropriate.

- Genetics evaluation and counseling
- Parental chromosomes
- Periodic ophthalmology evaluations
- Periodic audiology evaluations
- ENT referral for management of chronic otitis media
- Cardiology evaluation
- Renal ultrasound
- Orthopedic evaluation for management of foot abnormalities
- Monitor for scoliosis and kyphosis
- Neurology if concerns for seizures are present
- Gastrointestinal/nutritional evaluation of failure to thrive, gastroesophageal reflux, constipation, EoE
- Endocrinology evaluation for short stature, to include evaluation for growth hormone deficiency
- Referral for developmental services and therapy

## Family Planning and Genetic Counseling

Many parents wonder, “If we have another child, what is the chance that our next child will have Tetrasomy 18p?”

In the grand majority of cases, the isochromosome is a *de novo* event. That means that it is a unique change that only occurs in that individual. Siblings do not have a significantly increased risk to have Tetrasomy 18p.

If a person with Tetrasomy 18p has a child, there is a chance that their child would have Tetrasomy 18p as well. However, it should also be noted that there are no case reports of a person with full Tetrasomy 18p having children. If you have questions about the implications of a chromosome change for other family members, we recommend contacting a genetics provider.

### For Additional Information:

The information provided here is general information based on the literature as well as the experiences in the Chromosome 18 Clinical Research Center. However, every person with Tetrasomy 18p is different. Therefore, this information should not replace professional medical advice, diagnosis, or treatment. If you have questions or concerns, you may find it helpful to talk with a clinical geneticist or genetic counselor. You can locate a genetics provider at one of these sites:

[GeneTests Clinic Directory](#)

[National Society of Genetic Counselors](#)