CARPENTER SYNDROME

Otherwise known as?

Carpenter syndrome is also known by the following names:

1. Acrocephalopolysyndactyly type II (ACPS II)
2. Craniofacial syndrome
3. Craniofacial dysostosis, type II
4. Craniosynostosis with polydactyly

These names reflect the key features of the condition, which include craniosynostosis (premature fusion of skull sutures) and polydactyly (extra fingers or toes), among other physical differences.

Signs & Symptoms

Carpenter syndrome is a rare genetic disorder that primarily affects craniofacial development and can lead to a variety of physical differences.
The signs and symptoms of Carpenter syndrome may vary from person to person but typically include the following:

1. Craniofacial Differences

- Craniosynostosis: premature fusion of the skull sutures, leading to differences in head shape. This can result in a bulging forehead, flattened skull, and underdeveloped facial features.
- Broad, low-set ears: ears may appear large and positioned lower than usual.
- Flattened facial features: the face may be flat, with a wide, prominent nose and underdeveloped midface (hypoplasia).
- Beaked nose: the nose may have a characteristic "beak" shape due to the flattening of the nasal bridge.
- Strabismus (crossed eyes): differences in eye alignment can lead to vision problems.
- Cleft palate: a gap or opening in the roof of the mouth that can cause feeding and speech difficulties.

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2. Limb Differences

- Polydactyly: extra fingers or toes, which may be fully developed or partially fused. This is one of the characteristic features of Carpenter syndrome.
- Syndactyly: fusion of two or more fingers or toes, which can occur alongside polydactyly.
- Shortened limbs: limbs may be shorter than average due to bone differences.

3. Intellectual and Developmental Delays

- Developmental delays: individuals with Carpenter syndrome may experience delays in motor skills, speech development, and cognitive abilities.
- Learning difficulties: some individuals may have intellectual disabilities or learning difficulties, although this can vary widely from person to person.

4. Other Possible Characteristics

- Heart problems: some individuals with Carpenter syndrome may have congenital heart defects, such as ventricular septal defects (VSD), which are holes in the heart's walls.
- Obesity: people with Carpenter syndrome may be prone to obesity due to metabolic or hormonal imbalances.
- Hearing loss: due to craniofacial differences and possible ear problems, individuals may experience some degree of hearing loss.

5. Other Rare Features

- Genital differences: in some cases, there may be differences in the genitalia, including ambiguous genitalia (where male and female genital characteristics may not be clearly differentiated).
- Clubfoot: the foot is twisted out of shape or position.
- Hydrocephalus: the accumulation of excess fluid in the brain, which can lead to increased pressure and potential neurological problems.

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CARPENTER SYNDROME

Causes

Carpenter syndrome is a genetic condition caused by mutations in certain genes that affect skull, limb, and facial development. The primary causes include:

1. Gene Mutations

- RAB23 gene (most common cause)
- MEGF8 gene (less common)

These genes are involved in cell signalling and development, particularly in the formation of bones and tissues. Mutations in these genes disrupt normal skeletal and facial growth, leading to the characteristic features of Carpenter syndrome.

2. Inheritance Pattern

- Carpenter syndrome follows an autosomal recessive inheritance pattern.
- This means a child must inherit two mutated copies of the gene (one from each parent) to develop the syndrome.
- If both parents are carriers (each having one mutated gene but no symptoms), there is a 25% chance with each pregnancy that their child will have Carpenter syndrome.

Since Carpenter syndrome is genetic, it cannot be prevented, but genetic counselling can help families understand their risks.

Testing & Diagnosis

Testing and diagnosis of Carpenter syndrome typically involve a combination of physical examination, genetic testing, and imaging studies to confirm the presence of characteristic features and identify associated differences. The condition is diagnosed based on clinical symptoms and genetic confirmation, as it is caused by mutations in the RAB23 gene.

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CARPENTER SYNDROME

1. Physical Examination

A thorough physical examination is often the first step in diagnosing Carpenter syndrome. The doctor will evaluate the child’s physical features, focusing on key signs of the condition such as:

- Craniofacial Differences (e.g., craniosynostosis, flattened facial features, beaked nose, broad low-set ears).
- Limb Differences (e.g., polydactyly, syndactyly, shortened limbs).
- Developmental and cognitive delays: signs of developmental or intellectual delay

2. Genetic Testing

Genetic testing is the definitive method for diagnosing Carpenter syndrome. The condition is caused by mutations in the RAB23 gene, located on chromosome 6. This gene plays a role in regulating the development of the cranial and limb structures during foetal development. Testing typically involves:

- DNA testing: A blood or saliva sample is taken to analyse the DNA and look for mutations in the RAB23 gene.
- Genetic counselling: It is often recommended for families to understand the inheritance pattern of the condition (autosomal recessive) and the risks for future pregnancies.

3. Imaging Studies

Imaging studies help evaluate the extent of craniofacial differences and detect any associated features that may not be obvious on physical examination.

- X-rays: These may be used to assess craniosynostosis and limb Differences, such as polydactyly and syndactyly. X-rays may also help assess other skeletal Differences.
- CT scan (Computed Tomography): A CT scan of the head may be performed to further evaluate craniosynostosis and other skull differences. It provides detailed images of the bones and cranial sutures.
- MRI (Magnetic Resonance Imaging): An MRI can be used to assess the brain and detect any neurological issues, including hydrocephalus or any other structural differences.
- Echocardiogram: If heart defects are suspected (such as ventricular septal defects), an echocardiogram may be performed to assess heart structure and function.

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4. Additional Evaluations

- Hearing tests: If hearing loss is suspected due to craniofacial differences or other symptoms, audiological evaluations can assess the degree of hearing loss.
- Developmental assessments: If developmental delays or intellectual disabilities are suspected, a neurodevelopmental assessment may be conducted to evaluate motor skills, speech, and cognitive development.

Differential Diagnosis

Carpenter syndrome shares some features with other craniofacial syndromes, such as Crouzon syndrome, Apert syndrome, and Saethre-Chotzen syndrome. Genetic testing is essential to differentiate between these conditions, as the treatments and prognoses may vary.

Once diagnosed, a multidisciplinary approach is often used to manage symptoms and improve the quality of life for those affected by Carpenter syndrome. Treatment may involve surgeries to address craniosynostosis, limb or other differences, as well as therapies for developmental support.

Treatment

The treatment for Carpenter syndrome often involves multiple surgical interventions to address skull, hand, foot, and other differences. The exact procedures depend on the severity of symptoms but typically include the following:

1. Craniosynostosis Surgery (Cranial Vault Remodelling - i.e., surgery to reshape the skull)

- Purpose: To address premature skull bone fusion and allow brain growth.
- Procedure:
  - Surgeons remove and reshape fused skull bones.
  - Expand the skull to create more space for the brain.
  - Sometimes, distractors (devices that slowly move bones apart) are placed to help with skull expansion over time.
- Timing: Usually performed within the first year of life to prevent pressure on the brain and allow for normal head shape development.

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2. Hand and Foot Surgeries

- Syndactyly Release (Separation of fused fingers/toes)
  - To improve hand function and mobility.
- Addressing Polydactyly (Removal of extra fingers/toes)
  - If extra digits cause difficulty with movement or wearing shoes.

3. Facial and Jaw Surgery

- Mandibular (Jaw) Surgery
  - If the lower jaw is underdeveloped (micrognathia), surgery can help improve breathing, chewing, and speech.
- Midface Advancement
  - If needed, to address facial differences and improve airway function.

4. Heart Surgery (If Needed)

- Some individuals with Carpenter syndrome may have congenital heart defects that require surgery.

5. Other Potential Surgeries

- Ear, Nose, and Throat (ENT) Procedures
  - To improve breathing and hearing (e.g., if there is airway obstruction or recurrent ear infections).
- Soft Tissue Surgery
  - To address skin or muscle Differences related to the syndrome.

Since Carpenter syndrome affects multiple parts of the body, treatment usually requires a team of specialists, including craniofacial surgeons, orthopaedic surgeons, neurosurgeons, and geneticists.

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What next?

We are here to help. Explore support services on our website by scanning the QR code below. You can also explore more information on our online Resource Hub.

Did you know?

Although Carpenter described this condition in 1901, it was not firmly established as an entity until 1966.

Carpenter Syndrome is part of a group of conditions called acrocephalopolysyndactyly syndromes (ACPS), which also includes other rare disorders like Apert and Pfeiffer syndromes.

In Australia approximately 1 baby in 1,000,000 births is diagnosed with Carpenter syndrome.

References:

White J, Boldt DB, David DJ, Sheffield L, Simpson DA. (1981) Carpenter syndrome with normal intelligence and precocious growth. Acta Neurochirurgica, 57(1-2):43-9. https://doi.org/10.1007/BF01665112

*Junaid, M., Slack-Smith, L., Wong, K., Bourke, J., Baynam, G., Calache, H., & Leonard, H. (2022). Epidemiology of Rare Craniofacial Anomalies: Retrospective Western Australian Population Data Linkage Study. The Journal of Pediatrics, 241, 162-172.e169 https://doi.org/10.1016/j.jpeds.2021.09.060

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How we can support you:

- Care packs
- Financial assistance
- Family support coordinator
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