Anatomical Basis of Craniofacial Birth Defects

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Development of the Face I

- 5 facial primordia
  - Frontonasal prominence
  - Paired maxillary prominences
  - Paired mandibular prominences
- Surround primordial mouth (stomodeum)
- Neural crest: source for almost all connective tissues in the face
- Frontonasal prominence forms forehead and nose and a short margin of mouth
- Lower jaw and lip form first
- Nasal placodes (and pit): surrounded by medial & lateral nasal prominences
- Nasal pit remains connected to mouth
- Maxillary prominences grow toward each other, pushing nasal prominences medially

From Moore 1982
Development of the Face II

- Medial nasal prominences merge with each other and with lateral nasal & maxillary prominences
- Nasolacrimal groove: between lateral nasal and maxillary prominences
  - Becomes nasolacrimal duct
  - Duct forms as solid epithelial cord that later canalizes
  - Nasolacrimal duct atresia
    - Failure to completely canalize
    - 6% of newborns
- Intermaxillary segment
  - Merger of medial nasal prominences
  - Gives rise to philtrum, premaxillary bones, primary palate

From Moore 1982
Summary of Facial Development

From Moore 1982

Disruptions in the formation of these prominences leads to facial clefting and other defects.

1. Frontonasal prominence: forehead, dorsum & apex of nose
2. Lateral nasal prominence: sides of nose
3. Medial nasal prominence: nasal septum, philtrum, premaxilla, primary palate
4. Maxillary prominence: upper cheek, most of upper jaw and lip
5. Mandibular prominence: lower jaw, chin, lower lip, lower cheek
Defects of the Frontonasal Prominence

Excess tissue in frontonasal prominence: Frontonasal Dysplasia
• Broad nasal bridge, hypertelorism, cleft nose, median cleft lip
• Can be associated with other defects (e.g. tetralogy of Fallot in Heart

From Carlson 1999
Defects of the Frontonasal Prominence II

Deficient tissue in frontonasal prominence: Holoprosencephaly

- Defective formation of forebrain (prosencephalon) manifests as midfacial defects
- Caused by: excessive alcohol, genes (sonic hedgehog), excessive retinoic acid
- Wide range of facial defects
  - Mild: short, upturned nose; deficient philtrum; arched palate; microcephaly
  - Extreme: medial nasal prominences, intermaxillary process fail to form; absence of nasal septum & ethmoid bone; single nostril (cebocephaly); hypotelorism or even cyclopia with proboscis

From Larsen 1998

From Moore & Persaud 1998
Development of the Palate: 1. Primary Palate

- Palatal development begins in week 5, but weeks 6-9 are most critical
- Formation of intermaxillary segment from merged medial nasal prominences
- Primary palate forms from median palatine process
- Ossifies as the premaxillary portion of the maxilla
Development of the Palate: 2. Secondary Palate

- Lateral palatine processes
  - Ingrowths from maxillary prominences
  - Eventually project horizontally above the tongue
  - Fuse with each other, primary palate, and nasal septum
- Nasal septum
  - Downtgrowth of med. nas. promin.
  - Fusion with lateral palatine processes starts anteriorly, then moves back
- Hard palate
  - Primary palate: premaxilla
  - Lateral palatine processes: maxilla
- Soft palate: unossified portion of lateral palatine processes

From Moore 1982
Cleft Lip & Palate I: Unilateral Cleft Lip

- Cleft lip and cleft palate are related embryologically but are distinct entities
- Cleft lip: 1 in 750; Cleft palate: 1 in 2500
- Effects on appearance, speech, feeding

Unilateral Cleft Lip

- Forms as a persistent labial groove
- Labial groove should disappear as the maxillary prom. fuse with merged medial nasal prominences
- Stretching of epithelium causes tissue breakdown and cleft formation
- Simonart band: bridge of tissue spanning the cleft (arrow below)

From Moore 1982

From Moore & Persaud 1998
Cleft Lip & Palate II: Bilateral Cleft Lip

• Similar to unilateral cleft lip
• Central soft-tissue mass that moves freely

From Moore & Persaud 1998
Cleft Lip & Palate III: Anterior Cleft Anomalies

- Clefting of alveolar process of maxilla as well as lip
- Complete cleft extends to incisive foramen
- Complete bilateral anterior cleft isolates the anterior and posterior parts of the palate
- Result from failure of lateral palatine processes to fuse to primary palate

From Moore & Persaud 1998
Clefts extending through both soft and hard (bony) palate to the incisive fossa
Isolates anterior and posterior parts of palate
Result from failure of lateral palatine processes to grow medially and fuse to each other

From Moore & Persaud 1998
From Moore 1982
From Moore & Persaud 1998
Cleft Lip & Palate V: Complete Cleft Palate

Complete bilateral cleft of the lip and alveolar process of the maxillae with bilateral cleft of the anterior palate and unilateral cleft of the posterior palate

Complete bilateral cleft of the lip and alveolar process of the maxillae with complete bilateral cleft of the anterior and posterior palate

From Moore 1982
<table>
<thead>
<tr>
<th>Type</th>
<th>Embryol. Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anterior Cleft Palate</strong></td>
<td>• Lateral palatine processes fail to fuse with primary palate</td>
</tr>
<tr>
<td><strong>Posterior Cleft Palate</strong></td>
<td>• Lateral palatine processes fail to fuse with each other and with nasal septum</td>
</tr>
<tr>
<td><strong>Complete Cleft Palate (Anterior &amp; Posterior)</strong></td>
<td>• Lateral palatine processes fail to fuse with (1) each other, (2) with nasal septum, and (3) with primary palate</td>
</tr>
</tbody>
</table>

From Moore 1982
### Cleft Lip & Palate VII: Summary II

<table>
<thead>
<tr>
<th>Cleft Lip</th>
<th>Mechanism</th>
<th>Underlying Cause</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>• Hypoplasia in maxillary prom. leading to inadequate contact with medial nasal prom. &amp; intermaxillary segment</td>
<td>• Multifactorial (genetics, teratogens)</td>
</tr>
<tr>
<td></td>
<td>• Due to (1) inadequate migration of neural crest cells; (2) excessive cell death</td>
<td>• Teratogenic drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Anticonvulsants (dilantin)</td>
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<tr>
<td></td>
<td></td>
<td>• Vitamin A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Vitamin analogs: oral anti-acne drug Accutane</td>
</tr>
<tr>
<td>Cleft Palate</td>
<td>• Failure of lateral palatine processes to fuse</td>
<td>• Multifactorial (genetics, teratogens)</td>
</tr>
<tr>
<td></td>
<td>• Due to: (1) inadequate growth; (2) failure to elevate above tongue; (3) excessively wide head; (4) failure to fuse; (5) secondary rupture after fusing</td>
<td>• Genetics: trisomy 13</td>
</tr>
<tr>
<td></td>
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<td>• Teratogenic drugs: anticonvulsants</td>
</tr>
</tbody>
</table>

- Higher incidence of cleft palate in females: may be due to lateral palatine processes fusing about a week later—prolongs sensitive period
**Craniosynostosis**

Definition: premature closure of cranial suture
- Primary craniosynostosis: due to abnormalities of skull development
- Secondary craniosynostosis: due to failure of brain growth and expansion—produces microcephaly

For most workers: “craniosynostosis” = “primary craniosynostosis”

Incidence: 1 in 2000-3000; much more common in males
Mechanism: unknown, perhaps cranial base abnormalities cause dural forces that disrupt normal suture development

Classified on sutures closed
- sagittal
- coronal
- lambdoid

From Sadler 1985
Craniosynostosis

From Moore & Persaud 1998

Scaphocephaly
• Most common form; more common in males
• Premature closure of sagittal suture

Occipital Plagiocephaly
• More common in immobile children
• Premature closure of lambdoid suture on one side

Frontal Plagiocephaly
• Next most common; more common in females
• Premature closure of coronal suture on one side

Trigonocephaly: premature closure of metopic suture

Occipital Plagiocephaly
• More common in immobile children
• Premature closure of lambdoid suture on one side

Trigonocephaly
• Premature closure of coronal suture

From Larsen 1998
References