Common Craniofacial Anomalies: Facial Clefts and Encephaloceles

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Learning Objectives: After studying this article, the participant should be able to: 1. Understand the cause and pathogenesis of facial clefting and encephaloceles. 2. Recognize and classify facial clefts and encephaloceles. 3. Understand the different treatment plans for reconstruction of facial clefts and encephaloceles.

The wide variety of craniofacial malformations makes classification difficult. A simple classification system allows an overview of the current understanding of the causes, assessments, and treatments of the most frequently encountered craniofacial anomalies. Facial clefts and encephaloceles are reviewed with respect to their diverse causes, pathogenesis, anatomical features, and treatments. Approaches to the surgical treatment of these conditions are reviewed. (Plast. Reconstr. Surg. 112: 606, 2003.)

CRANIOFACIAL EMBRYOLOGICAL DEVELOPMENT

Normal embryological development of the human face and cranium was described by Sperber.4 After union of the male and female gametes, the formed zygote rapidly divides to form the morula and subsequently the blastocyst. The primary germ layers of the embryo, namely, the ectoderm and the endoderm, form in the inner cell mass of the blastocyst, with the ectoderm differentiating into cutaneous and neural portions by approximately day 20. At that stage, the neural portion of the blastocyst is called the neural plate; with midline folding of this neural plate, the neural tube is formed.

Of particular importance to the embryological development of craniofacial structures are neural crest cells. The neural crest ectomesenchymal tissue arises from the crests of the neural fold and forms a separate pluripotential tissue layer. Neural crest ectomesenchyme has great migratory propensities and is the major source of connective tissue throughout the body, because translocated neural crest cells differentiate into cartilage, bone, ligaments, muscles, and arteries. Any disruption in the orderly migration and differentiation of these cells can have severe consequences, manifested by congenital defects.5
The first 12 weeks of gestation represent the crucial period of organogenesis, and it is during this period that the majority of congenital craniofacial anomalies are established.\textsuperscript{4,5} The earliest signs of the future face appear at approximately day 23 or 24 of embryonic life, as paired mandibular processes of the first visceral arch. Next, the medial nasal processes combine with the intervening forebrain to form the frontonasal process, which is destined to become the forehead and the dorsum of the nose. The lateral nasal folds separate the olfactory pits from the gradually developing eye region. By the end of the fifth embryonic week, the maxillary and mandibular processes have begun to increase in size but have not yet fused; it is not until the sixth week that definitive jaws are formed. By the end of the eighth week, the face assumes most of the characteristics that make it recognizable as human. The face is derived from five facial prominences that surround the future mouth, namely, the single frontonasal process and the paired maxillary and mandibular processes.

The grooves between these facial prominences usually disappear by day 46 or 47 of gestation, as the processes meet their equivalents from the contralateral side and fuse in the midline. Any persisting groove between meeting or adjoining processes results in a congenital facial cleft. Slavkin et al.\textsuperscript{6} demonstrated that this process of fusion was attributable in part to the ability of preprogrammed cells to differentiate independently and allow normal development.

Causes of Craniofacial Anomalies

Identification of the genetic bases for most craniofacial syndromes has exploded in the past decade, and our knowledge continues to expand. For conditions without an identified genetic pattern of inheritance, four general categories of environmental "cleftogens" have been identified to date, as follows.

- Radiation. Large doses of radiation have been associated with microcephaly.
- Infections. The children of mothers with toxoplasmosis, rubella, or cytomegalovirus infections exhibit increased frequencies of facial clefts.
- Maternal idiosyncrasies. Mothers of children with cleft lips and palates have been noted to exhibit a higher-than-normal incidence of phenylketonuria, and the oculoauriculovertebral spectrum has been observed with unusual frequency among infants with diabetic mothers.\textsuperscript{7} Many studies have suggested maternal factors such as age, weight, and general health as potential causes of malformations.
- Chemicals. Vitamin deficiencies are associated with increased incidences of cleft lips and palates, which may be reduced with vitamin-supplementation diets for the mothers. Vitamin A, its derivatives, and related compounds such as isotretinoin (Accutane; Hoffman-La Roche, Inc., Nutley, N.J.) have been implicated in the development of facial clefting and hemifacial microsomia. Maternal smoking has been demonstrated to be associated with craniosynostosis.\textsuperscript{8}

Other drugs are strongly suspected to be contributors in craniofacial syndromes. Gardner et al.\textsuperscript{9} observed associations between craniosynostosis and exposure to chlorpheniramine, chlordiazepoxide, and nitrofurantoin but no associations with hydantoin, valproic acid, or cocaine.

Facial Clefts

Anatomical Classification

The broad spectrum of anomalies attributable to facial clefting makes classification difficult. In 1976, Tessier\textsuperscript{10} described an anatomical classification system in which a number is assigned to each malformation on the basis of its position relative to the sagittal midline. This system has become internationally accepted and allows concise effective communication among clinicians (Fig. 1).

For orientation, the orbit is divided into two hemispheres; the lower lid, cheek, and lip demonstrate facial clefts, and the upper lid and cranium demonstrate cranial clefts. According to Tessier’s scheme, clefts of the bones and soft tissues do not always coincide and frequently several different clefts coexist. This classification system remains in wide use today because of its accuracy and because it is relatively easy to learn and allows communication with other clinicians. David et al.\textsuperscript{11} demonstrated a complete series of these craniofacial clefts in three-dimensional computed tomographic scans. Clefting may present as a tissue deficiency or a tissue excess. The tissue-deficiency disorders, namely, arhinencephaly and holoprosencephaly, are secondary to failure of embryonic prosencephalon cleavage and of the normal longitudinal split into cerebral hemispheres.
The tissue-excess deformities result from failure of complete tissue development and range from a slight midline notch of the upper lip to severe orbital hypertelorism.

**Embryological Classification**

Van der Meulen et al. attempted to correlate clinical features of disorders with embryological events. They envisioned the craniofacial skeleton developing along a helical course symbolized by the letter S (Fig. 2).

Their scheme uses “focal fetal dysplasia” in preference to “cleft” to describe an arrest in skin, muscle, or bone development and names the dysplastic anomaly on the basis of the areas involved. For malformations characterized by
dysostoses, an additional distinction is made between transformation defects and developmental arrests that occur before fusion of the facial processes.12

In the frontosphenoidal area, dysplasia may manifest as a Tessier no. 9 cleft, a cloverleaf skull or kleeblattschädel deformity, or less often plagiocephaly. Frontal dysplasia is associated with orbital hypertelorism and nasal dysplasia, a widow’s peak, and dystopia of the eyebrow. This area corresponds to Tessier no. 10 and 11 clefts. Interfrontal dysplasia is associated with bone defects with or without encephaloceles, as observed with Tessier no. 0 to 14 clefts. Nasal aplasia with proboscis corresponds to the ethmocephaly or cebocephaly described by DeMyer et al.13 Nasoschizis (Tessier no. 1 cleft) involves deformity of one-half of the nose, with a normal septum and nasal cavity.

The cleft lip produced with medial nasomaxillary dysplasia is usually observed in combination with other deformities. When associated with lateral nasomaxillary dysplasia, it is known as the Morian I, Tessier no. 3, or naso-ocular cleft. The median (Tessier no. 4, Morian II) and lateral (Tessier no. 5, Morian III) oro-ocular clefts are dysplasias of the orbit and maxilla that spare the nose. The deformity known as maxillozygomatic dysplasia is equivalent to a Tessier no. 6 cleft or incomplete Treacher-Collins syndrome. The complete form of Treacher-Collins syndrome is characterized by zygotemporoauromandibular dysplasia and corresponds to Tessier no. 6, 7, and 8 clefts. Temporoauromandibular dysplasia is also known as auromandibular dysostosis, hemifacial microsomia, or first and second branchial arch syndrome.

Maxillomandibular dysplasia is a failure of the maxillary and mandibular processes to fuse, resulting in macrostomia. Mandibular dysplasias, exemplified by the Pierre Robin syndrome, are associated with micrognathia, glossoptosis, and respiratory distress.
Holoprosencephaly

The holoprosencephaly malformation represents a hypoplastic Tessier no. 14 cleft in association with a tissue deficiency or a tissue excess.\textsuperscript{12,13} Cohen and Sulik\textsuperscript{14} presented a modern analytical review of the holoprosencephalic disorders, in which the central nervous system findings and craniofacial anatomical features were discussed, syndromes and associated anomalies were updated, and the differential diagnosis was reviewed.

Elias et al.\textsuperscript{15} reviewed holoprosencephaly and midline facial anomalies in an attempt to redefine their classification and treatment. They noted that true holoprosencephaly encompasses a series of midline defects of the brain and face, with a spectrum of expression. In most cases, holoprosencephaly is associated with severe malformations of the brain that are incompatible with life. At the other end of the spectrum are patients with midline facial defects and normal or nearly normal brain development. With computed tomographic findings and a period of observation, patients who could benefit from surgical treatment can be selected.

Pathogenesis of Facial Clefts

There are two leading theories of facial cleft formation. The classic theory, championed by Dursy\textsuperscript{16} and His,\textsuperscript{17} holds that clefts are caused by the failure of fusion of the facial processes.\textsuperscript{18} In this theory, the face forms as the fingerlike ends of the maxillary processes meet and coalesce with the united paired globular processes beneath the nasal pits. Once epithelial contact is established, mesenchymal penetration completes the fusion and the lip and hard palate are formed. When the sequence is disturbed, clefting occurs.

The mesodermal penetration theory was described by Pohlmann\textsuperscript{19} and Veau\textsuperscript{20} and was later advocated by Stark and Saunders.\textsuperscript{21,22} Proponents of the mesodermal penetration theory think that free-end facial processes do not exist and the face consists of a bilaminar ectodermal membrane, with epithelial seams demarcating the major processes. The mesenchyme migrates into this double wall of ectoderm, penetrates it, and smoothes out the seams. If mesenchymal penetration fails, then the unsupported epithelial wall dehisces and a cleft is produced. The severity of the cleft is
inversely proportional to the success of mesodermal penetration, with different degrees of incomplete and complete clefts (Figs. 3 and 4).

**Treatment of Facial Clefts**

By far the most common craniofacial anomaly is cleft lip/palate, followed by isolated cleft palate as a distant second. The incidence of rare clefts is estimated to be 1.4 to 4.9 cases per 100,000 live births. Reconstruction initially focuses on soft-tissue closure, with excision of all scar within the cleft until normal tissue is reached, followed by meticulous, layered, soft-tissue closure. Because of underlying bony hypoplasia, skeletal reconstruction is often necessary, although it is delayed until the child is older.

Van der Meulen provided a thorough review of the pathological features, causes, and reconstruction of oblique facial clefts. He agreed with Tessier’s principle of combining skeletal and soft-tissue realignment in one major surgical procedure. Resnick and Kawamoto, Galante and Dado, and Fuente del Campo provided specific recommendations for the treatment of unusual facial clefts, on the basis of their respective experiences with Tessier no. 4, 5, and 8 clefts. Tissue expansion and its application in facial clefting were described by Menard et al., who reported soft-tissue closure for eight patients with facial clefts. In summary, the goals of surgical treatment of facial clefts include functional correction of macrostomia, soft-tissue reconstruction of the eyelid to prevent globe exposure, separation of the confluent oral, nasal, and orbital spaces, and aesthetic correction of the deformity.

**ENCEPHALOCELES**

An encephalocele is a protrusion of part of the cranial contents through a defect in the skull. The mass may contain meninges (meningocele), meninges and brain (meningoencephalocele), or meninges, brain, and ventricle (meningoencephalocystocele). Encephaloceles are categorized according to their positions in the skull and can be basal, sincipital, or convexity. The sincipital group can be further divided into frontoethmoidal, interfrontal, and associated with clefts. The frontoethmoidal group can be subdivided into nasofrontal, naseothmoidal, and naseobital types. Boonvisut et al. reviewed the morphological features of 120 skull base defects and classified the defects as involving either a single opening (type I) or multiple openings (type II) between the frontal, nasal, ethmoidal, and orbital bones. The groups were further divided into type IA/IIA, in which the defect was limited to two bones within the area, and type IB/IIB, in which the defect extended laterally to involve adjacent structures (Fig. 5).

The presence of an encephalocele may be detected on antenatal ultrasonograms or with elevated α-fetoprotein levels. The differential diagnosis of frontal midline masses includes encephaloceles, teratomas, gliomas, and dermoids, and high-resolution computed tomographic scans can establish the intracranial component of encephaloceles. In a frontoethmoidal or nasal encephalocele, the cranial defect is in the anterior midline between the frontal bone (preformed in membrane) and the ethmoid process (preformed in cartilage). The craniofacial deformity involves hypertelorism, orbital dystopia, elongation of the face, and dental malocclusion, reflecting the distorting effects on facial bone growth of the extruded intracranial contents.

The pathogenesis of frontoethmoidoencephaloceles is as follows. Early in embryogenesis, diverticula of dura project anteriorly through the fonticulus nasofrontalis (a small
fontanelle between the developing nasal and frontal bones) or inferiorly through the developing frontal bone into the prenasal space. These diverticula may come in contact with skin and adhere to it. Normally, the diverticula regress and the bone closes, creating the normal nasofrontal suture anteriorly and, passing through the skull base just anterior to the crista galli, the foramen cecum. In a frontoethmoidal encephalocele, the diverticulum does not recede and the bone does not close. The causes of encephaloceles are unknown but involve racial, genetic, environmental, and paternal factors. Encephaloceles also occur with a number of craniofacial syndromes.

The worldwide incidence of encephaloceles is one case per 5000 births. In Western Europe, North America, Australia, and Japan, back-of-the-head encephaloceles predominate; of 265 encephaloceles recorded in more than 20 years, 196 were occipital. In Southeast Asia and Russia, however, anterior encephaloceles outnumber posterior encephaloceles in a 9.5:1 ratio. The reason for this discrepancy is unknown (Figs. 6 and 7).

The principles of encephalocele treatment include incision of the sac, amputation of excess tissue to the level of the surrounding skull, closure of the dura, and closure of the skin. David, Forcada et al., and Smit et al. reviewed the spectrum of cranial and cerebral malformations that may occur with frontoethmoidal encephaloceles and discussed the diagnosis and treatment of these deformities. David analyzed the experience of the Australian Craniofacial Unit from 1975 to 1993 and reached the following conclusions with respect to frontoethmoidal encephaloceles. (1) Early complete surgical treatment is indicated to allow the developing brain and eyes to remodel the facial deformity. (2) Intracranial abnormalities are common. (3) Frontoethmoidal encephaloceles differ from other neural tube defects in the absence of a familial pattern and the peculiar geographic distribution. (4) Treatment with a craniofacial technique is best. (5) Established deformities can be effectively treated with craniofacial osteotomies. (6) Most patients exhibit abnormal intercanthal

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**Table 1**

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**Fig. 5.** Type IA and IB skull defects, representing nine subtypes. F, frontal; N, nasal; E, ethmoidal; O, orbital; B, bilateral; C, cephalad (reprinted from Boonvisut, S., Ladpli, S., Sujatanan, M., et al. Morphologic study of 120 skull base defects in frontoethmoidal encephalomeningoceles. Plast. Reconstr. Surg. 101: 1784, 1998).
distances but normal interpupillary and lateral canthal measurements. (7) The frontal sinus region often requires repeat bone grafting, and nasal bone grafts often must be replaced as patients age. (8) Treatment of craniofacial clefts should be postponed until growth is complete. (9) Early treatment of patients with basal encephaloceles is indicated, to prevent further damage and infection. (10) Surgical treatment of extensive basal encephaloceles is complex and probably should be performed through a facial hemisection approach.

Holmes et al. reported their experience with 35 cases of frontoethmoidal encephaloceles. The goals of treatment are (1) urgent closure of open skin defects, to prevent infections and desiccation of brain tissue, (2) removal or invagination of nonfunctional extracranial tissue, (3) watertight dural closure, and (4) total craniofacial reconstruction, particularly avoiding the “long-nose deformity.” To correct the deformity caused by hypertelorism and a long midface, Holmes et al. lower the supraorbital bar by rotating it medially, posteriorly, and downward in the midline, with lateral widening to correct the trigonocephalic deformity. Successful correction is dependent on (1) an understanding of the pathological anatomical features, (2) careful planning of osteotomies and bone movements that correct the entire deformity (including trigonocephaly and the long-nose deformity), (3) nasal reconstruction with a cantilever graft, to avoid the long-nose deformity, (4) skin closure that removes abnormal skin, with careful attention to the positioning of scars, (5) transnasal canthoplasty to reposition the medial canthi, and (6) single-stage surgical treatment, involving craniofacial and neurosurgical expertise.

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Self-Assessment Examination follows on the next page.
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1. REGARDING CRANIOFACIAL ORGANOGENESIS, THE CRUCIAL PERIOD OF DEVELOPMENT TAKES PLACE IN THE:
   A) First 48 hours
   B) First week
   C) First trimester
   D) Second trimester
   E) Third trimester

2. ENVIRONMENTAL CLEFTOGENS IDENTIFIED IN THE DEVELOPMENT OF CRANIOFACIAL ANOMALIES INCLUDE ALL OF THE FOLLOWING EXCEPT:
   A) Radiation
   B) Cytomegalovirus
   C) Isotretinoin
   D) Cocaine
   E) Vitamin deficiency

3. WHICH OF THE FOLLOWING PRINCIPLES OF RECONSTRUCTION OF FACIAL CLEFTING IS LEAST IMPORTANT?
   A) Excision of all scars within the cleft
   B) Initial soft-tissue closure
   C) Meticulous, layered, soft-tissue closure
   D) Immediate skeletal reconstruction
   E) Separation of oral, nasal, and orbital spaces

4. THE CRANIOFACIAL DEFORMITY OF NASAL ENCEPHALOCELE INCLUDES ALL OF THE FOLLOWING EXCEPT:
   A) Hypertelorism
   B) Orbital dystopia
   C) Elongation of the face
   D) Dental malocclusion
   E) Alveolar cleft

5. THE WORLDWIDE INCIDENCE OF ENCEPHALOCELES AMONG LIVE-BORN INFANTS IS:
   A) One in 1000
   B) One in 2000
   C) One in 3000
   D) One in 4000
   E) One in 5000

6. WHICH OF THE FOLLOWING IS AN INDICATION FOR AN EMERGENCY OPERATION AMONG CHILDREN WITH ENCEPHALOCELES?
   A) Bone defect of more than 5 cm
   B) Ulceration of skin with exposure of the brain or dura
   C) Presence of ventricle within the encephalocele
   D) Concomitant presence of a facial cleft
   E) Elevated α-fetoprotein level

To complete the examination for CME credit, turn to page 722 for instructions and the response form.