Cleft Lip and Palate

Mary-Alice Abbott, MD, PhD* Editor's Note: In the recently published article "Causal Attributions of Cleft Lip and Palate Across Cultures" (Cleft Palate Craniofac J. 2013;50[6]:655–661), the authors state that, across the world, culturally held beliefs concerning cleft lip and palate can have deleterious social effects on children and their families. Our readers should keep this in mind as they read the following article.

Joseph A. Zenel, MD Editor-in-Chief

Educational Gap

Physicians should be aware of the potential associated medical problems with orofacial clefts, including airway obstruction, feeding difficulties, speech and language abnormalities, otitis media, and underlying genetic syndromes.

Objectives After completing this article, readers should be able to:

- 1. Understand the role of genetics and environmental factors in the incidence of orofacial clefts.
- 2. Be aware of the availability of special nipples and bottles for feeding some infants with orofacial clefts.
- 3. Recognize the associations between cleft palate and airway issues (Pierre Robin sequence) and palatal dysfunction and otitis media.

Introduction

Oral-facial clefts are a common birth defect, occurring in approximately 1 in 600 US live births. (1) Epidemiologic studies have found that incidence varies according to sex and ethnic background; clefts occur most commonly in Native American and Asian populations and are least common in those with African heritage. Clefts of the lip are associated with a palatal cleft in approximately two-thirds of affected individuals. Cleft lip with or without cleft palate occurs more often in males, whereas isolated cleft palate is seen more often in females; cleft lip with or without cleft palate is more frequent that cleft palate alone.

Etiology and Pathogenesis

Facial development is a complex process. Five structures are involved in the development of the fetal face: the median frontonasal prominence, the paired maxillary prominences, and the paired mandibular prominences, both derivatives of the fetal first branchial arch. Upper lip formation is essentially complete by the sixth week of gestation and requires accurate fusion between the maxillary prominences and the medial nasal tissues, an outgrowth of the frontonasal prominence. Palatal fusion occurs later, between the 5th to 12th weeks of gestation, and proceeds anteriorly to posteriorly, ending with fusion of the uvula. Palatal development involves primary and secondary palatal structures. The primary palate (medial palatine process) is derived from the fused medial nasal tissues and forms the philtrum, part of the alveolus, and the most anterior segment of the hard palate. The secondary palate is derived from swellings of the maxillary prominence (the lateral palatine processes) and forms the hard palate, the soft palate, and uvula. When the accurate coordination of these

*Department of Pediatrics, Division of Medical Genetics, Tufts University School of Medicine, Baystate Medical Center, Springfield, MA.

Author Disclosure Dr Abbott has disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/ investigative use of a commercial product/ device. developmental processes fails, orofacial clefts can result. Understanding of the complex genetic and cellular mechanisms required for normal orofacial development remains limited.

Clinical Characteristics

Orofacial clefts are categorized by their location and by descriptive terms, such as *unilateral*, *bilateral*, or *midline* and *complete*, *incomplete*, or *submucus*. Clefts can involve the nasal tip, philtrum, lip, lip vermillion, alveolus (gum), hard palate, soft palate, or uvula. Less common are facial clefts, such as eyelid coloboma (a feature of craniofacial microsomia syndrome), and oblique facial clefts, which extend from the upper lip to the inner canthus of the eye, following the course of the lacrimal duct. This rare cleft involves the line of fusion along the maxillary process and lacrimal nasal fold tissues.

Differential Diagnosis

Clefts occur in 2 categories: syndromic or isolated. Syndromic clefts are typically accompanied by abnormalities in other developmental fields or organ systems (eg, skeletal, craniofacial, and eye). Syndromes associated with clefts have many origins, including intrauterine exposures and genetic disorders. Prenatal exposure to alcohol, antiepileptic drugs (phenytoin and others), isotretinoin, cigarette smoking, maternal diabetes, and low folic acid have all been linked with the development of oral-facial clefts. Genetic causes of clefts range from aneuploidy (abnormal number of chromosomes, such as trisomy 13) and microdeletion syndromes, including 22q11.2 deletion syndrome or velocardiofacial syndrome, to single-gene disorders, such as van der Woude syndrome, ectodermal dysplasia and clefting syndromes, Stickler syndrome, Smith-Lemli-Opitz syndrome, and Treacher Collins syndrome.

Genes play a role in the formation of isolated clefts, but in contrast to syndromic clefting, the occurrence of isolated clefts is due to complex or multifactorial inheritance. Numerous factors interact to support or disrupt the complex embryologic development of craniofacial structures, and a complex interaction of genetic, environmental, and unidentified factors leads to the expression of a cleft. Genetic syndromes can be a factor in craniofacial clefts; however, the clefting is an isolated finding in twothirds of individuals with cleft lip with or without cleft palate and in half of individuals with cleft palate only.

Diagnostic Approach

For any infant with an orofacial cleft, the pediatrician must first determine the nature and extent of the cleft and then determine whether the clefting is isolated or syndromic. This evaluation is relatively straightforward but must be rigorous and thorough because it reveals vital information about prognosis and risk of recurrence. Typically, the most effective evaluation is accomplished in consultation with a geneticist and collaboration with a craniofacial team. History should include a careful family history of clefts and other features of clefting syndromes, such as skin disorders, speech abnormalities, or other craniofacial abnormalities. Any history of prenatal exposures should be elicited (alcohol, cigarettes, medicines).

A careful examination for clefts is essential in all neonates, with consideration for neonatal transfer to a specialty center as needed for respiratory or nutritional support and/or assessment and treatment of other associated anomalies. Careful visualization and palpation of the hard and soft palate are necessary to identify a bifid uvula or submucous cleft of the soft palate. Palatal clefts are more likely to be syndromic than cleft lip or cleft lip and palate. The presence or absence of lip pits, eyelid coloboma, or dysmorphic facial features should be noted. Some palatal clefts are associated with Pierre Robin sequence (the triad of palatal cleft, micrognathia, and airway obstruction or glossoptosis). Pierre Robin sequence is important to identify because affected neonates are at high risk of airway obstruction and need close monitoring. Vision and hearing assessments should be conducted as early as possible.

Management, Therapy, and Follow-up

Most centers use a team-based approach for the management of craniofacial problems. Team members may include specialists in plastic surgery, oral and maxillofacial surgery, dentistry, orthodontics, otolaryngology, neurosurgery, genetics, nutrition, and child development. Multidisciplinary teams are poised to address the clinical problems that accompany clefts, including speech, middle ear disease and hearing, and dental. The challenge faced by the craniofacial team is to achieve optimal outcomes for both function and cosmesis. Lip clefts are usually repaired at approximately 10 weeks of age. Palatal clefts are repaired later; closure is usually completed between ages 9 months and 1 year. The benefits of early closure (speech development) are weighed against the risks of infant and complications related to earlier repair (eg, fistula formation). Because a crucial outcome measure for repair is speech, close attention is paid to the functionality of the levator musculature. There are now excellent online resources available to parents, including preoperative and postoperative photographs that can help them

understand the staged approach to craniofacial cleft repairs and to manage expectations.

Many parents are concerned about feeding their newborn with a cleft. Breastfeeding can be successful in many cases of isolated cleft lip, but direct breastfeeding is rarely successful as the sole means of feeding an infant with cleft palate. The presence of a cleft palate prevents an infant from effectively creating suction, despite having normal suck and swallow reflexes. Access to a high-quality breast pump is important for mothers who want to provide their infants with all the benefits of breast milk. There are a variety of special nipples available to facilitate feeding infants with clefts; some are assisted-delivery bottles, whereas others are not. Because of increased air intake while feeding, infants with a cleft require more frequent burping. It is helpful to place the infant upright for feeding and monitor the pattern of sucking and swallowing, followed by a breath. Nasal regurgitation is common when there is a palatal opening or dysfunction, and this does not herald choking. The treatment of gastroesophageal reflux disease can help prevent airway inflammation in infants with Pierre Robin sequence. Growth and nutrition must be carefully monitored while feeding techniques are established. Detailed information about feeding methods is available in the Cleft Palate Foundation publication "Feeding Your Baby."

Children with palatal clefts are at substantially increased risk for eustachian tube dysfunction, recurrent otitis media, and conductive hearing loss. Serous otitis media with effusion is virtually universal in children with palatal clefts; therefore, tympanostomy tubes are routinely placed at the time of palatal repair. Audiology evaluations should occur on an annual or semiannual basis for any child with a palatal cleft, and referral to an early intervention developmental program for speech therapy should occur as soon as possible. Submucous clefts and velopharyngeal insufficiency are part of the spectrum of palatal clefts and can be associated with syndromes; a bifid uvula can be associated with a submucous cleft palate, velopharyngeal insufficiency, and middle ear effusion. Children with these more subtle palatal problems should receive a complete evaluation so that appropriate speech therapy, and in some cases surgical repair, can be pursued and the best possible outcome ensured.

In addition, children with clefts are at increased risk for the psychosocial problems associated with any atypical physical trait. They often display hypernasal speech or other speech abnormalities that may elicit teasing from peers. Social work intervention and family support groups are an important component of care for both the child with a cleft and the family. A forthright approach by family members, as well as adequate preparation for the child with strategies for dealing with potential negative social interactions, is important for promoting successful psychologic and social adjustments. Cleft lip or palate parent support groups are strong advocates.

Additional Considerations

Recurrence Risk

Family members of an individual with a cleft may predictably have questions regarding their chance of conceiving a child with a cleft. To provide families with accurate recurrence risks, the etiologic basis of the cleft must be investigated. Many syndromes associated with clefting are inherited in an autosomal dominant pattern, with variable penetrance. In these cases, each offspring of an affected individual has up to a 50% chance of inheriting the syndrome. In sharp contrast, the recurrence rate of isolated clefts is low. The chance that unaffected parents of a child with a cleft will have another child with a cleft is estimated to be from 2% to 6%: cleft lip with or without cleft palate has a different rate of recurrence than cleft palate alone. The risk increases with the number of affected individuals in the family and decreases with the distance of relatedness.

Prenatal Diagnosis and Prevention

The availability and increased use of fetal ultrasonography have led to a prenatal diagnosis of many birth defects, including oral-facial clefts. Some, but not all, clefts can be diagnosed antenatally by ultrasonography, yet in many instances a cleft, particularly a palatal cleft, is first identified in the delivery room and can be quite unexpected. Some syndromes associated with clefts (eg, trisomy 13) can be diagnosed prenatally, but most syndromes cannot. Level 2 ultrasonography is frequently offered to women who themselves were born with a cleft or who have a first-degree relative with a cleft. Folic acid supplementation (from preconception until the transition to prenatal vitamins) is recommended to all women of reproductive age and for women at increased risk in particular because some data suggest that folic acid deficiency is a contributing factor to clefting.

Summary

- On the basis of strong evidence, orofacial clefts are birth defects identified in approximately 1 in 600 US births, an estimate supported by a recent epidemiologic study of birth defects. (1)
- On the basis of strong evidence, a cleft may be an isolated anomaly or part of an underlying genetic syndrome, usually associated with other abnormalities.

- In a newborn with a cleft whose airway is secure, the first important clinical issue is feeding.
- There are a number of techniques and interventions that clinical experience has found to be useful in establishing early nutrition.
- It is also important to recognize the association with mandibular hypoplasia or micrognathia and upper airway obstruction, such as in Pierre Robin sequence.
- Other problems include speech, hearing, middle ear effusion, and dental issues.
- It is important to recognize more subtle forms of cleft, such as bifid uvula and submucous cleft palate (an apparently intact palate with underlying defects in the bony and/or muscular components of the palate), which can be associated with velopharyngeal insufficiency and middle ear disease.

Resources for Providers and Families:

FACES: The National Craniofacial Association (http://www.faces-cranio.org)

The Cleft Palate Foundation (http://www.cleftline. org/)

Reference

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Additional Reading

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NOTE: Learners can take Pediatrics in Review quizzes and claim credit online only at: http://pedsinreview.org.

- 1. You are examining an infant in the newborn nursery and note a cleft palate. Of the following genetic syndromes, you should give HIGHEST consideration to:
 - A. Neurofibromatosis.
 - B. Noonan syndrome.
 - C. Russell-Silver syndrome.
 - D. Trisomy 21.
 - E. Velocardiofacial syndrome (22q11.2 deletion syndrome).
- 2. You are discussing incidence of cleft lips and palates with parents at a prenatal visit. Among the following, you are MOST likely to say:
 - A. Cleft lip with or without cleft palate is more frequent than cleft palate alone.
 - B. Cleft lip with or without cleft palate occurs more often in females.
 - C. Clefts occur most commonly in African American populations.
 - D. Isolated cleft palate is seen more often in males.
 - E. Orofacial clefts are relatively uncommon, occurring in approximately 1 in 5000 US live births.

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- 3. A mother brings her 2-week-old son with a cleft palate in for well-child care. Of the following, the statement you are MOST likely to make when counseling the mother is:
 - A. Infants with a cleft require less frequent burping.
 - B. Children with clefts do not have normal suck or swallow reflexes.
 - C. Direct breastfeeding is rarely successful as the sole means of feeding an infant with a cleft palate.
 - D. Special nipples are useful to facilitate feeding this child.
 - E. Use of a breast pump should be discouraged to maximize the infant's oral training at the breast.
- 4. You are seeing a 6-month-old girl for well-child care and note an isolated bifid uvula. Among the following, you should evaluate the child for:
 - A. Eyelid coloboma.
 - B. Otitis externa.
 - C. Pierre-Robin sequence.
 - D. Submucous cleft palate.
 - E. Upper airway obstruction.
- 5. A 10-month-old infant from your practice is about to undergo repair of her cleft palate. At the time of her surgical repair under anesthesia, you should anticipate that the child will MOST likely also undergo:
 - A. Central venous catheter placement for hyperalimentation.
 - B. Dental examination.
 - C. Percutaneous endoscopic gastrostomy.
 - D. Tracheostomy.
 - E. Tympanostomy tube placement.

Parent Resources from the AAP at HealthyChildren.org

- http://www.healthychildren.org/English/family-life/health-management/pediatric-specialists/Pages/What-is-a-Pediatric-Plastic-Surgeon.aspx
- Spanish: http://www.healthychildren.org/spanish/family-life/health-management/pediatric-specialists/paginas/what-isa-pediatric-plastic-surgeon.aspx
- http://www.healthychildren.org/English/health-issues/conditions/developmental-disabilities/Pages/Congenital-Abnormalities. aspx
- Spanish: http://www.healthychildren.org/spanish/health-issues/conditions/developmental-disabilities/paginas/congenital-abnormalities.aspx

Cleft Lip and Palate Mary-Alice Abbott Pediatrics in Review 2014;35;177 DOI: 10.1542/pir.35-5-177

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