TREACHER COLLINS SYNDROME

Otherwise known as?

Treacher Collins syndrome is known by a few other names:

1. Treacher Collins-Franceschetti Syndrome – Sometimes used to acknowledge the contributions of Dr Franceschetti, who helped describe the syndrome alongside Dr Treacher Collins.
2. Mandibulofacial Dysostosis – This term refers to the characteristic facial differences seen in the syndrome, which include underdeveloped bones of the mandible (jaw) and facial bones.
3. TCS – An abbreviated form of Treacher Collins syndrome.

These names are used less frequently, with Treacher Collins syndrome being the most common and accepted term.

Signs & Symptoms

Treacher Collins syndrome is a genetic condition that primarily affects the development of the bones and tissues of the face. The severity of symptoms can vary greatly from person to person, ranging from mild to more severe manifestations.

1. Facial differences

Facial differences are the most prominent characteristic of Treacher Collins syndrome and may include:

- Underdeveloped cheekbones (malar hypoplasia), which give the face a sunken appearance.
- Small jaw and chin (micrognathia), which can make the chin appear recessed.
- Malformed or absent ears: This can include:
  - Microtia (small or absent external ears).
  - Atresia (absence of the ear canal), leading to hearing loss.
  - Malformed ear structures, causing cosmetic and hearing difficulties.
- Downward-slanting eyes: The eyes may appear tilted downward, which is characteristic of the condition.
- Cleft palate: Some individuals may have a cleft palate, which is a gap in the roof of the mouth.

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- Sparse eyelashes or absence of eyelashes in some individuals.
- A wide mouth
- Hair growth extending from the sideburn area onto both upper cheeks.

2. Hearing Loss

- Conductive hearing loss is common in Treacher Collins syndrome due to differences in the middle ear (especially the ossicles – the tiny bones in the ear that help transmit sound).
- Ear malformations and absence of ear canals can also contribute to hearing impairment.
- In some cases, hearing loss may be severe and may require hearing aids or, in extreme cases, surgical interventions like a cochlear implant.

3. Breathing Problems

- Due to the underdevelopment of the jaw and airway, individuals may experience difficulty breathing, especially in infancy, as the airway may be too narrow.
- Sleep apnoea can also be a concern, where breathing stops and starts during sleep.

4. Dental Issues

- Malocclusion: Misalignment of the teeth, often resulting in difficulty with chewing or speaking.
- Teeth problems: Missing teeth or irregular tooth development can be common in individuals with Treacher Collins syndrome.

5. Hearing and Speech Difficulties

- Due to the combination of hearing loss and craniofacial differences, children with Treacher Collins syndrome may experience delays in speech development or articulation issues.
- Speech therapy is often recommended to help individuals develop effective communication skills.

6. Skin differences

- In some cases, individuals may have skin tags or extra skin near the ears or on the face, particularly in the area around the ears.

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7. Cognitive Ability

- Intelligence in individuals with Treacher Collins syndrome is usually normal, and most individuals have no significant cognitive impairments.
- Learning difficulties may occur, but these are typically due to other factors (e.g., hearing loss or speech delays) rather than being directly associated with intelligence.

8. Other Possible Symptoms

- Hearing loss may affect one or both ears, and the degree can vary.
- Problems with speech may arise due to hearing loss and jaw malformations, but these can often be addressed with speech therapy.
- Some people may experience vision problems (due to differences in the eyelids or eye development), although these are less common.

Causes

Treacher Collins syndrome is caused by genetic mutations that affect the development of the facial bones and tissues. The condition is most commonly associated with mutations in the TCOF1 gene, though mutations in POLR1C and POLR1D genes can also cause the syndrome.

1. Genetic Mutations

- TCOF1 Gene: The most common cause of Treacher Collins syndrome is a mutation in the TCOF1 gene, located on chromosome 5. The TCOF1 gene provides instructions for making a protein called treacle, which is involved in the development of facial structures during early embryonic development.
    - Impact of Mutation: Mutations in the TCOF1 gene lead to a reduction in treacle protein levels, which impairs the development of certain facial bones and tissues, especially those that form the jaw, cheeks, ears, and palate. This causes the characteristic features of the syndrome, including underdeveloped facial bones.
    - Inheritance Pattern: Treacher Collins syndrome is typically inherited in an autosomal dominant manner, meaning one copy of the altered gene in each cell is sufficient to cause the condition. However, 50% of cases are due to new (de novo) mutations, meaning the mutation occurs for the first time in the affected individual and is not inherited from their parents.

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- POLR1C and POLR1D Genes: In rare cases, mutations in the POLR1C and POLR1D genes, which are involved in the formation of RNA, have also been found to cause Treacher Collins syndrome. These mutations may lead to impaired RNA processing and affect craniofacial development.

2. Inheritance

- Autosomal Dominant Inheritance: The majority of individuals with Treacher Collins syndrome inherit the condition in an autosomal dominant pattern. This means that an affected individual has a 50% chance of passing the mutation on to each of their children.
- De Novo Mutations: In some cases, Treacher Collins syndrome occurs as a de novo mutation, meaning the mutation happens for the first time in the affected individual and is not inherited from the parents. This can happen if there is a mutation in the TCOF1 gene during the early stages of embryonic development.
- Affected Parents: In families where one parent has Treacher Collins syndrome, there is a 50% chance that any given child will inherit the condition, regardless of gender.

3. Pathophysiology

- Craniofacial Development: Treacher Collins syndrome primarily affects the development of structures derived from the first and second branchial arches (embryonic structures that contribute to the development of the face and neck). These include:
  - Maxilla (upper jaw)
  - Mandible (lower jaw)
  - Zygomatic bones (cheekbones)
  - External ear structures
- Disrupted Cell Growth and Development: The mutations in the TCOF1 gene lead to impaired growth and development of these facial structures. As a result, affected individuals may have underdeveloped facial bones, particularly the cheekbones, jaw, and ears, as well as cleft palate or other craniofacial differences.

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Testing & Diagnosis

Testing and diagnosis of Treacher Collins syndrome generally involve a combination of clinical evaluation, genetic testing, and imaging studies to confirm the presence of characteristic features and mutations.

1. Clinical Diagnosis

The first step in diagnosing Treacher Collins syndrome usually involves a thorough physical examination. A doctor will assess the facial features, hearing, and other related symptoms, such as:

- Underdeveloped cheekbones (malar hypoplasia).
- Small jaw and chin (micrognathia).
- Malformed or absent ears (microtia, atresia).
- Downward-slanting eyes.
- Cleft palate or other palate differences.
- Hearing loss (conductive due to ear malformations).
- Speech or feeding difficulties.

If these signs are present and consistent with Treacher Collins syndrome, the diagnosis may be strongly suspected.

2. Genetic Testing

Genetic Testing is the definitive method to confirm the diagnosis of Treacher Collins syndrome.

- The most common cause of TCS is a mutation in the TCOF1 gene, located on chromosome 5. Genetic testing can identify mutations in the TCOF1 gene in approximately 60-70% of individuals with TCS.
- In rare cases, mutations in the POLR1C and POLR1D genes can also cause the syndrome, and genetic testing for these mutations can be performed if necessary.

Genetic testing methods include:

- DNA sequencing: This is used to identify specific mutations in the TCOF1, POLR1C, or POLR1D genes.
- Chromosomal microarray analysis: This technique can detect large deletions or duplications in the genome that may cause the syndrome.
- Exome sequencing: This tests the parts of the genome that are actively involved in making proteins and can help identify rare mutations that cause the condition.

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3. Family History and Inheritance Pattern

Family history can be important for diagnosing Treacher Collins syndrome. If a family member has been diagnosed with Treacher Collins syndrome, genetic testing may be recommended to determine if the condition is inherited in an autosomal dominant pattern.

In cases where Treacher Collins syndrome is caused by a de novo mutation (not inherited from either parent), there may be no family history of the condition, making genetic testing even more crucial.

4. Imaging Studies

Imaging techniques like CT scans (computed tomography) or X-rays can be used to evaluate the craniofacial differences characteristic of Treacher Collins syndrome, such as:

- Bony differences in the maxilla (upper jaw), mandible (lower jaw), and zygoma (cheekbones).
- Cleft palate or other facial structural differences.
- Middle ear differences, which can contribute to hearing loss.
- In mild cases, one of the key signs on X-rays or scans may be a groove, notch, or small gap in the cheekbone arch.

These imaging studies are particularly useful in planning surgical interventions to address appearance and functioning, such as ear reconstruction or jaw surgery.

5. Hearing Evaluation

Audiological testing is essential because hearing loss is common in Treacher Collins syndrome, often due to ear anomalies such as absent or malformed ear canals. Hearing tests such as audiograms and tympanometry can help assess the degree and type of hearing loss (conductive vs. sensorineural).

- Otoscopy: A visual examination of the ear canal and tympanic membrane (eardrum) to assess for differences.
- Tympanometry and auditory brainstem response (ABR) testing can help assess middle ear function and neurological hearing pathways.

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6. Evaluation for Other Associated Conditions

In some cases, individuals may have additional craniofacial or systemic issues that need to be evaluated, such as:

- Cleft palate or feeding difficulties.
- Breathing difficulties due to underdeveloped airways, particularly if there are issues with the jaw or throat.
- Speech delays related to hearing loss or structural issues in the mouth and throat.

7. Prenatal Diagnosis (In Some Cases)

Prenatal genetic testing may be considered if there is a family history of Treacher Collins syndrome or if the condition is suspected due to ultrasound findings of facial anomalies (such as micrognathia or cleft lip/palate) during the pregnancy.

Chorionic villus sampling (CVS) or amniocentesis can be performed to obtain foetal DNA and conduct genetic testing for mutations in the TCOF1, POLR1C, or POLR1D genes.

Treatment

The treatment for Treacher Collins syndrome is multidisciplinary and focuses on managing the various physical and functional challenges that arise due to the condition. The primary aim of treatment is to improve quality of life by addressing specific symptoms such as hearing loss, breathing difficulties, facial differences, and speech delays.

1. Hearing Loss Management

- Hearing aids: Most individuals with Treacher Collins syndrome experience conductive hearing loss due to ear anomalies (such as missing or malformed ear canals). Hearing aids can amplify sound and help individuals with mild to moderate hearing loss.
- Bone-anchored hearing aids (BAHA): For those with more severe hearing loss or who cannot benefit from traditional hearing aids, a BAHA may be used. This device is surgically implanted and transmits sound through the bone, bypassing the outer and middle ear.

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- Cochlear implants: If the hearing loss is more severe or cannot be adequately addressed by hearing aids, a cochlear implant (a surgically implanted device that stimulates the auditory nerve) may be considered. This is usually recommended for individuals with profound hearing loss.

2. Surgical Treatment for Craniofacial Differences

- In severe cases, early intervention to maintain the airway may be necessary. This may include a soft nasopharyngeal airway/tube, tracheostomy, and lower jaw distraction.
- Facial reconstructive surgery: Surgical interventions may be necessary to address craniofacial differences and address the appearance and function of the face. Some procedures include:
  - Jaw surgery (orthognathic surgery): If there are issues with micrognathia (a small or underdeveloped jaw), surgery may be done to reposition the jaw and improve alignment, which can also help with breathing and speech.
  - Zygomatic and maxillary reconstruction: To address underdeveloped cheekbones and upper jaw, reconstructive surgery may address facial appearance and function.
- Ear reconstruction (otoplasty): Individuals with microtia (small or absent external ears) may undergo ear reconstruction. This can be done using autologous tissue (tissue taken from the patient) or prosthetic ears.
- Cleft palate repair: If an individual has a cleft palate, surgery is typically needed to repair the gap in the roof of the mouth, improving the ability to speak and eat. This is usually performed during infancy or early childhood.

3. Speech and Language Therapy

- Since many individuals with Treacher Collins syndrome experience speech delays due to hearing loss and craniofacial differences, speech therapy is an essential part of treatment.
  - Speech therapists) can help children develop their speech, language, and communication skills. Therapy may focus on articulation, language comprehension, and using alternative communication devices if needed.
- Feeding therapy: If there is a cleft palate or difficulty with feeding, a speech therapist or feeding specialist may assist in oral motor exercises and feeding techniques to ensure proper nutrition.

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4. Respiratory Support

- Breathing difficulties may arise due to micrognathia (small jaw), which can narrow the airway and lead to problems such as sleep apnoea. Management may involve:
- Positive pressure ventilation or a CPAP machine if sleep apnoea is present.
- Surgical interventions to improve airway patency, especially if there is a significant obstruction.
- Continuous monitoring of airway function and sleep patterns is important, especially in infants and young children.

5. Psychological and Social Support

- Psychosocial support is essential, as individuals with Treacher Collins syndrome may face emotional and social challenges due to the physical appearance and possible hearing impairment associated with the condition.
- Psychological counselling can help individuals cope with the psychological aspects of living with a visible craniofacial condition.
- Support groups and peer counselling can provide emotional support and resources for both individuals and families affected by Treacher Collins syndrome.

6. Genetic Counselling

- Since Treacher Collins syndrome is an inherited genetic condition, genetic counselling is recommended for individuals and families affected by the syndrome. Counsellors can provide information about:
- The inheritance pattern (autosomal dominant).
- The risks of recurrence in future pregnancies.
- Genetic testing options for family members.

7. Regular Monitoring and Follow-up

- Regular follow-up visits with a craniofacial team, including geneticists, ENT specialists, audiologists, surgeons, and speech therapists, are important for monitoring the progression of the condition and managing any evolving needs.
- Hearing tests should be performed regularly to assess any changes in hearing ability.
- Facial and jaw growth should be monitored, especially in children, to determine when surgical interventions may be necessary.

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8. Early Intervention Services

- Early intervention programs for speech therapy, occupational therapy, and physiotherapy can help children with Treacher Collins syndrome reach developmental milestones. These programs are crucial for addressing any delays in speech, motor skills, or social development.

By addressing the multiple aspects of Treacher Collins syndrome, including hearing, speech, facial appearance, and respiratory function, individuals can lead fulfilling lives with appropriate treatment and support. Early intervention and a multidisciplinary approach are essential for the best outcomes.

Did you know?

In Australia, approximately 1 baby per 100,000 births is diagnosed with Treacher Collins syndrome.*

Treacher Collins syndrome was first identified by Edward Treacher Collins, a British surgeon, in 1900.

References:

*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. J Pediatr, 241, 162-172.e169. https://doi.org/10.1016/j.jpeds.2021.09.060

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