CROUZON SYNDROME

Crouzon syndrome is a genetic condition characterized by craniosynostosis (premature fusion of skull bones), which affects the shape of the head and face.

Otherwise known as?

Craniofacial dysostosis

Signs & Symptoms

The severity of symptoms varies among individuals.

1. Craniofacial differences

- Craniosynostosis: Premature skull fusion leading to:
  - a short, wide, or tall skull (brachycephaly).
  - a bulging forehead (frontal bossing).
- Shallow Eye Sockets (ocular proptosis):
  - bulging or protruding eyes.
  - eyes may appear widely spaced (hypertelorism).
- Midface Hypoplasia:
  - underdeveloped upper jaw (maxilla), giving a flat midface appearance.
  - possible breathing and feeding difficulties.
- Beaked Nose: A nose with a narrow and pointed appearance.
- Dental Problems:
  - Crowded, misaligned, or missing teeth.
  - High-arched or cleft palate in some cases.

2. Vision Problems

- Strabismus (Crossed or Misaligned Eyes).
- Exposure Keratitis (damage to the cornea due to bulging eyes).
- Optic Nerve Compression (can lead to vision loss in severe cases).

3. Hearing and Ear Issues

- Frequent ear infections due to structural anomalies in the ear.
- Possible hearing loss (conductive or sensorineural).

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Craniofacial Australia
204 Melbourne Street
North Adelaide
South Australia, 5006

W: craniofacial.com.au
E: familysupport@acmff.org.au
P: (08) 8267 4128

4. Neurological Symptoms

- Increased Intracranial Pressure (ICP): Due to fusion of the bones in the skull restricting brain growth. Symptoms may include:
  - Headaches
  - Vomiting
  - Irritability
- Hydrocephalus (in some cases): Excess cerebrospinal fluid build-up in the brain.

5. Intellectual Development

- Normal Intelligence: Most individuals have typical cognitive development.
- Learning Difficulties (occasionally): If complications like increased intracranial pressure or hydrocephalus occur.

Mechanism (*the how*)

A baby's skull is made of several plates joined by flexible seams called sutures, and deeper growth plates in the skull base.

In Crouzon, a growth-signal pathway (controlled by genes FGFR2/FGFR3) is over-active.

This over-signalling makes bone-forming cells around some sutures mature and lock too early, so those seams turn into solid bone sooner than they should. Once a suture closes, growth in that direction stops and growth is redirected to areas that remain open.

The same over-signalling also alters how the skull base growth plates develop, changing the forward growth pattern of the face.

These changes begin early in foetal development and then shape skull and facial growth over time.

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Causes (*the why*)

Crouzon syndrome is a genetic condition caused by mutations in the FGFR2 (fibroblast growth factor receptor 2) gene and, in rare cases, the FGFR3 gene. These genes play a role in bone growth and development during foetal development.

1. Genetic Mutation

- The FGFR2 mutation causes the early fusion of skull bones (craniosynostosis), leading to the characteristic facial and skull differences of Crouzon syndrome.
- In rare cases, FGFR3 mutations may also be involved, sometimes leading to a variant form called 'Crouzon syndrome with acanthosis nigricans' (which includes dark, velvety patches on the skin, usually in areas like the neck and armpits).
- Inherited (autosomal dominant):
  - A child has a 50% chance of inheriting the condition if one parent has Crouzon syndrome.
- Spontaneous (De Novo) Mutation:
  - In about 50% of cases, the mutation occurs randomly in a baby with no family history of the condition.

Crouzon syndrome is not caused by environmental factors or anything a mother does during pregnancy. It is purely genetic.

Testing & Diagnosis

Crouzon syndrome is typically diagnosed through a combination of physical examination, genetic testing, and imaging studies. Early diagnosis allows for better management and treatment of symptoms.

1. Physical examination

- Clinical evaluation is usually the first step. A doctor will examine the child's features for characteristic signs, such as:
  - Craniosynostosis: Premature fusion of skull bones leading to a difference in head shape.
  - Protruding eyes (ocular proptosis) due to shallow eye sockets.
  - Midface hypoplasia (underdeveloped upper jaw, leading to a flat face).
  - Beaked nose and other facial differences.
  - Dental problems, including misaligned or crowded teeth.

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2. Genetic Testing

- FGFR2 gene mutation testing can confirm the diagnosis.
  - This test involves analysing a blood sample to detect mutations in the FGFR2 gene, which is the most common cause of Crouzon syndrome.
  - In some cases, mutations in the FGFR3 gene may also be involved.
  - Genetic counselling may be recommended to discuss inheritance risks and recurrence in future pregnancies.

3. Imaging Studies

- X-rays or CT Scans of the skull are used to:
  - Assess the fusion of skull bones (craniosynostosis).
  - Identify any differences in the shape of the skull and face.
  - Determine the extent of brain involvement, such as hydrocephalus or increased intracranial pressure.
- MRI (Magnetic Resonance Imaging) may be used to:
  - Examine the brain for any associated conditions like hydrocephalus or brain compression.
  - Evaluate optic nerve function to assess potential vision problems or nerve damage.

4. Additional Tests

- Hearing and vision tests may be conducted to identify issues such as hearing loss or vision problems due to craniofacial differences.
- Cognitive and developmental assessments might be performed if there are concerns about learning or developmental delays, although intelligence is typically normal in most individuals with Crouzon syndrome.

Treatment

Crouzon syndrome requires a multidisciplinary approach to address the various aspects of the condition, particularly craniofacial differences, hearing, vision, and developmental concerns. Treatment involves a combination of surgical procedures, therapies, and long-term monitoring.

1. Surgical Treatments

Surgical intervention is often required to address the craniofacial differences associated with Crouzon syndrome and improve both function and appearance.

a. Cranial Surgery

- Craniosynostosis Repair:
  - Surgery is typically performed in infancy or early childhood (around 6-12 months of age) to address skull shape and allow normal brain growth.

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- Cranial vault remodelling is the most common procedure, where surgeons remove fused bone and reshape the skull.
- Multiple surgeries may be needed as the child grows, especially if the fusion of skull bones affects brain development or pressure.

b. Facial Surgery

- Midface Advancement Surgery:
  - Performed around 3-5 years of age to address the underdeveloped midface (upper jaw), improving facial appearance and allowing for better function in terms of breathing and speech.
  - This procedure involves advancing the upper jaw and repositioning bones in the face.
- Nose Surgery (Rhinoplasty):
  - A beaked nose can be addressed through surgical procedures as the child grows, addressing appearance and improving function.

c. Orthognathic Surgery

- If jaw misalignment persists, jaw surgery may be done in the teenage years to address bite and improve facial balance.

2. Hearing and Vision Care

Because Crouzon syndrome can lead to hearing loss and vision problems due to facial differences, ongoing care is important.

- Ear Tubes (Tympanostomy Tubes):
  - To prevent ear infections and reduce the risk of hearing loss, ear tubes may be placed early in life.
  - Regular hearing tests are needed to monitor any potential hearing issues.
- Eye Care:
  - Early intervention with an ophthalmologist to address any vision issues caused by bulging eyes or optic nerve compression.
  - Surgery may be needed in some cases to relieve pressure on the optic nerve.

3. Speech and Language Therapy

- Children with Crouzon syndrome may have speech delays or difficulties due to the structure of their face and mouth.
- Speech therapy can help improve speech clarity and communication.
- Feeding therapy may also be required in infants who have trouble feeding due to facial differences.

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4. Dental and Orthodontic Care

- Children with Crouzon syndrome often experience dental issues such as misaligned teeth, overcrowding, or a high-arched palate.
- Early orthodontic treatment is essential to ensure proper alignment of teeth and jaw structure.
- Bone grafting may be performed to fill gaps in the upper jaw and support tooth development.
- Regular dental check-ups will be required as the child grows.

5. Long-Term Monitoring and Support

- Neurological Evaluation: Children should have regular neurological assessments to monitor for conditions like increased intracranial pressure or hydrocephalus.
- Psychological and Developmental Support:
  - Children with Crouzon syndrome may benefit from psychological counselling and developmental support to help with emotional well-being and learning difficulties.
  - Special education services can also assist children with developmental delays.

Did you know?

In Australia, approximately 2 babies in 100,000 births are diagnosed with Crouzon syndrome.*

Crouzon syndrome was the first identified genetic syndrome linked to craniosynostosis and was originally described in both a mother and daughter by a French physician, Octave Crouzon, in 1912.

References:

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How we can support you:

- Care packs
- Financial assistance
- Family support coordinator
- Connection to other families