Moebius Syndrome

Courtney Clayton, D.D.S.
1st Year Orthodontics Resident
Moebius Syndrome

- rare neurological condition that primarily affects the muscles that control facial expression and eye movement (3)
  - Though exact incidence is unknown
  - 1 in 50,000 to 1 in 500,000 newborns (3)
- Combination of congenital palsies of the abducens and facial nerves ➔ orofacial malformations, limb defects, and musculoskeletal behavioral and cognitive abnormalities (1)
- Signs and symptoms are present from birth (3)
- Weakness or paralysis of the facial muscles
  - symmetrical or asymmetrical facial palsy
- Affected individuals lack facial expressions; they cannot smile, frown, or raise their eyebrows (3)
- Can also affect speech, chewing, and swallowing
Other Names for Moebius Syndrome

- congenital facial diplegia
- congenital ophthalmoplegia and facial paresis
- Möbius sequence
- Mobius syndrome
- Moebius congenital oculofacial paralysis
- Moebius sequence
- Moebius spectrum
Etiology

• Unknown cause of condition
• Combination of environmental and genetic factors
  • A small percentage of all cases have been reported to run in families; no clear pattern of inheritance
• Two Hypotheses:
  • 1. rhombencephalic maldevelopment
  • 2. ischemia during the first trimester
• Regions of chromosomes 3, 10, or 13 in some families
• HOXA1, HOXB1, and TUBB3 genes are reported to cause atypical forms of Moebius syndrome
• Possible risk factors: certain medications during pregnancy; cocaine abuse
• Many of the signs and symptoms of Moebius syndrome result from the absence or underdevelopment of cranial nerves VI and VII
• Researchers speculate that Moebius syndrome may result from changes in blood flow to the brainstem during early stages of embryonic development
Characteristic Features

- At birth: feeding, swallowing, and choking problems
- Excessive drooling
- Eye Sensitivity
- Crossed Eyes
- must move their head from side to side to read or follow the movement of objects (3)
- difficulty making eye contact and strabismus (1)
- the eyelids may not close completely when blinking or sleeping → dry or irritated eyes
- bone abnormalities in the hands and feet, weak muscle tone (hypotonia), and hearing loss
- Affected children often experience delayed development of motor skills (3)
- small chin (micrognathia) and a small mouth (microstomia) with a short or unusually shaped tongue
- The roof of the mouth may have an abnormal opening (cleft palate) or be high and arched. These abnormalities contribute to problems with speech,
- Dental abnormalities, including missing and misaligned teeth, are also common
• Dysmorphic facial appearance
• Dysphagia and respiratory problems are frequently associated features resulting from lower brainstem dysfunction (2)

In 2007 at the biannual Moebius Syndrome Foundation research meeting, clinicians and researchers defined the minimum diagnostic criteria (MDC) for classic Moebius syndrome as “congenital, uni- or bilateral, nonprogressive facial weakness and limited abduction of the eye(s).”

To optimize genetic analysis, we propose adding “full vertical motility” to the MDC for Moebius syndrome. (1)
Participants were grouped on the basis of the presence or absence of abduction limitation and facial palsy, which define the currently accepted MDC for Moebius syndrome.
<table>
<thead>
<tr>
<th>Classic Moebius Syndrome Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial nerve palsy</td>
<td>100%</td>
</tr>
<tr>
<td>Severe abduction deficit</td>
<td>100%</td>
</tr>
<tr>
<td>Full vertical gaze</td>
<td>100%</td>
</tr>
<tr>
<td>Full adduction</td>
<td>17%</td>
</tr>
<tr>
<td>Mildly reduced adduction deficit</td>
<td>27%</td>
</tr>
<tr>
<td>Severe adduction deficit</td>
<td>56%</td>
</tr>
<tr>
<td>Orthotropia in primary gaze</td>
<td>41%</td>
</tr>
<tr>
<td>Esotropia in primary gaze</td>
<td>59%</td>
</tr>
<tr>
<td>Binocular vision</td>
<td>51%</td>
</tr>
<tr>
<td>Dysinnervation</td>
<td>41%</td>
</tr>
<tr>
<td>Volitional Bell's</td>
<td>45%</td>
</tr>
<tr>
<td>Intorsion with fixation</td>
<td>16%</td>
</tr>
<tr>
<td>Category of Anomaly</td>
<td>No. of Participants Affected</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Orofacial ∗</td>
<td>82 (93%)</td>
</tr>
<tr>
<td>Periorbital</td>
<td>31 (35%)</td>
</tr>
<tr>
<td>Ear shape/position</td>
<td>39 (44%)</td>
</tr>
<tr>
<td>Congenital hearing deficit</td>
<td>16 (18%)</td>
</tr>
<tr>
<td>Limb</td>
<td>54 (61%)</td>
</tr>
<tr>
<td>Lower limb only</td>
<td>23 (26%)</td>
</tr>
<tr>
<td>Upper limb only</td>
<td>18 (20%)</td>
</tr>
<tr>
<td>Upper and lower limbs</td>
<td>13 (15%)</td>
</tr>
<tr>
<td>Muscular or skeletal †</td>
<td>30 (34%)</td>
</tr>
<tr>
<td>Medical systemic or neurologic</td>
<td>21 (24%)</td>
</tr>
<tr>
<td>Developmental, cognitive, or behavioral</td>
<td>46 (52%)</td>
</tr>
<tr>
<td>Individuals having involvement of</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>1 category (as defined above)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>2 categories</td>
<td>20 (23%)</td>
</tr>
<tr>
<td>3 categories</td>
<td>20 (23%)</td>
</tr>
<tr>
<td>4 categories</td>
<td>14 (16%)</td>
</tr>
<tr>
<td>5 categories</td>
<td>13 (15%)</td>
</tr>
<tr>
<td>6 categories</td>
<td>6 (7%)</td>
</tr>
<tr>
<td>7 categories</td>
<td>8 (9%)</td>
</tr>
</tbody>
</table>
There are four recognized categories of Moebius syndrome:

- **Group I**, characterized by small or absent brain stem nuclei that control the cranial nerves
- **Group II**, characterized by loss and degeneration of neurons in the facial peripheral nerve
- **Group III**, characterized by loss and degeneration of neurons and other brain cells, microscopic areas of damage, and hardened tissue in the brainstem nuclei
- **Group IV**, characterized by muscular symptoms in spite of a lack of lesions in the cranial nerve.
Differential Diagnosis

- Poland syndrome, Klippel–Feil anomaly, Kallmann syndrome and Hanhart syndrome
- Brainstem dysgenesis and brainstem syndromes
- In pontine tegmental cap dysplasia and Pre- and perinatal total asphyxia
- The “TUBB3 E410K syndrome”
- Abducens nerve palsy
- Asymmetric crying facies
- Myotonic diseases
- Duane Syndrome
- Metabolic neuropathy
- Neuromuscular diseases
Diagnostic Methods

- assessment and medical history of the patient
- test ocular motility
  - patients must have both facial palsy and motility deficit
  - bilateral abduction deficits and full vertical gaze along with facial weakness
  - horizontal gaze palsies reported in approximately 50% of patients
  - if horizontal ductions are full, the patient does not have Moebius syndrome
- Blink reflex and direct facial nerve stimulation studies → various combinations of three patterns (supranuclear, nuclear, and peripheral) (7)
- Patients with exotropia, vertical gaze limitation, and ptosis do not have classic Moebius (1)
- autism spectrum disorders can be difficult to diagnose (3)
- MRI and thin-sliced CT should be performed
- Glabellar tap (1)
Eye alignment and horizontal ocular motility patterns in 2 participants with classic Moebius syndrome. Straight-ahead gaze (B, E), right gaze (A, D), and left gaze (C, F). A–C, An 18-month-old with a large esotropia and marked abduction deficit of each eye with good adduction. D–F, A 36-year-old man with relatively straight eyes (orthotropia) with limited horizontal gaze in both directions. (3)

Management

- There is no cure for Moebius Syndrome; requires early intervention
- Often left with comorbid conditions that render them technology-dependent
  - Home ventilator, tracheostomy, gastrostomy
- Unable to nurse properly; can't form “sucking” expression
- “Static Sling” - patients tissue transplanted to prop up drooping eyelids or lip area
- “Smile Surgery” or functional muscle transfer - muscle from thigh grafted to corners of mouth
- Eye drops for dry eyes, or tarsorrhaphy if necessary
- Surgery to correct crossed eyes
- Speech/Language Therapy
  - Body language, physical posture and tone of voice to compensate
- Psychosocial Support
- With proper care, life expectancy is normal
- Microvascular muscle transfer
- Cross facial nerve graft
The woman who couldn't smile
Dental Considerations

- Dental abnormalities, including missing and misaligned teeth, are also common
- The roof of the mouth may have an abnormal opening (cleft palate) or be high and arched → speech problems
- Many people with Moebius syndrome are born with a small chin (micrognathia) and a small mouth (microstomia) with a short or unusually shaped tongue (3)
  - more susceptible to crowded, fragile or misaligned front teeth
  - They may also have a harder time closing their mouths, leading to chronically dry lips and gums.
- Orthodontic devices → improving the child's bite and ability to close the mouth properly
- In more severe cases, a child may benefit from orthognathic surgery
- Cleft palate can be repaired with surgery before 12 years of age (4)
References


• http://www.childrenshospital.org/conditions-and-treatments/conditions/m/moebius-syndrome/treatments

• http://my.clevelandclinic.org/health/diseases_conditions hic_Mobius_Syndrome

• http://www.cranirare.eu/phenotypes/moebius/index.php

• The spectrum of Mobius syndrome: an electrophysiological study. Verzijl HT, Padberg GW, Zwarts MJ - Brain - July 1, 2005; 128 (Pt 7); 1728-36

Stickler syndrome
1965 Dr. Gunner Stickler and colleague described the stickler syndrome that they observed at Mayo clinic.

Hereditary disorder of connective tissue affected craniofacial, skeletal, audio and ocular systems.

COL2A1, COL2A2, COL11A1, and COL11A2 are autosomal dominant inheritance, except mutation in COL9A1 and COL9A2 cause autosomal recessive inheritance.

Also cause Pierre Robin Sequence and require obstruction of airway.

Incident: 1/10,000
Collagen type II and XI

- **Fibrillar collagen**
- Abundant in chondrocyte, osteoblast, and endothelial cells

### TABLE 1. Fibrillar collagens

<table>
<thead>
<tr>
<th>Type</th>
<th>Chains</th>
<th>Molecules</th>
<th>Representative tissues</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>α1(I), α2(I)</td>
<td>[α1(I)]_2 α2(I)</td>
<td>Skin, bone, tendon, dentin, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[α1(I)]_3</td>
<td>Dentin, skin (minor form)</td>
</tr>
<tr>
<td>III</td>
<td>α1(III)</td>
<td>[α1(III)]_3</td>
<td>Skin, vessels</td>
</tr>
<tr>
<td>V</td>
<td>α1(V),* α2(V), α3(V)</td>
<td>[α1(V)]_3, [α1(V)]_2 α2(V) α1(V) α2(V) α3(V)</td>
<td>Hamster lung cell cultures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fetal membranes, skin, bone</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placenta, synovial membranes</td>
</tr>
<tr>
<td>II</td>
<td>α1(II)</td>
<td>[α1(II)]_3</td>
<td>Hyaline cartilage, vitreous body</td>
</tr>
<tr>
<td>XI*</td>
<td>α1(XI), α2(XI), α3(XI)*</td>
<td>α1(XI) α2(XI) α3(XI)</td>
<td>Hyaline cartilage</td>
</tr>
</tbody>
</table>

* A chain similar in its triple helix, but different in its propeptides has been described and called α1(V') or α4(V').
* α3(XI) is probably identical to α1(II), except for posttranslational modifications.
* Often called 1α2α3α.
The molecular genetic mechanism

- Heterozygous base pair mutation in the gene
  - Type 1: COL2A1 at 54 exons on chromosome 12 and COL2A2
  - Type 2: COL11A1 and COL11A2
  - Nonocular type (Weissenbacher-Zweymüller syndrome): COL11A2

- Similar to Marshall syndrome (COL11A1 gene, splicing mutation at exon 54), Kniest dysplasia (COL2A1 gene, mutation site vary), Wagner syndrome (chondroitin sulfate proteoglycan 2, CSPG2 splicing mutation at exon 8, also cause vitreoretinal degeneration).

- Mutations occurred in COL2A1 and COL11A1 genes and resulted in other type of amino acids replacement or sequence termination.

- These mutations influence the synthesis of procollagen.
<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Gene</th>
<th>Mutation</th>
<th>Effect</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Ins 10bp, exon 4</td>
<td>Frameshift</td>
<td>53</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Arg9Ter, exon 7</td>
<td>Nonsense mutation</td>
<td>54</td>
</tr>
<tr>
<td>Stickler syndrome*†</td>
<td>COL2A1</td>
<td>A^2→G, IVS17</td>
<td>Aberrant splicing, frameshift</td>
<td>55</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Del A, exon 20</td>
<td>Frameshift</td>
<td>53</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Arg704Cys, exon 39</td>
<td>Missense mutation</td>
<td>23</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Arg732Ter, exon 40</td>
<td>Nonsense mutation</td>
<td>56</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Del T, exon 40</td>
<td>Frameshift</td>
<td>57</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Del T, exon 43</td>
<td>Frameshift</td>
<td>58</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Ins G, exon 48</td>
<td>Frameshift</td>
<td>53</td>
</tr>
<tr>
<td>Stickler syndrome*</td>
<td>COL2A1</td>
<td>Del C, exon 50</td>
<td>Frameshift</td>
<td>59</td>
</tr>
<tr>
<td>Stickler syndrome with type 2 vitreous</td>
<td>COL11A1</td>
<td>Del 1bp, acceptor splice site</td>
<td>Aberrant splicing, in frame exon skip</td>
<td>26</td>
</tr>
<tr>
<td>Stickler syndrome with type 2 vitreous</td>
<td>COL11A1</td>
<td>Gly97Val</td>
<td>Missense mutation</td>
<td>25</td>
</tr>
<tr>
<td>Stickler syndrome with type 2 vitreous</td>
<td>COL11A1</td>
<td>Del 40kb (multiple exons)</td>
<td>Large in frame deletion</td>
<td>26</td>
</tr>
</tbody>
</table>

*Families with COL2A1 mutations are likely to have the type 1 vitreous phenotype (see text).
†Original family reported by Stickler et al.¹²
Fig. 1  Approximate position of the mutations in the triple helix of type II collagen. Numbers refer to those in Table 1. Upper row: published cases; lower row: our own observations.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Molecular defects and resulting abnormalities in the type II procollagen chain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical disorder</strong></td>
<td><strong>Molecular defect</strong></td>
</tr>
<tr>
<td>Achondrogenesis II</td>
<td>Single base substitution</td>
</tr>
<tr>
<td>Hypochondrogenesis</td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td>SED congenita</td>
<td>Deletion exon 48</td>
</tr>
<tr>
<td></td>
<td>Duplication exon 48</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Duplication in exon 44</td>
</tr>
<tr>
<td>Knies dysplasia</td>
<td>Deletion of 28 bp intron 12/exon 12, skipping of exon 12</td>
</tr>
<tr>
<td></td>
<td>Single base substitution intron 20/exon 21, alternative splicing, skipping of part of exon 21</td>
</tr>
<tr>
<td></td>
<td>Deletion in exon 49</td>
</tr>
<tr>
<td>Stickler dysplasia</td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single bp deletion exon 40, frameshift→Stop in exon 42</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single bp deletion exon 43, frameshift→Stop in exon 44</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
<tr>
<td></td>
<td>Single base substitution</td>
</tr>
</tbody>
</table>
Mutated procollagens involved mechanism

- Misfold procollagens accumulated in the endoplasmic reticulum, produced aggregation, and induced ER stress. ER mediate stress could triggered cell apoptosis.
- Hsp47 chaperone cannot fold the collagen into triple helix.
- The procollagen α1 chain from collagen type II also failed assemble with type XI procollagen α1.
Clinical manifestations

- Craniofacial appearance:
  - Shortness of cranial base midface hypoplasia
  - Maxillary and mandibular hypoplasia
  - Long total facial length
  - Increased height of the lower face
The mutations diversity contributes different phenotypes in the clinical observation.
Clinical manifestations

- Skeletal defect
  - Pierre Robin sequence
  - Joint problem (80%)
Mandibular abnormality
• Short ramus
• Antegonial notching of the body
Before surgery

After surgery

Normal dentition after 54 months
Joint hypermobility
Clinical manifestations

- Neural defect
  - High myopia and glaucoma
  - Sensorineural hearing deficit

Typical pigmented paravascular retinal lattice degeneration
Clinical manifestations

- Sensorineural hearing deficit (continue)
- Studies from 313 patients (102 families) individually described in 46 articles.
- Hearing loss 62.9%, ranges from mild and moderate.
- Hearing impairment sensorineural (67.8%).
- Conductive (14.1%) and mixed (18.1%) hearing loss primarily found in young patients or patient with a palatal defect.
Diagnosis

- Imaging test.
- Eye exam.
- Hearing test.
- Genetic test
  - Hard to diagnose due to great viability in symptom.
Treatment and drugs

- Medications:
  - Pain relievers.
  - Glaucoma drugs.

- Therapy:
  - Speech therapy.
  - Physical therapy.
  - Hearing aids.
  - Special education.

- Surgery
  - Tracheostomy
  - Jaw surgery
  - Cleft palate repair
  - Ear tubes
  - Eye surgery
  - Joint replacement
Reference

Thank you!
What is Carpenter Syndrome?

- **Carpenter syndrome** belongs to a group of rare disorders known as “acrocephalopolysyndactyly” (ACPS) disorders
  - Carpenter syndrome is also known as **ACPS type II**
- First described in 1909 by Dr. Carpenter
Epidemiology

- A disease is defined as rare in the USA when it affects fewer than 200,000 Americans at any given time.
- Occurs in approximately 1 in 1,000,000 births.
- Currently less than 300 known cases in the US.
Clinical Presentation

- Carpenter syndrome is typically evident at or shortly after birth

- **Primary findings** include
  - Premature fusion of cranial bones (craniosynostosis)
  - Webbing or fusion of toes and fingers (syndactyly)
  - Conical shaped head (acrocephaly)
  - More than the normal number of digits (polydactyly)
  - Obesity
  - Reduced height
Additional sign and symptoms

- Downsloping eyelid folds (palpebral fissures)
- Flat nasal bridge
- Low-set ears
- Underdeveloped maxilla or mandible
- Many individuals have mild to moderate ID.
Carpenters syndrome: Deformities of cranium and polydactylism of hands/feet.
Causes

- Inherited as a **autosomal recessive disorder**
- Associated with mutations in the **RAB23** or **MEGF8** gene
Diagnosis

- Prenatal diagnosis of this syndrome is possible by ultrasound during pregnancy.
- Diagnosis is usually made at or shortly after birth based upon a thorough clinical examination.
- Molecular genetic testing can confirm diagnosis and is often used for research purposes.
Treatment

- Therapies are directed toward the specific symptoms that appear in each individual:
  - Surgeries to prevent or correct premature closure of cranial sutures
  - Corrective or reconstructive surgeries to address polydactyly, syndactyly, and other skeletal defects
  - Hearing aids to address hearing impairment
Questions?
References

Crouzon Syndrome

Nicha Ungvijanpunya

1st year Orthodontic Resident
What is Crouzon syndrome?

- Described by a French neurosurgeon Octave Crouzon in 1912
- Genetic disorder
- Premature fusion of certain skull bones (Craniosynostosis)
  - prevent normal growth of skull & affect the shape of the head & face
What is Crouzon syndrome?

- Usually begins in the first year of life and is completed by the second or third year.
- May sometimes be apparent at birth or during childhood (Rare).
- 16 per million newborns (1:60,000) in the US, 1:25,000 worldwide.
- Patients usually have a normal lifespan.
Signs & Symptoms

- Wide-set, bulging eyes (exophthalmos)
- Shallow eye sockets —> vision problems
- Divergent strabismus
- Beaked nose —> might cause difficulty in breathing
- Hearing loss, narrow/obstructed ear canals
Signs & Symptoms

- 97% have normal intelligence
- Increased risk to develop hydrocephalus
- Raised intracranial pressure → blindness
- Acanthosis nigricans (in some cases)
- Mostly no abnormalities of the hands & feet → can be used in differential diagnosis
Signs & Symptoms

- Dental problems
  - Underdeveloped upper jaw —> Relative mandibular prognathism (class III malocclusion)
  - High & narrow upper arch —> Upper arch crowding
  - Cleft lip and cleft palate (Rare)
  - Oligodontia, Macrodontia, peg-shaped and widely spaced teeth (Occasionally)
Causes

- Mutations in **FGFR2** gene on chromosome 10 [locus 10q25 - 10q26] (>50%)
  - or **FGFR3** gene on chromosome 4 —> Acanthosis Nigricans
- **FGFR2** gene
  - Making a protein called “fibroblast growth factor receptor 2”
  - This protein signals **immature cell** —> **bone cells** during embryonic development
  - Mutation in this gene —> overstimulate signaling by FGFR2 protein —> bone skull fuse prematurely
- Inherited in an **autosomal dominant** pattern or **new mutations** (50:50)
Diagnosis

- Skull examination
- Facial features
- Radiographic findings: CT imaging, Lateral Skull view
  - “Copper beaten appearance”
- Obliterated sutures
- Underdeveloped maxilla
Diagnosis

- Genetic test → check mutations in FGFR gene
- A sample of skin cells
- Check for acanthosis nigricans
- Family history
Differential Diagnosis

- Beare-Stevenson syndrome
- Carpenter syndrome
- Jackson-Weiss syndrome
- Pfeiffer syndrome
- Saethre-Chotzen syndrome
- Apert syndrome
Treatment Options

Directed toward the specific symptoms that are apparent in each individual

Skull

- Surgery —> To remove closed sutures & expand & reshape the skull

Eyes

- Early fronto orbital advancement
- Visit an ophthalmologist on regular basis

Brain

- Evaluation of severe recurrent headaches
- Checked for signs & symptoms of hydrocephalus —> need surgery
Treatment Options

➤ Hearing
  ➤ Periodic hearing check
  ➤ Speech difficulties —> speech therapy

➤ Breathing
  ➤ Require placement of a surgical tracheostomy
  ➤ Sleep apnea —> Midface advancement (LeFort III) or Adenoidectomy

➤ Teeth
  ➤ Orthodontic treatment to correct crowding
  ➤ Jaw surgery


http://ghr.nlm.nih.gov/condition/crouzon-syndrome#glossary
http://www.seattlechildrens.org/medical-conditions/bone-joint-muscle-conditions/crouzon/
https://rarediseases.org/rare-diseases/crouzon-syndrome/
http://www.chla.org/crouzon-syndrome