VAN DER WOUDE SYNDROME

Otherwise known as?

Van der Woude syndrome is sometimes referred to by other names, though "Van der Woude syndrome" is the most widely recognized. Some other names or descriptions used for this condition include:

1. Cleft lip-palate syndrome – This refers to the fact that Van der Woude syndrome often involves a cleft lip and/or cleft palate, which are the characteristic features of the condition.

2. Cleft lip-palate syndrome with lower lip pits – A description that highlights the two main features of Van der Woude syndrome: cleft lip/palate and lower lip pits (a distinctive characteristic of the condition).

3. Van der Woude's syndrome – An alternative spelling of the syndrome's name.

Signs & Symptoms

Van der Woude syndrome is a genetic condition primarily characterized by cleft lip and/or cleft palate and lower lip pits. These are the most noticeable features, but the syndrome can also cause other associated symptoms. Here's a detailed breakdown of the signs and symptoms:

1. Cleft Lip and/or Cleft Palate

- Cleft Lip: A gap or split in the upper lip, which can range from a small notch to a complete separation that extends into the nose. This can occur on one or both sides of the lip.
- Cleft Palate: A gap or opening in the roof of the mouth (palate), which may involve only the soft palate or extend into the hard palate as well.
    - These conditions can cause difficulty with feeding, speech, and hearing, and often require surgical repair.

2. Lower Lip Pits

- Lip Pits: Small, usually symmetrical depressions or indentations in the lower lip, which are considered a characteristic feature of Van der Woude syndrome. The pits may vary in size and can sometimes be accompanied by sinus tracts (small tunnels under the skin). These can be prone to infection.
    - The presence of bilateral lower lip pits is particularly indicative of this syndrome.

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3. Other Facial Features

- Some individuals may have mild to moderate facial asymmetry or subtle facial dysmorphology.
- Teeth differences: Children with Van der Woude syndrome may have missing teeth (hypodontia), especially the lower incisors.

4. Hearing Issues

- Hearing loss can occur in some individuals due to associated middle ear problems, such as Eustachian Tube dysfunction. This can lead to fluid accumulation in the middle ear, resulting in conductive hearing loss.

5. Speech and Language Delays

- Children with Van der Woude syndrome may experience speech and language delays, especially if they have an untreated cleft palate. Speech therapy is often required to address these issues.

6. Developmental and Growth Delays

- While growth and intellectual development are usually normal, some individuals may experience slightly delayed motor milestones, though they typically catch up to peers as they age.

7. Inherited Patterns and Family History

- Since Van der Woude syndrome is inherited in an autosomal dominant manner, the signs and symptoms often appear in multiple family members. However, in some cases, it may arise de novo (new mutation) in an individual with no family history of the condition.

8. Rare Features

In rare cases, there may be associated conditions such as:
- Hypertelorism: Increased distance between the eyes.
- Syndactyly: Webbing or fusion of fingers or toes, although this is not common.

Causes

Van der Woude syndrome is primarily caused by mutations in the IRF6 gene (Interferon Regulatory Factor 6). This gene plays a crucial role in the development of the lip, palate, and other facial structures during embryonic development.

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Key Causes:

1. Genetic Mutations (IRF6 Gene)

- IRF6 gene mutations: Van der Woude syndrome is most commonly caused by mutations or deletions in the IRF6 gene, located on chromosome 1. This gene is essential for regulating the development of the facial tissues during embryonic growth.
- The mutation in the IRF6 gene disrupts normal cellular signalling and leads to the impaired development of the lip, palate, and lower lip.
- These mutations may result in cleft lip and/or cleft palate, as well as the distinctive lower lip pits that characterize the condition.

2. Inheritance Pattern

- Autosomal Dominant Inheritance: Van der Woude syndrome follows an autosomal dominant inheritance pattern, meaning that an individual needs only one copy of the mutated gene (from either parent) to develop the condition.
    - If one parent carries the mutation, there is a 50% chance that the condition will be passed on to each child.
    - In some cases, the mutation may arise de novo (new mutation) in an individual with no family history of the condition.

3. Environmental and Other Factors (Less Common)

- While genetic mutations are the primary cause of Van der Woude syndrome, certain environmental factors may contribute to the risk of cleft lip and palate development in general, though this is not typically the case for this syndrome.
- Maternal health, nutrition, medications, and smoking during pregnancy can increase the risk of cleft lip and palate in the general population, but these factors are not directly responsible for Van der Woude syndrome.

Testing & Diagnosis

The diagnosis of Van der Woude syndrome typically involves a combination of clinical evaluation, genetic testing, and family history analysis.

1. Clinical Diagnosis

- The first step is a physical examination by a doctor, usually a geneticist, paediatrician, or craniofacial specialist. The doctor will look for characteristic features of Van der Woude syndrome, including:

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  - Cleft lip and/or cleft palate: A split or gap in the upper lip and/or roof of the mouth.
  - Lower lip pits: Small indentations or depressions in the lower lip, which may be accompanied by sinus tracts (small tunnels under the skin).
  - Other facial anomalies such as slight asymmetry or dental differences (missing teeth or extra teeth).

The presence of both cleft lip/palate and lower lip pits is strongly suggestive of Van der Woude syndrome.

2. Genetic Testing

- Genetic testing is essential for confirming the diagnosis of Van der Woude syndrome and identifying the underlying cause. The IRF6 gene mutation is the primary cause of this syndrome. The testing involves:
  - DNA sequencing: This method is used to look for mutations in the IRF6 gene on chromosome 1. If a mutation is found, it confirms the diagnosis of Van der Woude syndrome.
  - Genetic counselling: This is recommended for individuals and families to understand the inheritance pattern (autosomal dominant) and to discuss the risks for future pregnancies.

3. Family History

- A family history of cleft lip, cleft palate, or lower lip pits can be a helpful diagnostic clue. Since Van der Woude syndrome is inherited in an autosomal dominant pattern, it is common for multiple family members to be affected. In some cases, the condition can arise de novo (without a prior family history) due to a new mutation in the IRF6 gene.

4. Prenatal Diagnosis (In Some Cases)

- If there is a known family history of Van der Woude syndrome, prenatal testing may be done. This can involve chorionic villus sampling (CVS) or amniocentesis to analyse the foetal DNA for mutations in the IRF6 gene.
  - Ultrasound may also detect cleft lip or cleft palate during pregnancy, which could prompt genetic testing for further confirmation.

5. Imaging and Evaluation for Associated Issues

- While not always necessary for diagnosis, imaging may be performed to assess cleft palate or other craniofacial differences. Imaging techniques like X-rays or CT scans may be used to evaluate the structure of the palate or upper jaw if surgical intervention is planned.

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- Audiological testing may be recommended to check for hearing loss, which can sometimes be associated with cleft lip and palate conditions, although it is not typically a prominent feature in Van der Woude syndrome.

6. Diagnostic Criteria

The diagnosis of Van der Woude syndrome is often confirmed when both:

- Cleft lip and/or cleft palate and lower lip pits are present.
- A mutation in the IRF6 gene is detected via genetic testing.

Treatment

The treatment of Van der Woude syndrome is multidisciplinary, aimed at addressing the primary symptoms and improving quality of life. The condition typically requires interventions from various doctors, including surgeons, and audiologists, speech therapists, and genetic counsellors. Here's a breakdown of the common treatment approaches:

1. Surgical Treatment for Cleft Lip and/or Cleft Palate

- Cleft Lip and Cleft Palate Repair:
  - Surgical repair is often required to address the cleft lip and/or cleft palate. These surgeries are typically performed in infancy or early childhood to close the gap and allow for proper feeding, speech, and breathing.
    - Cleft lip repair is usually done between 2-3 months of age.
    - Cleft palate repair is often done around 9-18 months to help with speech development and prevent complications like ear infections.
  - Early surgical interventions can greatly improve the appearance of the face and help with functional issues like feeding, speaking, and swallowing.

2. Lip Pit Treatment

- Lower Lip Pits:
  - Lip pits are a characteristic feature of Van der Woude syndrome. Although they may not require surgical treatment if they do not cause problems, they can become prone to infection or abscess formation.
  - Surgical excision may be considered for individuals who have infections, pain, or cosmetic concerns related to the lip pits.
  - Regular cleaning and proper care can help prevent infections in the pits.
  - Sinus tracts (small tunnels under the skin) associated with the lip pits may also require surgical attention if they become problematic.

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3. Hearing Management

- Hearing Loss:
  - Hearing problems may occur due to middle ear fluid, a common issue with cleft palate. This can lead to conductive hearing loss.
  - Regular hearing assessments are important for monitoring any hearing loss.
  - Ear tubes (ventilation tubes) may be recommended for children with persistent fluid in the middle ear to help prevent ear infections and promote normal hearing.
  - Hearing aids or bone-anchored hearing aids (BAHA) might be considered for more severe hearing loss.

4. Speech and Language Therapy

- Since many individuals with Van der Woude syndrome have cleft palate, speech therapy is essential to help with:
  - Speech delays and issues with articulation, especially if the palate is not repaired at an early age.
  - Feeding difficulties may also require therapy to ensure proper nutrition and development.
- Speech therapists work with children to improve their speech, language, and communication skills, often beginning in infancy to address developmental delays.

5. Orthodontic Care

- Dental and orthodontic treatment may be required for individuals with Van der Woude syndrome, particularly those with missing teeth or misaligned teeth (hypodontia). Treatment may include:
  - Orthodontic interventions to align the teeth and jaws properly.
  - Dental implants or prosthetics may be used to address missing teeth.

6. Psychological and Social Support

- Psychosocial support is essential, especially for children who may experience social or emotional challenges due to the visible nature of their clefts or lip pits. Support can include:
  - Counselling to help individuals and their families cope with the psychological impact of living with a craniofacial condition.
  - Support groups can provide valuable resources and emotional support from others who are affected by Van der Woude syndrome.

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7. Genetic Counselling

- Since Van der Woude syndrome is inherited in an autosomal dominant pattern, genetic counselling is important for families. A genetic counsellor can:
  - Explain the inheritance pattern and risks for recurrence in future pregnancies.
  - Offer prenatal testing options if desired, especially in families with a known history of the syndrome.

8. Regular Monitoring and Follow-up

- Regular follow-up with a craniofacial team and specialists (geneticists, paediatricians, speech therapists, audiologists) is important to monitor growth, hearing, speech, and any changes in the condition.
  - Hearing evaluations, speech assessments, and facial development monitoring are crucial to track the individual's progress and address any new issues as they arise.

Did you know?

In Australia, approximately two babies per 100,000 births are diagnosed with Van der Woude syndrome.*

Van der Woude syndrome was first identified by Dutch dermatologist Dr. R. Van der Woude in 1954.

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