# Cri du Chat Syndrome

*Information from the Cri du Chat Support Group of Australia*

## A Message for New Families

Children with Cri du Chat Syndrome can lead happy, fulfilling lives as valued members of their families and communities. Many aspects of the condition described below will worry new parents a great deal but they must remember that not every child has every one of these, many are minor problems which can be dealt with and you will overcome your initial shock and fear of the future as you find ways to help your child develop and learn.

As parents ourselves, our major concern is for other parents. We want them to know what we wished we had been told when our babies were born. Not knowing enough about this syndrome caused us to experience more pain and confusion than necessary. We were often angry and frustrated as we tried to find out how to help our children. We want to give you the information you need and offer all parents and carers the opportunity to share what they have learned about living with Cri du Chat Syndrome.

We understand that the knowledge of what might go wrong in the future can be very frightening and may make you want to hide from the reality but it can also prepare you in advance. We know that knowing what to expect helps you to anticipate and plan so that the future is not so scary. And best of all, knowing what is possible gives you goals to work towards and hope for the future. Knowledge can be frightening but it can also be empowering.

Your child is a unique individual with his or her own wonderful personality, gifts and shortcomings just like everyone else. He or she is not a syndrome! Regardless of how mild or severe your child's condition is, it will cause you a lot of grief, worry and sadness but at the same time **he or she** will bring you enormous joy and love. Whilst it can be very difficult to accept in the first days or months, yours and your family's lives can be enriched by the experience of raising a child with Cri du Chat Syndrome. We know this from our own experience.

## What is a Genetic Disorder?

Humans usually have 23 pairs of chromosomes in each cell of their body. These are named in pairs 1, 2, 3, 4, 5, 6 etc. A chromosome consists of smaller components called genes which contain instructions in a code made up of proteins. This code contains the plans or blueprint for each human being.

When something goes wrong with the chromosomes in the process of creating a new human being, the code cannot be read properly and the child's body and brain may not develop correctly. When a problem results from this genetic mistake it is called a genetic disorder. Cri du Chat Syndrome is a genetic disorder, it is not an illness or a disease. A child born with this disorder has specific physiological problems which result in their development being delayed both physically and intellectually. They may also have health problems because parts of their physiology have not developed correctly.

Remember, nothing the parents have done has caused this deletion to occur. It hasn't been shown to occur with higher frequency in any geographical location or in any cultural or racial group. There has never been a correlation demonstrated between the incidence of Cri du Chat Syndromeand any environmental factor such as radiation, pollution or medications. Except for the 10% or so where parents have a balanced translocation, the deletion which results in Cri du Chat syndrome is an accidental occurrence.

There are a number of genetic mishaps which can result in a child being born with Cri du Chat syndrome and all involve a missing or deleted part of the short arm of one of the pair of number five chromosomes. A chromosome has a narrow point called a centromere (see Diagram 1) separating the two segments or "arms" which are called the short and the long arms. The short arm is named p for the French word "petite" which means small, and the long arm is named q because the French word for tail is queue. Cri du Chat Syndrome is also called 5p- or 5p minus syndrome because part of the p arm is deleted.

It is called a **deletion** syndrome because part of the short arm is missing or deleted. That missing piece must contain a certain region of the short-arm for Cri du Chat syndrome to result. This critical region is known to be in the area (see Diagram 1) called band 15.2. The bands are distinct areas which show up as stripes when the chromosome is stained and viewed under a microscope.

**A variety of genetic arrangements can result in a child having Cri du Chat syndrome. These include:**

**Unbalanced Translocation**

A Translocation "occurs when a piece of one chromosome breaks off and attaches to another, different chromosome. When no material is lost or gained the translocation is said to be 'balanced' and the individual is not affected. An 'unbalanced' translocation results in the loss or gain of genetic material which may result in a genetic disorder." *(Fact Sheet from the Centre for Genetic Education in NSW. Australia - for more information on basic genetics look at their site http://www.genetics.com.au).* When a parent has a balanced translocation the child can be born with an unbalanced translocation. This happens in about 10% of cases of Cri du Chat syndrome. In a few cases the unbalanced translocation is spontaneous or de novo (new) in the child.

**Ring Chromosome**

In this rare situation the chromosome loses a piece from each end and the ends join to form a ring. In the child with Cri du Chat syndrome, this can result in additional problems depending on the amount of material lost from the long arm of the chromosome.

**Interstitial Deletion**

A section from within the short arm is deleted and the broken ends rejoin. The deleted section may be lost or attach itself to another chromosome.

**Inversion**

This occurs sometimes when a chromosome breaks at two points within the arm. The broken section flips or inverts before reattaching. It can result in a disorder because the code is reversed in that section.

**Duplication or Partial Trisomy**

A part of the short arm of the number five chromosome containing the critical region duplicates itself. This can be attached within the chromosome or at the tip. It also results in the code being misread.

**Mosaicism**

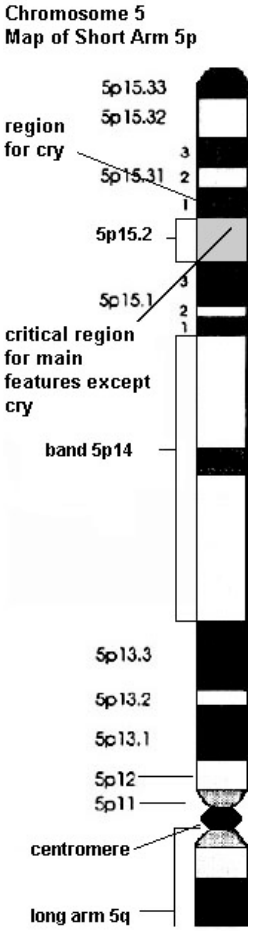
In a very few cases, the deleted chromosome is present in only some cells in the body.i.e. 20%, 50% or 75% etc. Children with this type of condition can be severely to very mildly affected depending on the percentage of cells with the deletion and which type of body cells are most involved. It is usually very difficult to diagnose since the cells containing the deletion can be hard to find and often missed in the process of taking blood or tissue samples. Children who are mosaic for Cri du Chat syndrome can be diagnosed with other conditions and syndromes by mistake. It is important that a correct diagnosis is made since it is possible for them to produce a child with Cri du Chat syndrome when they are adults if the deletion occurs in the cells of the reproductive organs.

## So What is Cri du Chat Syndrome?

- **Cri du Chat Syndrome** results from the loss or deletion of a significant portion of the genetic material from the short arm of one of the pair of number five chromosomes.
- **Cri Du Chat Syndrome** is also known as 5P Minus syndrome, Le Jeune's syndrome and Cat's-cry syndrome.
- It is a relatively rare genetic condition with an estimated incidence of between around 1:25000 to 1:50000 births. There are more children being diagnosed now that genetic testing is carried out more frequently and is more accurate. In addition, since records of this nature are not kept in most countries, the actual incidence is not known.
- The incidence appears to be the same in most countries, ethnic groups and regions. To date, there is no single environmental factor implicated in the incidence of this syndrome.
- It is thought that more girls than boys are born with the syndrome. The ratio is currently estimated to be 3 girls to 2 boys.
- Approximately 80% are caused by a spontaneous deletion in one of the child's number 5 chromosomes, 10-13% by an error in a number five chromosome in either parent and the remaining 7-10% result from rare genetic anomalies. Where there is an error in a parent's chromosomes, subsequent children or relatives may also be affected and it is therefore important that all parents of children with this syndrome receive genetic counselling.
- The critical region of the chromosome containing genes which are responsible for the main features of the syndrome appears to be located in band 5p15.2. (see Diagram 1 below)
- The gene causing the cry has been located in band 15.3. This would explain why some babies with other features of the syndrome do not have the characteristic cry and some babies have the cry but not the other characteristics.

- In most cases the deletion is spontaneous and no specific cause can be identified. The parents did nothing wrong to cause it to happen.
- It is possible to detect **Cri du Chat Syndrome** with amniocentesis or CVS (Chorionic Villus Sampling) in the first trimester of pregnancy. An ultrasound may lead the doctor to suspect a disorder of this type and carry out further investigations but it is not possible to diagnose it solely by this means. *(See the Fact Sheet from the Genetic Education Program of NSW. Australia - for more information on Prenatal Testing look at their site New South Wales Centre for Genetic Education Go to http://www.genetics.com.au for Genetic Fact Sheets and look at the index under **Genetic Testing, Screening and Prevention**.)*
- At present it is not possible to predict how severely affected the baby will be.
- There is no treatment for major genetic anomalies however there is therapy to help the child achieve his or her developmental potential.

## Diagram 1: Chromosome 5 - Map of the Short Arm 5p




## Characteristics of the Syndrome

The most distinctive characteristic, and the one for which the syndrome was originally named in 1963 by geneticist Jerome Lejeune, is the distinctive high-pitched, monotone, cat-like cry. "Cri du Chat" is French for "cat's cry". The cry is thought to be the result of structural abnormality and low muscle tone. Although the voice will naturally lower as the child grows, the characteristic high pitch often persists into adulthood.

In addition to the cry, there are a number of distinguishing characteristics present in infancy which aid in recognition of the syndrome. Not every child will have every feature. Those only mildly affected may have very few or they may be less obvious.

The size and location of the deletion appears to have some correlation with the severity of effect of the syndrome on the child. At present however, there is no way to determine with any accuracy how severely a particular child will be affected. All we can say at present is that those with very large deletions tend to be more severely affected and those with very small ones in and above band 15.2 tend to be more mildly affected. In general, babies with an unbalanced translocation are likely to be more severely affected.

Babies are often of low birth weight and many require help with feeding in infancy. Feeding difficulties often persist for the first few years with many experiencing reflux and swallowing problems.

**Major identifying characteristics**

- Monotone, weak, cat-like cry
- Small head (microcephally)
- High palate
- Round face
- Small receding chin (micrognathia)
- Widely spaced eyes (hypertelorism)
- Low set ears
- Low broad nasal ridge
- Folds of skin over the upper eyelid (epicanthic folds)
- Distinctive palmar creases (creases on the palms of the hands)

Some of the features change as the child ages. The cry may become less distinctive and the voice lower whilst still retaining its characteristic tone and pitch. Males usually undergo the same voice changes as other males in adolescence but most females with the syndrome retain the higher pitched, monotone voice throughout life. In adolescence the face becomes more elongated, the nasal bridge high and the epicanthic folds less distinct. The head remains smaller than normal throughout life becoming more evident in the first years, however, it is not particularly noticeable to the layperson.

**Problems reported in those with Cri du Chat Syndrome**

**Medical problems found in a minority of children**

- Heart defects (commonly Ventral Septal Defects and Atrial Septal Defects and rarely tetralogy of Fallot and endocardial cushion defects)
- Cleft Palate occurs but is rare
- Kidney abnormalities are also rare
- Minor skeletal problems including hip dislocation and deformities of the feet
- Scoliosis develops in some children
- Hernias (inguinal and abdominal) are sometimes present at birth
- Bowel abnormalities
- Epilepsy is not common
- Swallowing and sucking problems are often present in the newborn and swallowing problems may persist
- Problems with intubation for anaesthesia have been reported in a small number of cases due to malformations of the larynx and epiglottis

**Additional problems which may be noticed as the child gets older**

- Minor hearing impairments. Hearing impairment is occasionally severe and requires hearing aids.
- Strabismus or turned eye is fairly common and should be attended to as most do not grow out of it and it does affect vision. Treatment may help.
- Other visual problems.
- Low muscle tone (hypotonia) is common in infancy and may change to high muscle tone (hypertonia) later in life. Physiotherapy is an important aspect of intervention.
- Difficulty with sucking and swallowing (dysphagia). Sucking may be very weak and the child may gag and cough when swallowing. Swallowing should be investigated since aspiration pneumonia may occur and treatment is possible.
- Gastrointestinal abnormalities are present in some babies.
- Gastric reflux is common in infancy and usually requires treatment.
- Chronic constipation is common. It often starts in the first year or two and usually persists throughout life. It

is can be well-managed in most cases.

- Frequent ear infections - many children with Cri du Chat syndrome have ear infections often requiring grommets in childhood.
- Saliva control problems (drooling). In severe cases that have not resolved when the child is older, surgery is available to help correct this.
- Sexual development is usually normal and female fertility is possible since some instances of pregnancy have been reported.
- Dental problems are common.
- Feeding problems. Often not interested in eating.
- Failure to thrive. Due to illness, refusal to eat or drink or severe reflux.

**Problems reported by parents that have not been reported as a feature of the syndrome**

- Sudden, transient, high temperatures without obvious infection or illness. These should be reported to your doctor for further investigation.
- Apnoea (breathing stops occasionally, usually during sleep). This may not be related to the syndrome but is occasionally reported to us by parents. If this condition exists it must be monitored as it can lead to other problems with health and behaviour.
- Frequent upper respiratory infections. The increased rate of infection has not yet been identified as the result of a specific immune abnormality in this syndrome. Babies and children may develop pneumonia either from infection or from aspiration of food or liquids. Tests are available to determine if swallowing is likely to be causing infection or pneumonia.
- Sleep disorders. Early intervention and management is important to prevent long term difficulties. Behaviour problems can be exaggerated in children who are getting insufficient sleep.
- Sensory defensiveness including one or more of the following:
  Sensitivity to sound - often only particular frequencies.
  Tactile defensiveness.
  Sensitivity to touch on parts of the body usually the hands, feet, head and face.
  Oral defensiveness (also called oral aversion or oral tactile sensitivity).

For good information on health and behaviour issues in Cri du Chat Syndrome please see the UK support group website http://www.criduchat.co.uk/index.html

Life expectancy cannot be predicted and although a few children with serious health problems may have a reduced life-span, it is thought that most live well into adulthood. The oldest person reported to us to date was in her sixties.

In the past, doctors believed this syndrome resulted in severe to profound disability in all cases, however, early researchers like Professor Erik Niebuhr of Denmark, discovered that this is an extremely variable syndrome. The level of disability can range from very mild developmental delay to profound physical and intellectual disability. Most cases at present appear to fall into the moderate to severe range but even this is uncertain since more mild cases are being diagnosed.

The development of more sophisticated genetic testing technology has uncovered an increasing number of children who are only mildly affected but are only now being diagnosed. They have fewer of the features or problems usually associated with Cri du Chat Syndrome and those features are usually less obvious. They also have greater developmental potential than was previously thought possible for children with this syndrome.

## Development

The effects of this syndrome on the child are extremely variable but almost all children with this syndrome have a degree of intellectual disability, delayed speech and language acquisition and slow development of motor skills. Although problematic behaviours are not uncommon, they are usually bright, loving and sociable children with a great sense of humour who occupy a valued position within their families and communities.

**Major developmental issues in Cri du Chat syndrome**

- Intellectual disability ranging from mild to profound with the majority being moderate to severe
- Speech and language impairment varying from mild to profound. Research has shown children with Cri du Chat Syndrome have better receptive than expressive language which means they can understand more complex language than you would expect based on their ability to speak. A small number do not speak at all but all can communicate with one or a combination of methods. Early consultation with a speech pathologist is

important as is the early introduction of alternate means of communication.

- Low muscle tone and delayed motor development. The majority walk, most between 2 and 6 years of age. Physiotherapy is an important part of early intervention.
- Short attention span (almost 100%).
- Hyperactivity (approximately 25%)
- Challenging behaviours including obsessive, repetitive and sometimes self-harming behaviours such as head-banging and hitting, biting or scratching self.

No one can determine at birth how much a child will be affected by this syndrome and the best course of action for carers is to do as much as they can to maximize the child's developmental potential and provide him or her with as many opportunities to live as normal a life as possible.

## Treatment

Gene therapy is in its infancy and no techniques have yet been developed to treat these types of large chromosomal abnormalities. Although it is possible that some of the effects of this genetic deletion may eventually be treated by this method, it is unlikely in the near future.

Most of the medical problems can be treated successfully with current medical treatments. Early intervention programs, using a variety of therapies and educational strategies, focus on enhancing physical, intellectual, sensory and social development and have been shown to greatly improve the future outlook for the child.

**Early Intervention programs should include:**

Physiotherapy

Speech Therapy

Occupational Therapy

Behavioural management (if necessary)

Since most children with the syndrome experience severe speech development problems, speech and language therapy are vital. The early introduction of alternative means of communication, including a sign language such as Makaton along with a pictorial symbol system, will enhance the child's speech development, language acquisition and behaviour. Children with Cri du Chat Syndrome are usually keen to communicate and many will develop their own signs and gestures to get what they want often preferring these to the more difficult formal signs. Children who cannot communicate effectively experience a great deal of frustration and behaviour problems can develop as a result.

Improving a child's ability to communicate by any means not only helps them to make their needs known, but also helps them to develop intellectually and socially, improving the quality of their lives immeasurably.

Older children and adults who have not acquired adequate speech may benefit from using a communication device.

The level of independence a particular child achieves depends on their own inborn potential combined with the skill of those training them. Those most severely affected require full-time care throughout their lives. Most people with Cri du Chat Syndrome are capable of achieving a degree of independent self-care but require supervision and care for life. Some of those least affected by the syndrome are be able to live independently (or with minimal assistance) in the community.

## Education

Children with Cri du Chat Syndrome in Australia attend both mainstream and special schools and pre-schools. Although full inclusion should be the goal for all children with disabilities, decisions regarding placement in either a special or mainstream educational setting must take into account the most appropriate setting for the individual child, the education policy of the local government, available support and the wishes of the family.

Most children with Cri du Chat syndrome in a mainstream setting will require a teacher's aide to assist them although a few are able to manage with minimal assistance.

## Research

Research in the past has been concentrated in the area of medical genetics with very limited investigation of the developmental and behavioural aspects of the syndrome.

Current genetic research into Cri du Chat Syndrome is aimed at locating and identifying the critical genes responsible for the various features of the syndrome. The gene locations for the cry and the other features were found to be on separate bands of the chromosome. (see Diagram 1 above)

Researchers in the field of behaviour are still working to assess and describe the different aspects of development and behaviour which characterise this syndrome. The long-term goal is to more accurately target the various available interventions and therapies so that our children can live up to their potential and lead happier, more fulfilling lives.

Developmental researchers have been collaborating with genetic researchers for a number of years in an attempt to define how the varying genetic combinations (genotype) occurring in this syndrome affect the development and features a particular individual displays (phenotype). This collaboration assists the geneticist to track down the location of particular genes and identify their activity. In the future it is hoped that it will help developmental specialists to predict how severely a particular child's development will be affected. This is not possible with our current level of knowledge.

**Prominent English-speaking researchers in the field include:**

Professor Erik Niebuhr Medical Genetics Denmark
Dr. Kim Cornish Child development & genetic disorders Originally UK. Now in Canada.
Dr. Joan Overhauser Medical genetics USA
Professor Chris Oliver UK

There are many others not named who collaborate with these researchers or work independently and many in non-English-speaking countries such as Prof. Mainardi in Italy, Prof. Kristoffersen in Norway and others in Spain, China, Japan etc.

## Links to information for Medical Practitioners

**ORPHA.NET DATABASE: LISTING FOR CRI DU CHAT SYNDROME**

http://www.orpha.net/data/patho/GB/uk-criduchat.pdf

This document contains a very good overview of the syndrome written by Prof. Paola Cerruti Mainardi, an Italian scientist who has a research interest in Cri du Chat Syndrome.

## More information

The information for this page is based on the published results of the work of Prof. Erik Niebuhr (Denmark), Dr. Kim Cornish (UK), Dr. Joan Overhauser (USA), Dr. Mary Esther Carlin (USA, Margaret Collins (Ireland), Prof. Paola Mainardi (Italy), Dr Elisabeth Dykens and Dr. Richard Hoddap along with the reports of many tens of parents of children with Cri du Chat Syndrome we have spoken to and communicated with over the past 14 years. It is by no means all there is to say about this syndrome which is still relatively poorly researched in comparison with many of the better known and more common genetic syndromes.

For more information look at the published results of the research of these scientists, the handbooks published in the UK and the USA and contact your local support group (listed on our links page) for more personal contact with someone who has lived with the syndrome.