Update on the Management of Patients with Craniosynostosis
AAPOS 2011

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From March 4-6, 2010, the National Foundation for Facial Reconstruction (NFFR) hosted a multidisciplinary meeting in Atlanta, Georgia sponsored by the Centers for Disease Control and Prevention (CDC) entitled “Craniosynostosis: Developing Parameters for Diagnosis, Treatment, and Management.” The goal of this meeting was to create parameters for the care of children with craniosynostosis. The 55 conference attendees covered a broad range of expertise including anesthesiology, craniofacial surgery, pediatric dentistry, genetics, hand surgery, neurosurgery, nursing, ophthalmology, oral and maxillofacial surgery, orthodontics, otolaryngology, pediatrics, psychology, public health, radiology, and speech-language pathology. Sixteen professional societies were also represented at the meeting.

This workshop will provide:

1) The ophthalmology parameters of care for patients with syndromic and nonsyndromic craniosynostosis set forth by the CDC Ophthalmology Committee members
2) The workshop will present new genetic discoveries, and update the audience on the common ophthalmic complications and management/treatment guidelines: ocular adnexal abnormalities, ocular motility abnormalities and the multiple levels of visual pathway involvement in these conditions

Craniosynostosis: Developing Parameters for Diagnosis, Treatment, and Management

INTRODUCTION

Craniosynostosis is premature fusion of one or more cranial sutures. This relatively common developmental anomaly affects 1 in 2000 children. This condition can occur in association with more than 130 different syndromes, but most patients are nonsyndromic. Physical findings can include calvarial dysmorphology, midface hypoplasia, hydrocephalus, deafness, blindness, mental retardation, and extremity anomalies. The diagnosis, management, and treatment of craniosynostosis can be complex. While recognizing that adequate care can be provided outside of craniofacial centers, due to the complex nature of the disorder we strongly believe that optimal care is best accomplished by teams of interdisciplinary specialists who are dedicated to the care and management of patients with craniofacial anomalies and see a sufficient number of affected patients to understand the management complexities. Interdisciplinary team care has been practiced for many years in the care of children with cleft lip and cleft palate and complex
craniofacial anomalies. The American Cleft Palate –Craniofacial Association defines team care for these problems in its Parameters for the Evaluation and Treatment of Patients with Cleft Lip/Palate or Other Craniofacial Anomalies.\(^1\) For the management of craniosynostosis these interdisciplinary team may be comprised of professionals from the following disciplines: anesthesia, craniofacial surgery, genetics, hand surgery, intensive care, neurosurgery, nursing, ophthalmology, orthodontics, pediatrics, pediatric dentistry, prosthodontics, psychology, radiology, social work, and speech/language pathology. Consultation with clinicians from other specialties may also be warranted. The team should embrace family-centered care and view the family as equal partners in assuring quality care for the child.

**OPHTHALMOLOGY**

**EVALUATION AND TREATMENT**

Ocular and visual health, maintenance and restoration are integral components of the overall management of the child and adolescent with isolated and syndromic craniosynostosis. The ophthalmologist plays a particularly important role in the diagnosis and treatment of sight threatening complications of craniosynostosis and advises the craniofacial team about optic nerve health which may impact the timing of cranial vault surgery. It is important that the ophthalmologist have knowledge about the specific impact of craniosynostosis on the ocular and visual system and has experience in treating patients with craniosynostosis.

Qualifications of the ophthalmologist should include:
- board certification or eligibility in ophthalmology and state licensure
- membership in a craniofacial team or an ophthalmologist with experience in managing and treating patients with craniosynostosis

**Ocular Adnexa abnormalities**

Patients with syndromic craniosynostosis display more adnexal abnormalities than isolated craniosynostosis patients. Common abnormalities include orbital hypertelorism, telecanthus, abnormal slant of the palpebral fissures secondary to superior displacement of the medial canthi, ptosis, and nasolacrimal apparatus abnormality such as duct obstruction and punctal anomalies. Epiphora is a common finding and may be secondary to nasolacrimal apparatus obstruction, or poor blink secondary to proptosis.

**Proptosis**

Proptosis, or exorbitism, results from the reduced volume of the bony orbital space. It usually occurs in syndromic craniosynostosis. The severity of the proptosis is not uniform and frequently increases with age because of the impaired growth of the bony orbit. Proptosis is disfiguring and can be vision threatening due to corneal exposure and globe luxation.

**Corneal Exposure**

Because the eyelids may not close completely over the proptotic globes, corneal exposure may occur secondary to inadequate blink and/or nocturnal lagophthalmos with possible development of exposure keratitis. Exposure, in the short term, can lead to the following corneal complications: punctate epithelial erosions, epithelial defects, and subsequent infectious keratitis.
Resulting scarring of the cornea may lead to irregular astigmatism, with difficulty providing accurate spectacle corrections, and permanent corneal scars that may obstruct the visual axis. Aggressive lubrication in the form of artificial tears and ointment is necessary to prevent corneal drying. Tarsorrhaphies or lid occlusal sutures may be necessary if lubrication is not adequate for the prevention and treatment of exposure keratitis. Surgical expansion of the orbital volume, eliminating or reducing the proptosis, is the ultimate treatment when proptosis (exorbitism) and exposure are severe and lubrication and tarsorrhaphies fail.

**Globe Luxation**
Patients with extremely shallow orbits may suffer globe luxation when the eyelids are manipulated, as when giving eyedrops, or when there is increased pressure in the orbits, as occurs with a valsala maneuver. The globe is luxated forward, with the eyelids falling behind the equator of the globe. The condition can be very painful and may also compromise the blood supply to the globe, a medical emergency. For recurrent luxation the treatment is tarsorrhaphy or orbit volume expansion.

**Decreased Vision**
Patients with syndromic craniosynostosis often have decreased vision that can be due to a variety of causes: exposure keratitis and corneal surface irregularity, corneal scarring with obstruction of the visual axis or irregular astigmatism, uncorrected refractive errors with difficulty wearing glasses secondary to proptosis, hypertelorism and midface retrusion, amblyopia from high or asymmetric refractive errors or strabismus, and optic nerve atrophy. Most cases of permanent vision loss are preventable.

**Refractive errors**
Patients with syndromic craniosynostosis are at higher risk for unusual refractive errors that cause decreased vision. Patients with nonsyndromic craniosynostosis, namely unicoronal synostosis, are at risk for astigmatism in the eye opposite the coronal suture synostosis. Spectacles are the typical treatment for refractive errors.

**Amblyopia**
Amblyopia is common in patients with syndromic craniosynostosis, occurring in up to 40%, less common in nonsyndromic craniosynostosis patients. Amblyopia is secondary to high uncorrected refractive errors, asymmetric refractive errors or strabismus, all of which occur more frequently in this subset of patients. Occlusive patches or atropine eyedrops are the mainstay of treatment for amblyopia.

**Strabismus**
Syndromic craniosynostosis patients have a much higher incidence of strabismus than nonsyndromic craniosynostosis patients. This is secondary to the increased incidence of orbital abnormalities in syndromic craniosynostosis (particularly those patients with bicoronal and skull base suture fusion): exorbitism, orbital extorsion, shallow orbits, anomalous orbital pulleys and extraocular muscles.

Esotropia, and more frequently exotropia, are frequent horizontal deviations noted, particularly in patients with syndromic craniosynostosis. The treatment of horizontal strabismus is relatively straightforward and involves surgery on the medial and lateral rectus muscles.
Patients with coronal suture synostosis, syndromic or nonsyndromic, commonly experience a characteristic strabismus: V-pattern strabismus with a large exotropia on upgaze, diminishing in down gaze. Often accompanying this strabismus pattern is a marked apparent overaction of the inferior oblique muscle/s, with possible superior oblique underaction, ipsilateral to the coronal suture fusion. This leads to a hypertropia of the involved eye which worsens in adduction. This characteristic strabismus is likely due to the following: orbital and secondary globe extorsion with extraocular muscle displacement, superior orbital rim and secondary superior oblique trochlea retrusion causing superior oblique underaction, and/or anomalous extraocular muscles insertions or agenesis, and anomalous pulley system within the orbit. The outcome of strabismus surgery is better in nonsyndromic unicoronal synostosis patients, with increased chances for normal alignment and fusion postoperatively. Patients with syndromic craniosynostosis and strabismus are difficult to align. No single surgical procedure reliably treats the V-pattern, apparent inferior oblique overaction and hypertropias in side gazes. Often multiple procedures are required.

Optic nerve abnormalities
Papilledema and subsequent optic atrophy may occur secondary to elevated intracranial pressure, which is induced by multiple mechanisms:
- craniocerebral disproportion secondary to widespread cranial suture fusion which is more common in patients with syndromic craniosynostosis
- hydrocephalus, occurring more commonly in patients with the Crouzon phenotype
- sleep apnea, more common in children with syndromic craniosynostosis with midface retrusion, inducing episodes of nocturnal elevated intracranial pressure. The mechanism is poorly understood but episodes of elevated ICP occur after episodes of partial or complete upper airway obstruction, possibly increasing central venous pressure with secondary increased cerebrovascular volume, and cerebral vasodilation with subsequent increased intracranial pressure secondary to hypoxia and hypercapnia.
- Venous hypertension secondary to cranial base narrowing and anomalous venous drainage, particularly stenosis or complete nonopacification of the sigmoid/jugular sinus complex in association with collateral venous channels.

Treatment of the underlying cause of the papilledema may involve cranial vault expansion, control of sleep apnea or surgery for hydrocephalus. It must be remembered that the absence of papilledema (particularly in children less than 8 yrs) does not exclude the possibility of intracranial hypertension.

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<tr>
<th>Age Category</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Prenatal</td>
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<tr>
<td>Birth – 12 months</td>
<td>Isolated and syndromic craniosynostosis</td>
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<tr>
<td></td>
<td>• Diagnostic work-up: after diagnosis is made and before and after significant</td>
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<tr>
<td></td>
<td>craniofacial surgery- complete exam to assess for orbital/canthal dystopia, ptosis,</td>
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<tr>
<td>1 year – 9 years</td>
<td>Isolated</td>
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<tr>
<td>Diagnostic work-up: if no ocular abnormalities requiring treatment, then complete exam bi-annually.</td>
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<tr>
<td>Syndromic:</td>
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<tr>
<td>Diagnostic work-up; complete exam every 6-12 months. Consideration given to baseline optic nerve photography for comparison purposes.</td>
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</tr>
<tr>
<td>Treatment Options: Exam schedule may be more frequent depending on severity of visual and ocular abnormality. Treatment options: ptosis surgery, tarsorraphy if indicated, for spontaneous globe luxation or exposure keratopathy, nasolacrimal system and/or canthal surgery when indicated, spectacles for high or asymmetric refractive errors, amblyopia treatment, artificial tears or lubrication for exposure keratopathy, consider strabismus surgery if no impending orbital surgery</td>
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</tbody>
</table>

- Treatment options: Exam schedule may be more frequent depending on severity of visual and ocular abnormality. Treatment options: early ptosis surgery for severe sight threatening ptosis, nasolacrimal system surgery, tarsorraphy if indicated, e.g. for spontaneous globe luxation or exposure keratopathy, spectacles for high or asymmetric refractive errors, amblyopia treatment, artificial tears or lube for exposure keratopathy. Consider strabismus surgery if no impending surgical orbital manipulation.

Syndromic only
- Treatment options: for papilledema-
- Appropriate reconstructive surgery to relieve intracranial crowding, CSF diversion surgery for hydrocephalus, medical or surgical treatment for severe obstructive sleep apnea.
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<th>10 years – through adolescence</th>
<th>Syndromic</th>
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<td>- Diagnostic work-up: complete exam yearly</td>
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OVERVIEW OF KEY INTERVENTIONS BY AGE (all subspecialties)

PRENATAL

<table>
<thead>
<tr>
<th>PROBLEM</th>
<th>INTERVENTION</th>
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<tbody>
<tr>
<td>Craniofacial dysmorphology with or without extremity and visceral</td>
<td>• Consultation (craniofacial surgeon, neurosurgeon, geneticist, maternal-</td>
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<tr>
<td>anomalies identified on screening ultrasound. Gene mutation associated</td>
<td>fetal medicine)</td>
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<tr>
<td>with isolated or syndromic craniosynostosis identified on chorionic</td>
<td>• Family-Patient referrals</td>
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<tr>
<td>villous sampling or amniocenteses.</td>
<td>• Additional imaging for suspected craniofacial anomalies (standardized</td>
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<td></td>
<td>fetal ultrasound protocol +/- fetal MRI for suspected brain malformation)</td>
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<td></td>
<td>• Prenatal counseling - prenatal genetic evaluation</td>
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<td></td>
<td>• Refer to high risk OB / Neonatology</td>
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<td></td>
<td>• Refer to Craniofacial Team</td>
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<td></td>
<td>• Assess financial and insurance resources</td>
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<tr>
<td>PROBLEM</td>
<td>INTERVENTION</td>
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<tr>
<td>Craniofacial dysmorphology</td>
<td>• Participate in the diagnosis and collection of pertinent records (e.g., radiologic imaging, fundoscopic examination, photographs, genetics, psychometric). Distinguish syndromic vs. non-syndromic (birth/first visit)&lt;br&gt;• Early operative treatment for synostosis with elevated intracranial pressure (ICP): 1) craniectomy; 2) total cranial vault remodeling (CVR); 3) anterior or posterior skull expansion&lt;br&gt;• Early operative treatment for selected suture fusion: 1) endoscopic strip-cranietomy +/- external molding; 2) open cranial vault procedure; 3) spring-therapy</td>
</tr>
<tr>
<td>Oral health</td>
<td>• Orthodontists should collect baseline diagnostic records&lt;br&gt;• Oral examination</td>
</tr>
<tr>
<td>Visual and ocular status</td>
<td>• Diagnostic work-up&lt;br&gt;• Treatment options</td>
</tr>
<tr>
<td>Middle ear status, hearing, airway</td>
<td>• Diagnostic work-up (birth–1 month)&lt;br&gt;• Treatment options (birth–1 month)</td>
</tr>
<tr>
<td>General pediatric health</td>
<td>• Repeat brainsteam auditory evoked response (BAER) (birth/first visit)&lt;br&gt;• Pediatric care provider screening</td>
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<tr>
<td>Family’s need for information and psychosocial support and child development</td>
<td>• Family coping and understanding of diagnosis and treatment needs&lt;br&gt;• Address barriers to medical care&lt;br&gt;• Monitor parent-child issues&lt;br&gt;• Neurodevelopmental screening&lt;br&gt;• Referral to parent support groups</td>
</tr>
<tr>
<td>Speech and language development</td>
<td>• Physical assessment of oral and pharyngeal structures&lt;br&gt;• Assess feeding and swallowing with interdisciplinary team.&lt;br&gt;• Assessment of early vocal output and communicative behavior no later than three months</td>
</tr>
<tr>
<td>Imaging</td>
<td>• Single/Non-syndromic CT as indicated</td>
</tr>
</tbody>
</table>
- Complex/Syndromic CT as indicated
- 3DCT as indicated
- MRI [brain, cerebrospinal fluid (CSF), magnetic resonance venography (MRV)] as indicated
## 4 MONTHS – 3 YEARS

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<tr>
<th>PROBLEM</th>
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</table>
| Craniofacial dysmorphology    | • Typical primary operative treatment period: 1) fronto-orbital advancement (FOA) and CVR (4-12 months); 2) strip craniectomy +/- spring-assisted expansion +/- protective helmet (up to 6 months)  
  • FOA with midface distraction osteogenesis (DO) or monobloc DO for severe exorbitism, midfacial hypoplasia with airway issues |
| Hand problems                 | • Begin reconstructive process around 6 months-1 year  
  • Monitor developmental milestones and recommend occupational therapy if necessary  
  Apert Hand  
  • Incision and drainage of macerations and nail bed infections (1-6 months)  
  • Digital separation completed; joint releases completed. (6-36 months) |
| Oral health                   | • Baseline diagnostic records  
  • Oral examination/Caries risk assessment/ Anticipatory guidance (every 6 months or as indicated by risk assessment)  
  • Early midface surgical treatment (planning- i.e., cephalometric analysis; surgical predictions; appliance selection; fabrication and insertion of intraoral appliances; post-surgical follow-up and documentation)  
  • Monitoring dental development |
| Visual and ocular status      | • Diagnostic work-up  
  • Treatment options  
  Nonsyndromic diagnostic work-up: if no ocular abnormalities requiring treatment, then complete exam bi-annually.  
  Syndromic: Diagnostic work-up: complete exam every 6-12 months. |
| Middle ear status, hearing, airway | • Diagnostic work-up |
| General pediatric health      | • Pediatric care provider screening at 1–4 months, 5–11 months, 12 months, 18 months, 24 months, and 36 months |
| Family’s need for information and psychosocial support and child development | • Family coping and understanding of diagnosis and treatment needs  
• Address barriers to medical care  
• Monitor parent-child issues  
• Family coping and understanding of medical treatment plan  
• Neurodevelopmental screening; Early Intervention Services as indicated |
| --- |
| Speech and language development | • Counsel parents on early communication development  
• Assess communication development every six months  
• Reassess feeding and swallowing  
• Begin communication intervention |
| Imaging | • Single/Non-syndromic CT as indicated  
3DCT as indicated  
• Complex/Syndromic CT as indicated  
3DCT as indicated  
MRI (brain, CSF, MRV) as indicated |
## PROBLEM

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<tr>
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| Craniofacial dysmorphology                   | • Secondary cranial vault procedures as necessary  
• Severe midface hypoplasia causing obstructive sleep apnea, corneal exposure keratopathy, craniofacial dysmorphology treated with: 1) monobloc conventional or DO; or 2) subcranial LeFort III conventional or DO  
• Adjunct procedures |
| Hand problems                                | • Apert thumb clinodactyly correction, consider correction of persistent angular deformities, metacarpal synostoses, revisions as needed (4-6 years) |
| Oral health                                  | • Oral examination, caries risk assessment / preventive care (repeated every 6 months or as indicated by risk assessment)  
• Monitor dental development  
• Midface surgical treatment |
| Visual and ocular status                     | • Nonsyndromic: Diagnostic work-up: if no ocular abnormalities requiring treatment, then complete exam bi-annually.  
• Syndromic: Diagnostic work-up: complete exam every 6-12 months. |
| Middle ear status, hearing, airway           | • Diagnostic work-up: Continued ENT follow-up for patients with hearing loss, Eustachian tube dysfunction, myringotomy tubes, sleep apnea, airway issues, tracheostomy dependence, and recurrent ENT infections. (7–18 years) |
| General pediatric health                     | • Annual pediatric care provider screening |
| Family’s need for information and psychosocial support and child development | • Address barriers to medical care  
• Screen for school readiness and academic precursors of learning disability (3-5 years)  
• Monitor school achievement using standardized data  
• Refer for neuropsychological evaluation as indicated  
• Assess emotional and behavioral functioning using standardized instruments (3–8 years) |
| Speech and language development | • If the child is presenting for the first time, complete diagnostic work-up including physical exam of oral and pharyngeal structures, imaging studies if there is any type of resonance or swallowing problem (such studies may include standard radiography, nasopharyngoscopy, or videofluoroscopy), complete perceptual evaluation of speech and language skills  
• Assessment should include evaluation of language comprehension, language competence, phonologic development, feeding and swallowing, and phonetic development |
| --- | --- |
| Imaging | • Single/Non-syndromic CT as indicated  
3DCT as indicated  
• Complex/Syndromic CT as indicated  
3DCT as indicated  
MRI (brain, CSF, MRV) as indicated |
### 9 YEARS – 12 YEARS

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<td>Craniofacial dysmorphology</td>
<td>• Secondary cranial vault procedures as necessary</td>
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<td>Oral health</td>
<td>• Oral examination, caries risk assessment / preventive care (every 6 months or as indicated by risk assessment)</td>
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<tr>
<td></td>
<td>• Phase I orthodontic treatment (6 -15 years)</td>
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<td>• Phase II orthodontic treatment (12-21 years)</td>
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<td></td>
<td>• Presurgical orthodontics (12-21 years)</td>
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<tr>
<td></td>
<td>• Surgical treatment planning</td>
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<tr>
<td></td>
<td>• Complete post-surgical orthodontic treatment (12-21 years)</td>
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<tr>
<td>Visual and ocular status</td>
<td>• Syndromic: Diagnostic work-up: complete exam yearly (9 years – adolescence)</td>
</tr>
<tr>
<td>Middle ear status, hearing, airway</td>
<td>• Diagnostic work-up: Continued ENT follow-up for patients with hearing loss, Eustachian tube dysfunction, myringotomy tubes, sleep apnea, airway issues, tracheostomy dependence, and recurrent ENT infections.</td>
</tr>
<tr>
<td>General pediatric health</td>
<td>• Annual Pediatric Care Provider Screening</td>
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<td>Family’s need for information and psychosocial support and child development</td>
<td>• Address barriers to medical care</td>
</tr>
<tr>
<td></td>
<td>• Assess emotional and behavioral functioning using standardized instruments</td>
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<td></td>
<td>• Monitor school achievement using well standardized data and screen for learning disorders; neuropsychological evaluation should be conducted as indicated</td>
</tr>
<tr>
<td>Speech and language development</td>
<td>• Assessment should include evaluation of all aspects of language development and speech production capabilities</td>
</tr>
<tr>
<td>Imaging</td>
<td>• Single/Non-syndromic CT as indicated</td>
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<td>3DCT as indicated</td>
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<tr>
<td>Craniofacial dysmorphology</td>
<td>• Orthodontic therapy may begin in conjunction with orthodontist in preparation for midface advancement and/or orthognathic surgery</td>
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</tbody>
</table>
| Oral health                                       | • Oral examination, caries risk assessment / preventive care (repeated every 6 months or as indicated by risk assessment)  
|                                                  | • Phase I orthodontic treatment (6-15 years)                                 |
|                                                  | • Phase II orthodontic treatment (12- 21 years)                             |
|                                                  | • Presurgical orthodontics (12- 21 years)                                  |
|                                                  | • Surgical treatment planning                                              |
|                                                  | • Complete post-surgical orthodontic treatment (12-21 years)               |
| Visual and ocular status                         | • Syndromic: Diagnostic work-up: complete exam yearly (9 years – adolescence) |
| Middle ear status, hearing, airway               | • Diagnostic work-up: Continued ENT follow-up for patients with hearing loss, Eustachian tube dysfunction, myringotomy tubes, sleep apnea, airway issues, tracheostomy dependence, and recurrent ENT infections. |
| Family’s need for information and psychosocial support and child development | • Address barriers to medical care                                          |
|                                                  | • Assess emotional and behavioral functioning using standardized questionnaires |
|                                                  | • Assess quality of life for youth and family                              |
|                                                  | • Link child/youth to other youth                                          |
|                                                  | • Support during school absence                                            |
|                                                  | • Monitor school achievement including assessment of vocational planning if indicated |
|                                                  | • Begin to address transition to adult care                                 |
| Imaging                                           | • Complex/Syndromic CT as indicated                                         |
|                                                  | • 3DCT as indicated                                                        |
|                                                  | • MRI (brain, CSF, MRV) as indicated                                       |
## 18 YEARS – ADULTHOOD

<table>
<thead>
<tr>
<th>PROBLEM</th>
<th>INTERVENTION</th>
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<tbody>
<tr>
<td>Craniofacial dysmorphology</td>
<td>• Midface and/or orthognathic surgery</td>
</tr>
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<td></td>
<td>• Adjunct or refinement procedures</td>
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<tr>
<td>Oral health</td>
<td>• Oral examination, caries risk assessment / anticipatory guidance (repeated every 6 months or as indicated by risk assessment)</td>
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<td></td>
<td>• Phase II orthodontic treatment (12-21 years)</td>
</tr>
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<td>• Diagnostic work-up: Continued ENT follow-up for patients with hearing loss, Eustachian tube dysfunction, myringotomy tubes, sleep apnea, airway issues, tracheostomy dependence, and recurrent ENT infections.</td>
</tr>
<tr>
<td>Family’s need for information and psychosocial support and child development</td>
<td>• Address new barriers to care: change in family support, insurance issues, transportation needs, absence from school or work, language and cultural differences</td>
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<tr>
<td></td>
<td>• Assess social, emotional, and behavioral adjustment and readiness for independence</td>
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<td>• Address quality of life issues</td>
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<td>• Assess emotional and behavioral functioning</td>
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<td>• Assess transition to adult care if relevant</td>
</tr>
<tr>
<td>Imaging</td>
<td>• Complex/Syndromic CT as indicated</td>
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<td></td>
<td>• 3DCT as indicated</td>
</tr>
<tr>
<td></td>
<td>• MRI (brain, CSF, MRV) as indicated</td>
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**ACKNOWLEDGMENT**

The development of this document was supported by Grant number 1U50DD000470-01, “Development of Guidelines and Educational Materials for Craniofacial Malformation” from the Centers for Disease Control and Prevention awarded to the National Foundation for Facial Reconstruction (NFFR). The document is the product of the combined efforts of the participants, including the conference and parameters committee and representatives from 16 professional societies, in a consensus conference.
on recommended practices in the care of patients with craniosynostosis, “Craniosynostosis: Developing Parameters for Diagnosis, Treatment, and Management,” and the peer reviewers who suggested revisions to the original draft.

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Syndromic craniosynostosis (~ 20%)
- 40% involves coronal suture
  most have identifiable
  gene mutation
  chromosome aberration
  majority AD
  ~ 50% spontaneous mutations

Non-syndromic craniosynostosis
most are isolated single suture
may have underlying genetic basis

Osteoblast differentiation
• skull development:
  mesenchyme ➔ osteoblasts ➔ osteocytes / osteoids
• complex cascade: FGF, FGFR, bone morphogenic proteins (BMP) and more...

Mutated Genes
• Fibroblast growth factor receptors
  - FGFR 1, FGFR 2, FGFR 3
• Twist homologue 1 (Drosophila) - TWIST 1
• Others – RUNX2, MSX2, IFT122*, WDR 35*, RAB 23
  *Levin syndrome!

FGFR mutations
• Fibroblast growth factor (FGF) signaling
  22 FGFs bind to 4 FGFRs
  initiate downstream signaling

Gain-of-function mutations
enable FGF receptor to become over active
  - suture closure

Twist 1
Transcription factor
basic helix-loop-helix family
negative regulation of FGFR 1, 2, 3 & RUNX 2
**TWIST 1 mutations**

Loss-of-function mutations (haploinsufficiency)
- FGFR uninhibited
- Suture closure

**EFN-B1 (Xq12)**

- Ephrin B1 ligand
- Critical role in control of bone remodeling

**TWIST 1 mutations**

- Saethre-Chotzen
- Isolated coronal synostosis
- Isolated sagittal synostosis

**EFN-B1 mutations**

- Loss-of-function mutations (haploinsufficiency)
- X-linked Craniofrontonasal dysplasia (CFND)
  - Grooved nails, wavy hair, thoracic spine, pterygium...
- Paradoxically, more severe in heterozygous females than in hemizygous males (adverse interaction of two alleles?)

**And many more....**

- RECQL4 Baller-Gerold
- RAD23 Carpenter
- ...and more

**Genetic Testing**

- All syndromic patients
- Non-syndromic patients if coronal/multisuture involvement
- Targeted testing – if dx suspected

**Genetic Counseling**

- No molecular dx and Fanet's negative
- Sibling recurrence risk:
  - Sagittal/multisuture synostosis = 2%
  - Unisutural = ~5%
  - Bicoronal/multisuture = ~10%
- Offspring risk – not well-documented
  - Nonsyndromic sagittal/multisuture/familial = ~5%
  - Bicoronal/multisuture = ~50%

**Genetic Counseling**

- Identified single-gene disorder and parents clinical and DNA normal
- Recurrence (gonadal mosaicism):
  - FGFR mutations: <1%
  - EFNBI mutations: ~10%
  - TWIST mutations: ~2%
Genetic Counseling

Watch out for variable expression
Oculoplastic Considerations in Craniofacial Patients: The Wet and The Dry

AAPOS 2011, San Diego CA
William Rocamora Katowitz MD
Oculoplastic and Orbital Surgery
Assistant Professor of Clinical Ophthalmology
University of Pennsylvania
Children's Hospital of Philadelphia

Disclaimers

I have no financial interests in any of the materials presented in this talk.

Preserving a Healthy Cornea

- Dry Conditions
  - Increased tear evaporation
  - Corneal exposure
  - Abnormal tear secretion
- Wet Conditions
  - Reflexive hypersecretion
  - Decreased tear outflow
  - Agenesis of the tear system
  - Blockage
  - Iatrogenic injury

Amblyopia in CF

Visual Loss in CF Abnormalities


Vision Impairment in CF

- Both dry and wet conditions can impair vision
  - Dry as amblyogenic
    - Decreased tear film
    - Reflexive tearing
    - Pro-inflammatory
  - Wet as amblyogenic
    - Increased tear film
    - Increased tear lake
    - Pro-inflammatory

Preserving a Healthy Cornea
Preserving a Healthy Cornea

Tearing and Amblyopia


A Challenge to Corneal Health and Vision

- Crouzon
- Apert
- Pfeiffer
- Treacher-Collins
- Goldenhar
- Saethre-Chotzen
- Amniotic banding
- Hemifacial microsomia

Indications for Tarsorrhaphy

- Prophylaxis and/or Treatment
  - Shallow orbits
  - Eyelid coloboma
  - Eyelid malposition
    - Lateral canthal dystopia
    - Eyelid retraction, ectropion
  - Corneal disease
  - Neurotrophic keratitis

Timing for Tarsorrhaphy

- Recognizing insufficient eyelid closure
- Severe lagophthalmos
- Orbital insufficiency
- Intra-operative and post-operative prophylaxis

Types of Tarsorrhaphy

- Pharmacologic (Botox)
- Mechanical
  - Glue (Cyanoacrylate)
  - Tape
  - Suture
Suture Tarsorrhaphy

- Temporary
  - Lateral gray line
  - Bolster
  - Margin adhesion
- Permanent
  - Margin adhesion
  - Lamellar integration/fusion

Frost Suture

Central Gray Line

Lateral/Medial Gray Line

Complete Suture Tarsorrhaphy
Improving Tear Outflow
- Improving eyelid position
- Ectropion repair
- Lateral canthopexy
- Nasolacrimal surgery
  - Probing, irrigation and stenting
  - DCR
  - Jones bypass tube

Lateral Tarsal Strip
Oculoplastic Considerations

- Major goal is to preserve vision
- Recognize the risk of corneal disease before aggressively treating tear outflow abnormalities
- Multi-disciplinary approach to better anticipate risks and to time surgical interventions
- Many surgical approaches to protect the cornea

Thank You!

katowitzW@email.chop.edu
THE SYNDROMIC CRANIOSYNOSTOSES: STRABISMUS MANAGEMENT
Brian J. Forbes, MD, PhD
The Children's Hospital of Philadelphia
University of Pennsylvania

Craniosynostosis: Functional Issues
- Elevated intracranial pressure (>15mm Hg)
- Multiple sutural fusion: 42%
- Single sutural fusion: 13%
- Blindness: optic nerve atrophy, corneal exposure
- Abnormalities of the ocular axis and adnexa
- Abnormalities of the airway
- Abnormalities of speech and hearing
- Mental retardation
- Malocclusion

POSTERIOR CRANIAL VAULT RESHAPING
Age 2-6 months.
Periodically done prior to fronto-orbital advancement in the child with severe turribrachycephaly, to decompress the calvarium and prevent worsening of the deformity.

FRONTO-ORBITAL ADVANCEMENT AND RESHAPING IN INFANCY AND CHILDHOOD:
- Provides room for growing brain – 1 year or so of age
- Promotes frontofacial growth
- Protects and decompresses eye/orbit
- Frontal bone and SO rim advancement (one or both sides)

MONOBLOC ADVANCEMENT
- Useful for patients needing adv at the forehead, orbit and midface simul.
- Especially if breathing issues.
- High rate of complications in children older than age 6 years due to contamination from developing sinuses

Le Fort III (midface adv)
- Earliest performed 7-9 YO (after permanent teeth erupt)
- Will need to be repeated at adolescence due to recurrence of midface retrusion.
- Improves:
  - Mid-face retraction
  - Improves exorbitism by advancing the inferior and superior orbital rims, expands the orbital volume
Strabismus Surgery Guidelines

- Consider likelihood for fusion
  - Yes for surgery if:
    - History of fusion which has been lost
    - HT and fusing in AHP
    - Normal neuro status with chances to develop fusion
- Consider cosmesis (ocular and overall)
  - May be low on list of priorities.
- Do not operate before impending craniofacial surgery (Recommended less than 2 years away)

Specific Considerations

- ET and XT treated in standard fashion
- Orbital divergence
  - causes XT
- EOM agenesis or anomaly
  - Look at muscles on the MRI
  - Can be difficult to get done well at institutions unfamiliar with techniques.

Assessment of Extraocular Muscles Position and Anatomy By 3-Dimensional Ultrasonography: A Trial in Craniosynostosis Patients

- The 3D US yielded an acceptably accurate anatomic picture of the eye muscles. Anatomic variations in eye muscles may account for certain strabismic manifestations. Preoperative knowledge of such variations may provide additional information to the surgeon planning the procedure. This especially holds true in the craniosynostosis population in which a muscle that the surgeon was intending to operate on may be absent, malformed, or located in an abnormal position.
- It is less valuable as a tool for determining variations in muscle position.

Etiologies of Motility Disturbances in Craniosynostosis

- Orbital and ocular extorsion,
  - Causes “pseudo IOOA”, “SOUA” and V
- MR – adducts and elevates (simulates IOOA, SOUA)
- SR – elevates and abducts
- LR – abducts and depresses
- IR – depresses and adducts
- Desagitalization (retrusion) of the trochlea - SOUA, secondary IOOA

How to Treat “IOOA” with V Pattern

- Transpose MR down, +/- LR up
  - Treats HTs in side gaze and V pattern
- WR weakening +/- SO strengthening
  - Treats HTs in side gaze and V pattern
- Improves extorsion
- Anteriorization of the IOs
  - Treats HTs in side gaze and V pattern
- May hold the most promise for elimination of “IOOA”

Ocular Overelevation in Adduction in Craniosynostosis: Is It the Result of Excyclorotation of the Extraocular Muscles?

- If we recognize the EOM rotation as an important, or even the primary cause of the overelevation in adduction as is the case in some patients, then direct surgical intervention on the IOLs may be needed. The IOOAs are linked to the excyclorotation of the IOLs, and surgery to fix the IOOAs is more appropriate than surgery to fix the IOLs directly. In these patients, the EOM rotation is a likely cause of the overelevation in adduction.
- Guyton and Weingarten summarized the schools of thought regarding each surgical option in addressing “V” patterns. They highlighted the need to address torsion directly. As extorsion of the globe creates abnormal force vectors on the rectus muscles, some of these abnormal vectors should be eliminated with improvement in the extorsion by shortening the IOs. Guyton and Weingarten went on to emphasize that focal muscle transposition surgery is much more likely to make the extorsion worse.
- There is a significant association radiographically between excyclorotation of the EOM and elevation in adduction in these children.

Anterior and nasal transposition of the IO

- Anterior and nasal transposition of the IO muscle reduces overelevation in adduction and helps eliminate or reduce divergence of the eyes in upgaze, but esodeviation may persist in downgaze. This procedure was most effective in absence of the SO tendon.
- It is likely to benefit patients with severe congenital fourth nerve palsy in which standard IO muscle weakening procedures have been ineffective. Best in absence of SO muscle/tendon.

(Hussein et al. J AAPOS 2007;11:29-33)

Bilateral superior oblique tucks

- Bilateral superior oblique tucks are useful in addressing the excyclotorsion that leads to apparent inferior oblique overaction and V-pattern strabismus associated with craniosynostosis.
- Though frequently underdeveloped or absent.

(Holmes et al. Strabismus. 2010 Sep;18(3):111-5.)

Bottom line

- No one surgery is completely effective for “IOOA” and the V pattern in these pts as these pts have quite variable circumstances.
- Multifactorial causes for the deviation and multiple surgeries may be needed
  - IO weakening with or without ant trans
  - SO strengthening procedures/tucks
  - Vertical offsets of the horizontal muscles w PFS
  - SR muscle translation nasally w a PFS?
Unicoronal synostosis

• HTs
  – Reported that 50-75% of unicoronal synostosis pts will have HT on involved side, most with “IOOA” and less with “SOUA”
  – Also reported is “IOOA” on uninvolved side
• Extorsion of opposite orbit?
Craniosynostoses
• Premature closure of cranial sutures

Syndromic Craniosynostoses
• Apert, Pfeiffer, Crouzon
  – FGFR2 mutation
• Saethre-Chotzen
  – TWIST
• Craniofrontonasal dysplasia
• Unicoronal synostosis
  – FGFR3

Is there a problem with visual loss?
Visual Loss

- Is there a problem?

Risk factors in craniosynostotic syndromes: a review of 141 cases.

- Amblyogenic factors
  - STRABISMUS 70%
  - ANISOMETROPIA 18% > 1 D
  - ASTIGMATISM 40% > 1 D

Prevalence of Abnormal FGFRs in 114 Patients with Craniosynostoses

All Cases Pre-Intervention

Visual Loss ...why?

- Amblyopia
- Exposure keratopathy
- Optic Neuropathy
  - better considered as
  - VISUAL PATHWAY DYSFUNCTION

- FGFR2
- Isomer is KGFR
- Prophylactic lubrication
- Temporising tarsorraphy
Correlation of visual acuity, optic disc appearance and pattern visual evoked potentials in syndromic craniosynostosis pre and post cranial vault expansion.

Alki Liasis, Ken K Nischal, Bronwen Walters, Shafquet Mohammed, Robert Evans, Barry Jones, Andrew Thompson, Richard Elwell, Anthony Towell, David Dunaway


- 8 cases
- 50% showed NO optic disc swelling
- 12% (1 case) showed linear decrease in visual acuity
- All 8 cases trend for the N80 to P100 to decrease in amplitude prior to surgery. The decrease in amplitude was found to correlate with a rise in raised intracranial pressure prior to surgery where measured.
- In all but two cases after vault expansion surgery there was an opposite trend with an increase in the N80-P100 amplitude

**Why should optic nerve not swell?**

- **EXPRESSION OF FGFR-2 AND FGFR-3 IN THE NORMAL HUMAN EMBRYO ORBIT.**
  - Sajid H. Khan, Jonathan A. Britto, Robert D. Evans, and Ken K. Nischal

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Adenoid Tonsillectomy for Visual Dysfunction in Craniosynostosis


Pediatric Neurosurgery, Vol. 41, No. 4, 197 - 200, 2005
**Surveillance Protocol since 2000**
- Aggressive Amblyopia management
- VEP and optic disc appearance
  - Directed Craniofacial surgical intervention
  - Directed ENT intervention including CPAP

**Study**
- Retrospective case note review
- Between 2000 and 2003
- 5 years follow up
- Statistical comparison of VA's obtained with previous published departmental data

**Demographics**
- 60 patients – 25 syndromic
- Mean months of age at presentation was 16.2 (study 1= 23.3)
- Mean new cases per year- 6.25 (Study 1 = 7.05)

**Demographics cont...**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Current Cohort (Study 2)</th>
<th>Study 1 Cohort 2000</th>
</tr>
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<tbody>
<tr>
<td>Apert</td>
<td>28%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Crouzon</td>
<td>32%</td>
<td>10.6%</td>
</tr>
<tr>
<td>Pfeiffer</td>
<td>4%</td>
<td>13.5%</td>
</tr>
<tr>
<td>Saethre-Chotzen</td>
<td>36%</td>
<td>44.7%</td>
</tr>
</tbody>
</table>

**Comparison of Visual Acuity**

Better eye BCVA worse than 0.3 was found in 19% of study 2 cohort, compared to 40% in study 1 cohort.

- Pearson uncorrected \( \chi^2 = 3.891 (p<0.05) \)
Conclusions

- Visual loss in craniosynostosis is multifactorial

- Careful visual surveillance of children with craniosynostosis using the GOSH protocol has led to an improvement in visual acuity