Cleft Lip and Palate Malformations

5

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Abstract

This chapter describes the embryology and development of cleft lip and palate deformities in children. Schematic figures and clinical photographs illustrate the more common anomalies and surgeries used to correct these malformations.

Keywords

Cleft lip • Cleft palate • Embryology of oral cavity • Congenital oral malformations

Embryology

The formation of the face begins early in fetal development. The early oral pit, or stoma, is apparent at approximately 4 weeks of age. The facial structures continue to rapidly develop in the ensuing weeks. The nasal placodes are present laterally with the development of medial and lateral nasal prominences during the fifth week of development. During the sixth week, the medial nasal processes join in the midline to form the nasal tip, columella, prolabial segment, and primary palate. The maxillary prominences join with the lateral aspect of each medial nasal process to form the lateral components of the upper lip (Fig. 5.1). During this time, the secondary palate begins to form. Bilateral vertical outgrowths from the maxillary prominences develop during the sixth week. The paired palatal shelves, which initially are vertically oriented, rotate to a transverse position over the following 2 weeks. Once the shelves assume a horizontal orientation (eighth week), they begin to fuse in the midline, a process that is complete by 12 weeks gestation (Fig. 5.2). Thus, by week 8, the lips, primary palate, and secondary palate have all obtained their initial morphology [1]. The classic theory on the formation of a cleft lip holds that during week 6, the medial nasal processes fail to fuse with the maxillary prominences resulting in a cleft of the lip and/or primary palate [2, 3]. Failure of fusion of the palatal shelves during the eighth week

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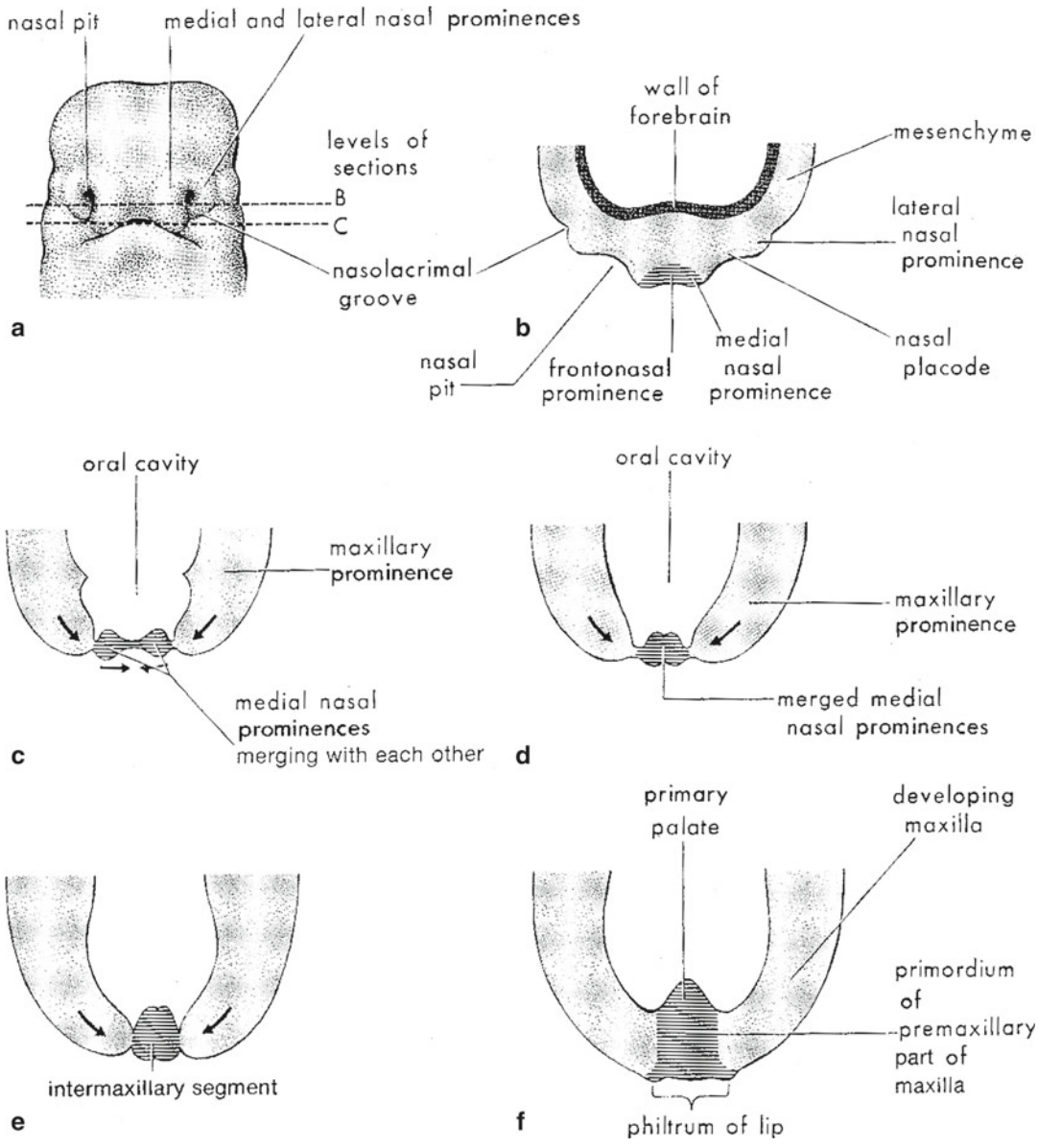

Fig. 5.1 Embryologic development of the lip (from Moore KL, Persaud TVN. *The Developing Human: Clinically Oriented Embryology*, 5th ed. Philadelphia: W.B. Saunders; 1993. Copyright Elsevier 1993)

results in a cleft of the secondary palate. A second theory of cleft pathogenesis invokes a failure of mesodermal penetration. This theory holds that the medial nasal processes and maxillary processes join but, due to a lack of mesoderm within this union, the processes are unable to maintain their fusion, resulting in breakdown and cleft formation [4].

Definition

Due to their differing embryologic development, cleft lip with or without cleft palate (CL/P) is an entity distinct from isolated cleft palate (CP). Clefting of the lip and primary palate results from incomplete fusion of the maxillary and medial

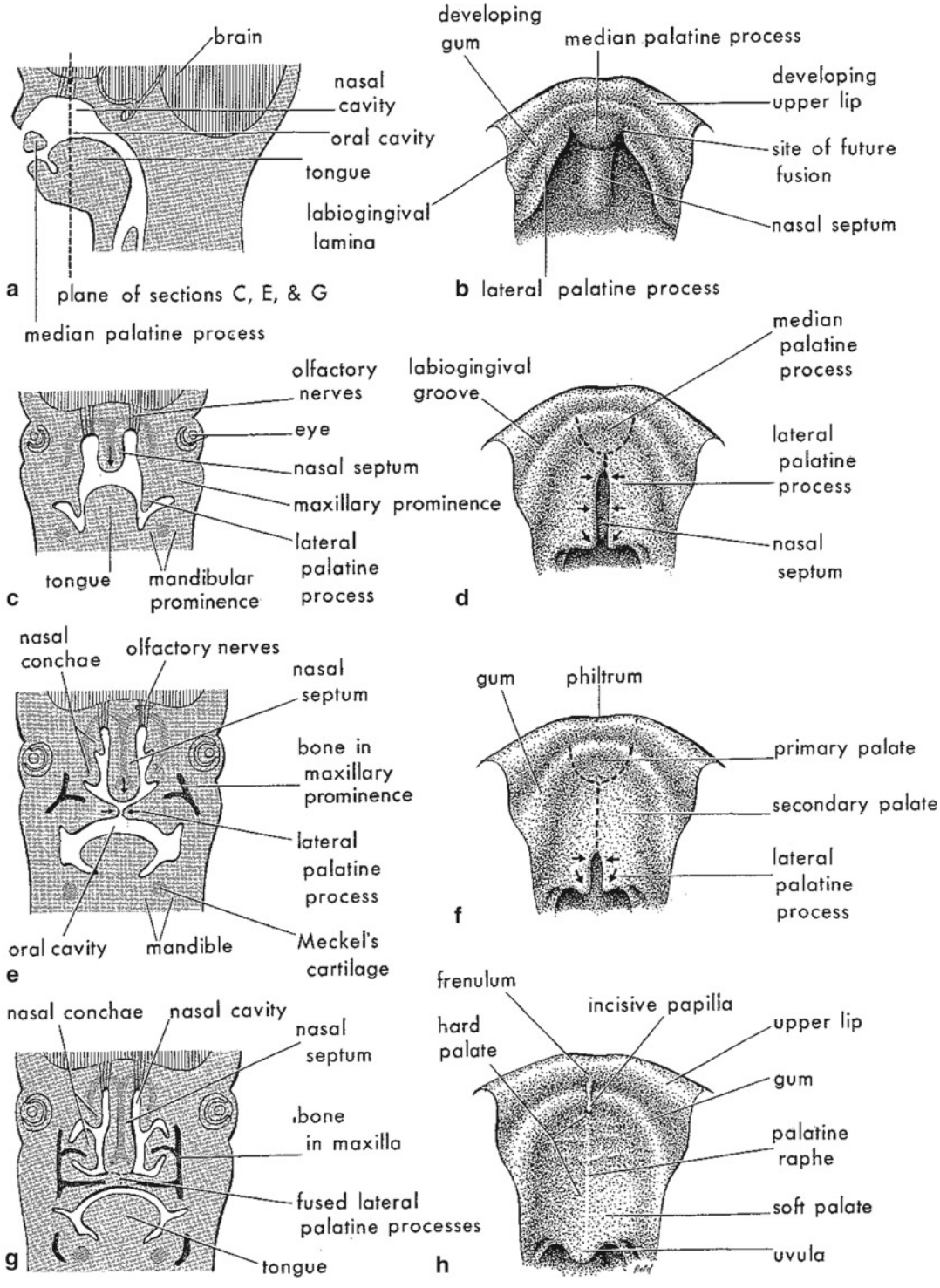

Fig. 5.2 Embryologic development of the palate (from Moore KL, Persaud TVN. *The Developing Human: Clinically Oriented Embryology*, 5th ed. Philadelphia: W.B. Saunders; 1993. Copyright Elsevier 1993)

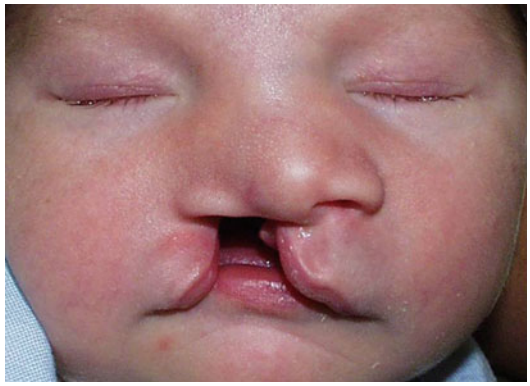

Fig. 5.3 Complete unilateral cleft lip and palate

nasal processes, whereas clefting of the secondary palate results from failure of fusion of the palatal shelves. Cleft lip/palate may be defined by the laterality of clefting (left, right, or bilateral) or by whether the cleft is incomplete or complete. In a complete cleft lip, no tissue connects the medial and lateral lip segments (Fig. 5.3). In an incomplete cleft of the lip, a band of tissue of variable width (Simonart's band) connects the medial and lateral lip segments in the superior portion of the lip (Fig. 5.4). Clefting of the secondary palate occurs from the incisive foramen posteriorly and may involve the soft palate alone or both the soft and hard palate (Fig. 5.5). A submucous cleft palate is identified as a bifid uvula, notching of the posterior hard palate, and a zona pellucidum within the soft palate [5] (Fig. 5.6). In a submucous cleft palate, the mucosa of the soft palate is intact but the muscular levator sling is disrupted, with the levator veli palatini aberrantly inserting onto the posterior edge of the hard palate.

Incidence

Cleft lip/palate has variable incidence depending upon race and gender of the patient. The relative occurrence of CL/P is a 6:3:1 ratio of left: right: bilateral. Cleft lip/palate is more common in males compared to females. Race plays a role in the incidence of CL/P as well, with Native Americans and Asians having the highest

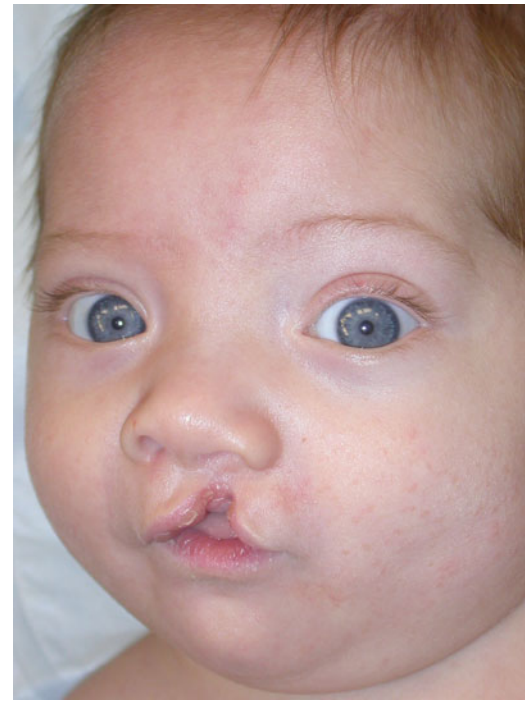

Fig. 5.4 Incomplete unilateral cleft lip and palate

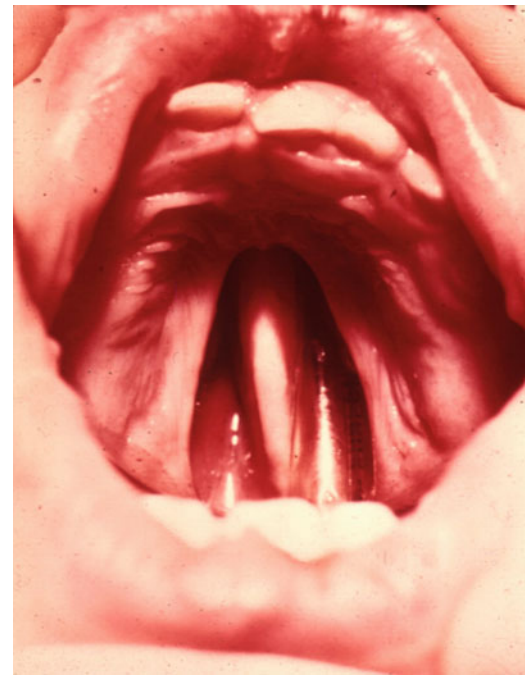

Fig. 5.5 Cleft of the secondary palate

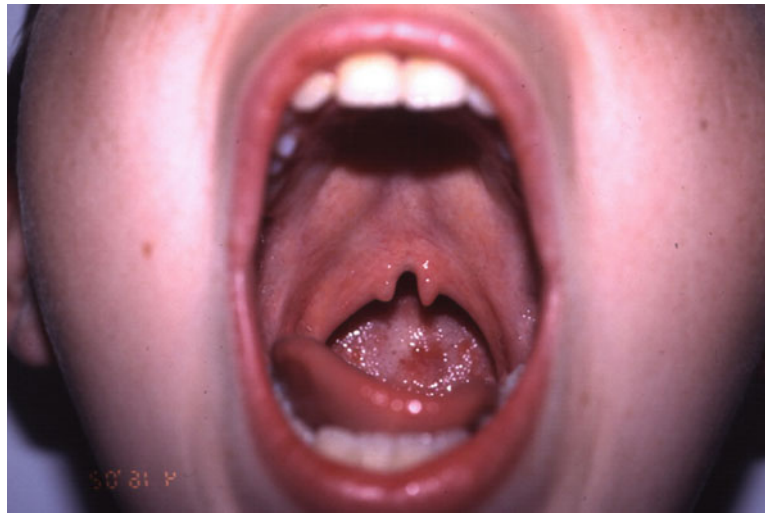

Fig. 5.6 Submucous cleft palate

incidence (3.6 and 2.1 per 1,000 live births, respectively). The incidence of CL/P in Caucasians is 1.0 per 1,000 live births, and that in African Americans is 0.5 per 1,000 live births [6]. Unlike CL/P, isolated cleft palate has a uniform incidence across all races (0.5 per 1,000 live births). CP occurs more frequently in females than in males.

History

The first cleft lip repair to appear in the world's literature was that performed by a Chinese surgeon on a poor farm boy in the fourth century AD. The patient, Wei Yang-Chi, would later become the Governor General of six Chinese provinces, an extraordinary historical testament to the social impact of cleft surgery. For more than a millennium thereafter, cleft lip surgery did not advance much beyond simple cauterization or paring of the cleft edges with simple approximation of the lip segments. Attempts to restore adequate lip length began with the use of curved incisions, as first described by von Graefe and later by Rose and Thompson, and later progressed to the use of rectangular (LeMesurier) and later triangular (Tennison and Randall) flaps from the lateral lip. The rotation-advancement technique, introduced by Millard in 1955, was based on the understanding that the entire Cupid's bow is invariably present on the medial lip segment and is rotated superiorly. Downward rotation of the entire philtral complex, noted Millard, levels the Cupid's bow and opens a gap in the superior lip into which a flap derived from the lateral lip element may be advanced. The rotation-advancement technique has been modified by many cleft surgeons since its introduction and remains widely used throughout the world.

The first anecdotal report of cleft palate repair in 1766 is attributed to LeMonnier, a French dentist. He simply placed several sutures across the cleft, cauterized the mucosa along the cleft margin, and then tied the sutures. In 1819, Dr. Philibert Roux reported repair of the cleft soft palate of a Canadian medical student named John Stephenson. Bernard von Langenbeck is credited with first describing closure of hard palatal clefts by elevating full-thickness mucoperiosteal flaps in 1861. His technique of raising the mucoperiosteum from the posterior edge of the cleft hard palate to the posterior aspect of the alveolus is still commonly used today in the procedure that bears his name (Fig. 5.7a–c). In the early twentieth century, cleft palate surgeons began to focus

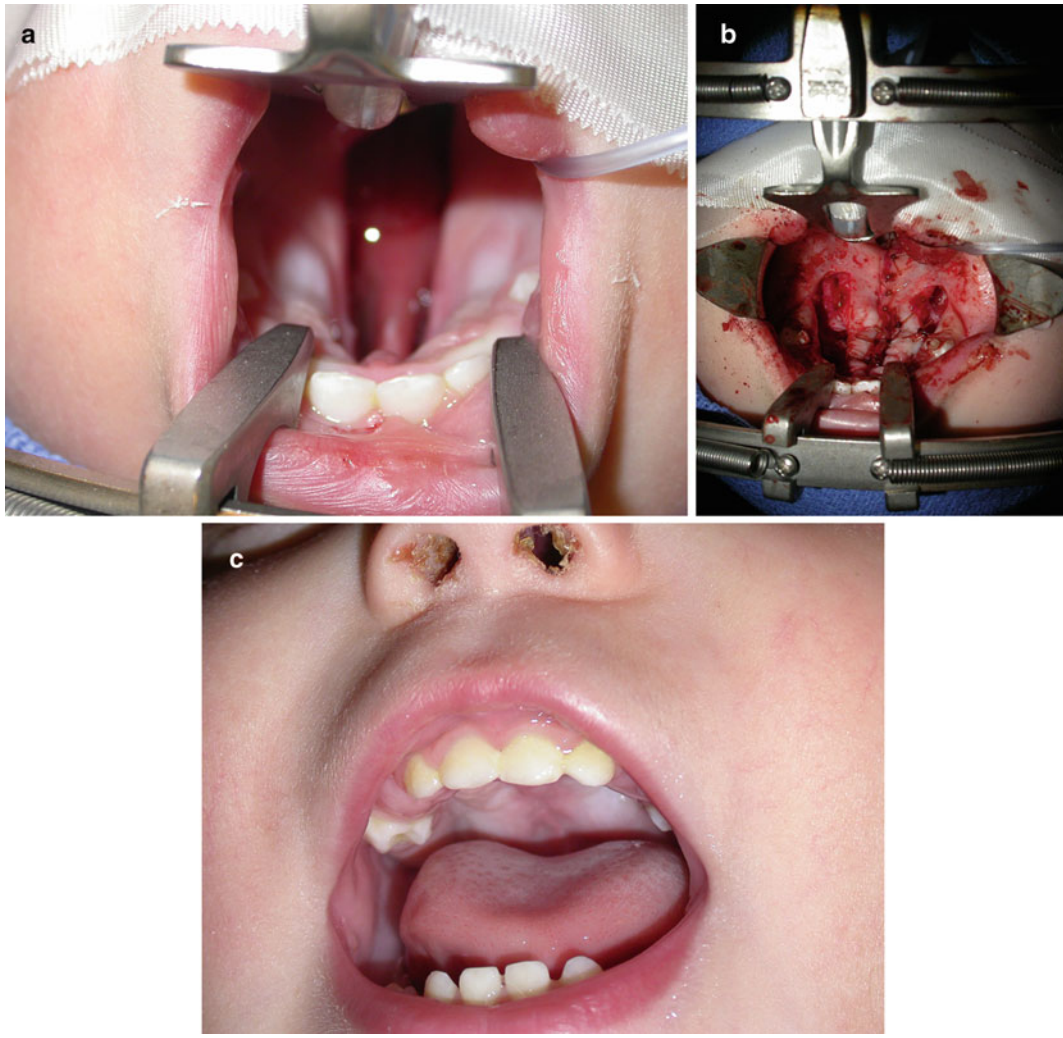

Fig. 5.7 (**a**–**c**) Von Langenbeck cleft palate repair (**a** and **b** demonstrates the surgeon's view from the top of the stretcher with the patient lying supine.)

their attention on means by which to improve speech outcomes by lengthening the palate at the time of repair. The most popular of these techniques, the V–Y pushback technique described by Wardill, and Kilner, remains in widespread use today. In 1978, Leonard Furlow of the University of Florida first described a novel technique of velar repair utilizing opposing mirror-image Z-plasties of the oral and nasal mucosa. The technique offered several advantages over straight-line techniques. Use of Z-plasty closure provided for palatal lengthening without the need for pushback procedures, and transposition of the posteriorly based myomucosal flaps reoriented the levator muscle bundles into anatomical position, reconstructing the levator sling [7] (Fig. 5.8a, b).

Heredity

Genetic analyses have shown that nonsyndromic cleft lip with or without cleft palate has complex inheritance patterns, and there is substantial data to support an etiologic role for genetic factors. Although segregation analysis has provided significant insights, the mode of inheritance for nonsyndromic orofacial clefts remains uncertain.

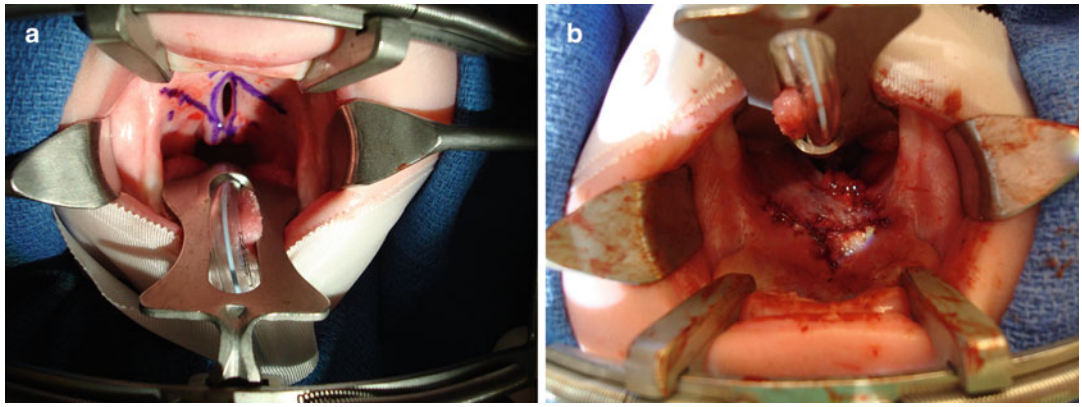

Fig. 5.8 (**a** and **b**) Furlow cleft palate repair (surgeon's view from the top of the stretcher)

It is widely believed that cleft lip with or without cleft palate is a heterogeneous disorder and that 3–20 genes may interact with one another and/or with environmental factors to produce orofacial clefting [8, 9]. Certainly, a family history is one of the strongest risk factors for cleft lip/palate and cleft palate alone. The risk of cleft lip/palate in first-degree relatives is approximately 4 %, increasing to 10 % when two first-degree relatives are affected. For cleft palate alone, the overall risk in first-degree relatives is approximately 2 %, increasing to 8 % when two first-degree relatives are affected [10].

Etiology

As noted above, there is clear evidence for a genetic etiology of nonsyndromic orofacial clefting. In addition, several environmental factors have been implicated, including pharmacologic agents (retinoids, anti-convulsants, folate antagonists, benzodiazepines, and corticosteroids), maternal diseases (diabetes mellitus), and maternal smoking.

Associated Conditions

Understanding the conditions associated with syndromic orofacial clefts are essential to proper clinical management. Over 400 distinct syndromes associated with orofacial clefts, some quite rare, have been described. Associated abnormalities are seen in 25–35 % of clefts of the lip with or without cleft palate in the fetal and newborn period, and yet only 10–15 % of older children with cleft lip with or without cleft palate have associated defects, indicating that many infants with associated severe malformations do not survive infancy [11, 12]. The most common syndrome associated with cleft lip with or without cleft palate is van der Woude syndrome, an autosomal dominant condition most often caused mutations in interferon inhibiting factor 6 (IRF6) [13]. In addition to orofacial clefts, the syndrome often presents with hypodontia and lower lip pits (Fig. 5.9). CHARGE Association (coloboma, heart defect, atresia choanae, retarded growth and development, genital anomalies and hypogonadism, and ear anomalies and deafness), an autosomal dominant condition most often associated with mutations in CHD7, is the second most common syndrome associated with cleft lip with or without cleft palate [14].

In contrast to clefts of the lip with or without cleft palate, the incidence of associated anomalies in infants with cleft palate alone is approximately 50 %. Clefts of the palate alone may be associated with Pierre Robin sequence, a constellation of anomalies including microretrognathia, glossoptosis, and upper airway obstruction (Fig. 5.10). Roughly half of all cases of Robin sequence are syndromic. Of the syndromes associated with cleft palate alone, Stickler syndrome is the most common (5 %), and Stickler

syndrome accounts for nearly half of all syndromic cases of Robin sequence. The syndrome is an autosomal dominant disorder caused by mutations in the genes that code for either type 2 or type 11 collagen [15]. Affected patients often present with a flattened midface, myopia, hypotonia, and joint laxity (see Fig. 1 in Chap. 1). The second most common syndrome associated with cleft palate is 22q11.2 deletion syndrome (velocardiofacial syndrome, DiGeorge syndrome), a disorder characterized by short palpebral fissures and hooded eyelids, a broad nasal root, hypoplastic alae, external ear anomalies, conotruncal cardiac defect, immune deficiency, and velopharyngeal dysfunction [16] (see Fig. 3 in Chap. 1).

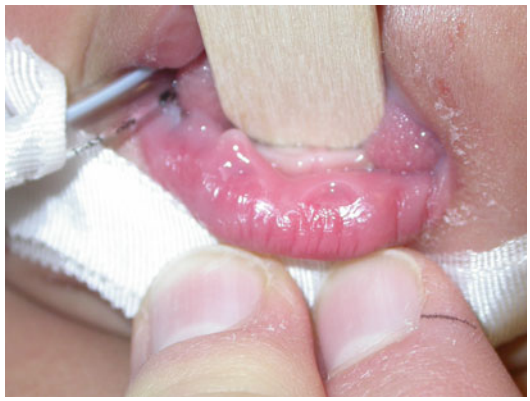

Fig. 5.9 Lip pits in van der Woude syndrome

Clinical Features

There is wide variability in cleft severity (Figs. 5.11, 5.12, 5.13, 5.14, and 5.15) Clefts of the lip with or without cleft palate may be complete (the cleft extends through the entire lip and into the nasal floor) or incomplete (a bridge of tissue remains in the upper portion of the lip). Such clefts may or may not involve the maxillary alveolus and the palate. Incomplete clefts may vary from microform types to more typical patterns. Isolated palatal clefts may involve the levator muscle alone (submucosal clefts), the muscle and mucosa of the velum alone, or the entire thickness of the velum and hard palate.

Some degree of nasal deformity accompanies all clefts of the lip, again varying from minor to severe. In the unilateral cleft, the ala is flattened and posterolaterally displaced. The septum of the nose tends form a C shape with the caudal end

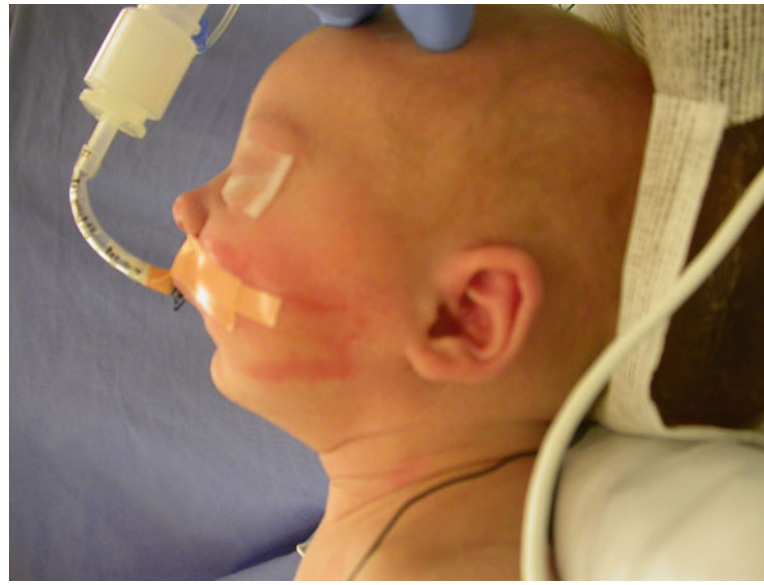

Fig. 5.10 Infant with Pierre-Robin sequence

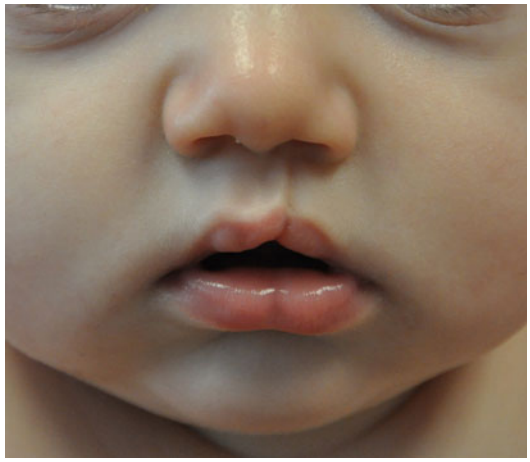

Fig. 5.11 Microform cleft lip

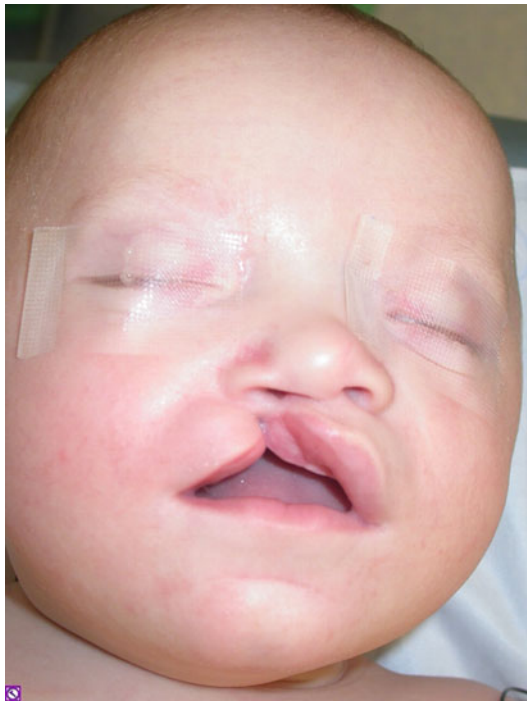

Fig. 5.12 Unilateral incomplete cleft lip

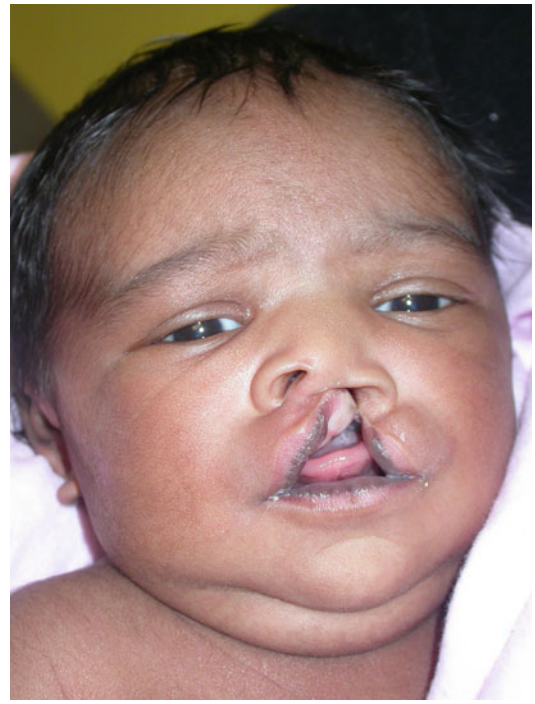

Fig. 5.13 Unilateral complete cleft lip

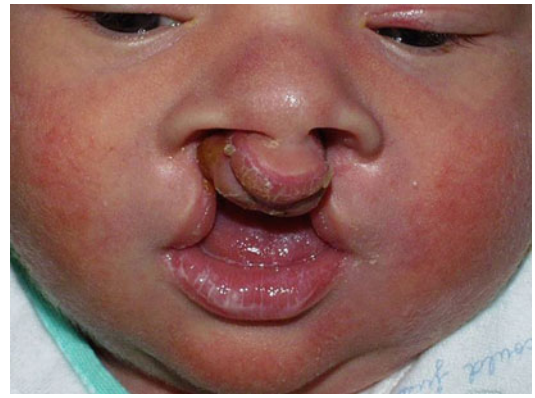

Fig. 5.14 Bilateral complete cleft lip and palate

lying in the normal side of the nares. The premaxilla rotates outward with collapse of the lateral maxillary segment (Fig. 5.16). The lateral incisor and/or canine can be missing in up to 56 % of all cleft patients [17]. In the child with bilateral cleft lip with or without cleft palate child, the nose and premaxilla may be even more severely affected. The premaxilla typically attains a ventral-dorsal alignment since it is not tethered by any soft tissue restraints. The lateral alar cartilages are flattened bilaterally, and the columella is foreshortened (Fig. 5.17).

Children with cleft palate often present with Eustachian tube dysfunction secondary to improper mechanics of the levator and tensor veli palatini muscles. The incidence of tympanostomy

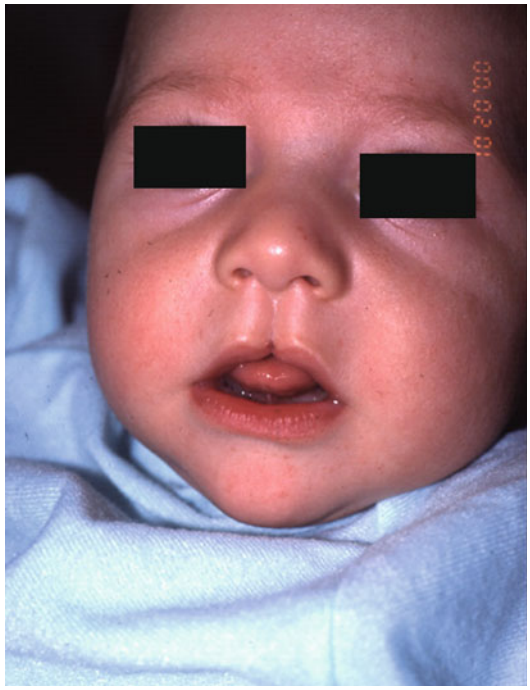

Fig. 5.15 Rare midline cleft lip

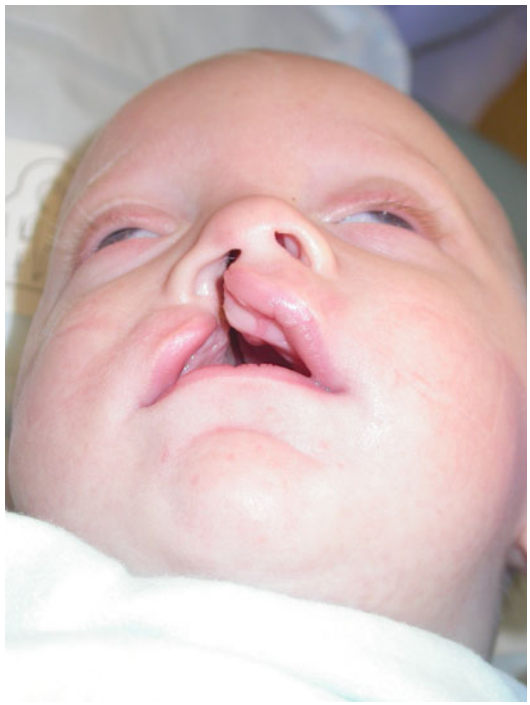

Fig. 5.16 Unilateral cleft nasal deformity

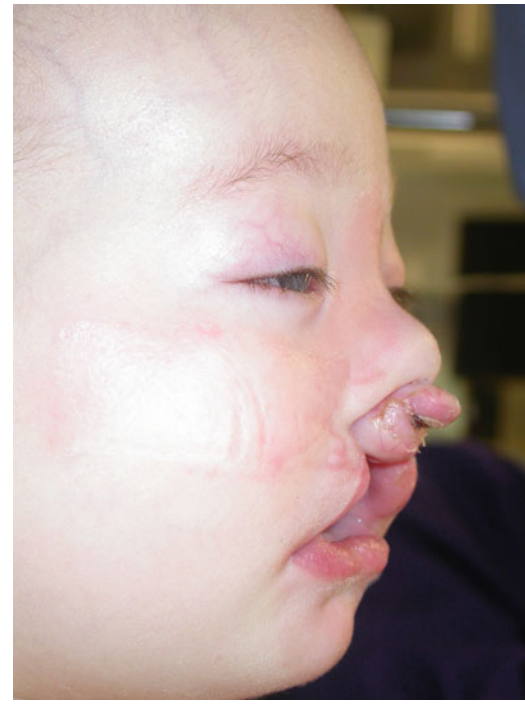

Fig. 5.17 Bilateral cleft nasal deformity

tube placement in children with palatal clefts approaches 90 % [18, 19]. Since the soft palate is an organ of speech, children may demonstrate velopharyngeal dysfunction, usually most evident as hypernasal resonance, even after cleft palate repair.

Diagnosis

Diagnosis can be made in the prenatal period or after delivery. The ability to detect clefts of the lip depends upon many factors including amniotic fluid volume, position of the child, cleft severity, and expertise of the sonographer. Clefts of the palate are more difficult to detect with sonography. Consequently, clefts of the palate alone are rarely identified prenatally. Prenatal MRI has been utilized to delineate clefts of the lip and palate, offering increased sensitivity and specificity when compared to sonography. Upon delivery, clefts of the lip are readily apparent, although microform clefts may elude early diagnosis.

Clefts of the palate can usually be diagnosed with proper intraoral examination, although submucosal clefts may be difficult to diagnose in the neonatal period.

Treatment

No consensus exists for the ideal timing of cleft lip repair. Some centers advocate early repair (within the first few weeks of life), while most centers begin surgery around 3–4 months of life. Presurgical orthopedics have become more popular with lip taping, obturators, nasoalveolar molding (NAM), and the Latham device all having their advocates. Surgical lip adhesion is also a technique for primary orthopedic work. All of these methods seek to improve the lip, nasal, and alveolar form and relationships prior to primary lip repair. The Millard rotation-advancement technique (or some variation thereof) is the most widely utilized technique for repair of the unilateral cleft lip (Figs. 5.18a–5.19b) For the bilateral cleft lip, a modification of the Millard bilateral cleft lip repair modification of this procedure is typically performed (Fig. 5.20a, b).

The approach to repair of alveolar clefts also demonstrates significant variability. Some surgeons advocate repair at the time of the initial cleft lip repair by performing a primary gingivoperiosteoplasty [20]. Other centers have advocated primary alveolar bone grafting in infancy. An abundance of evidence suggests, however, that this approach may result in significant maxillary growth restriction [21]. A more time-honored approach is that of secondary bone grafting performed during the mixed-dentition stage (7–9 years of age), with cancellous iliac bone grafts most commonly employed. More recently, some have advocated the use of bone morphogenic protein (BMP) in conjunction with biodegradable matrix scaffolds as a substitute for autologous bone [22]. While this method offers the advantage

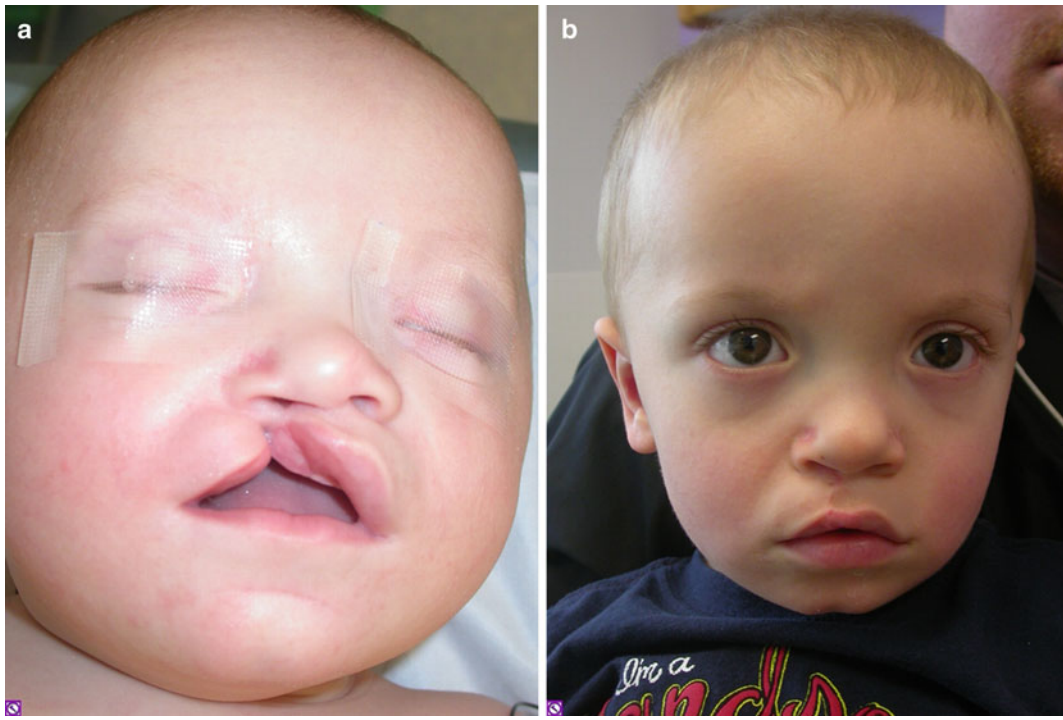

Fig. 5.18 (**a** and **b**) Unilateral incomplete cleft lip repair (Millard)

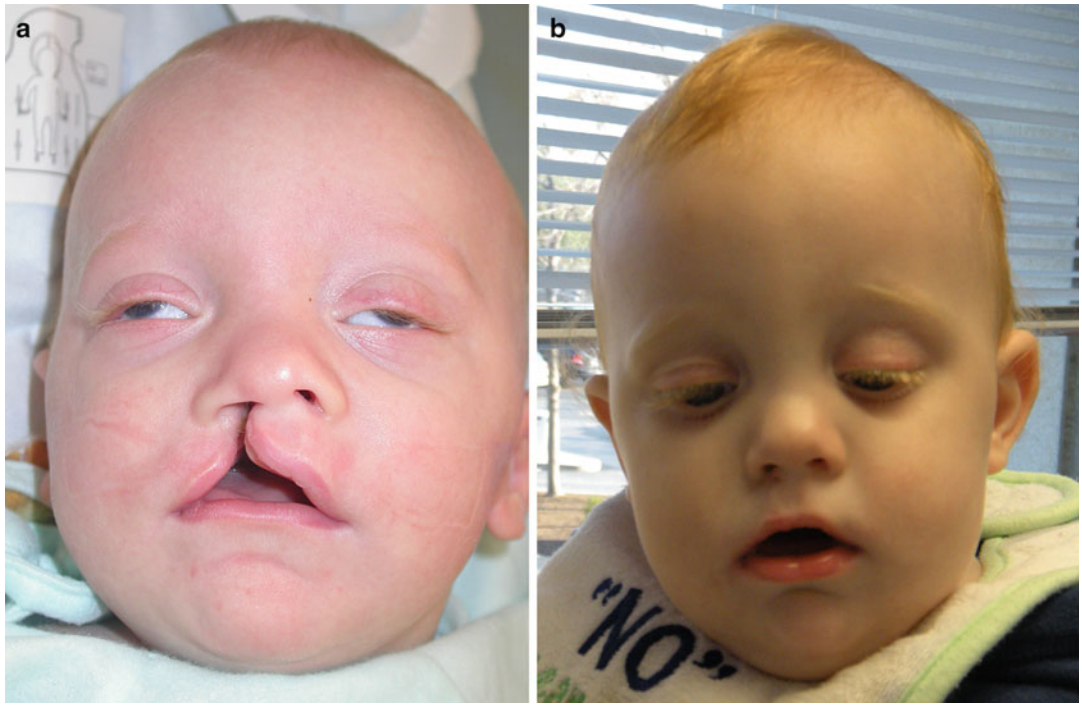

Fig. 5.19 (**a** and **b**) Unilateral complete cleft lip repair (Millard)

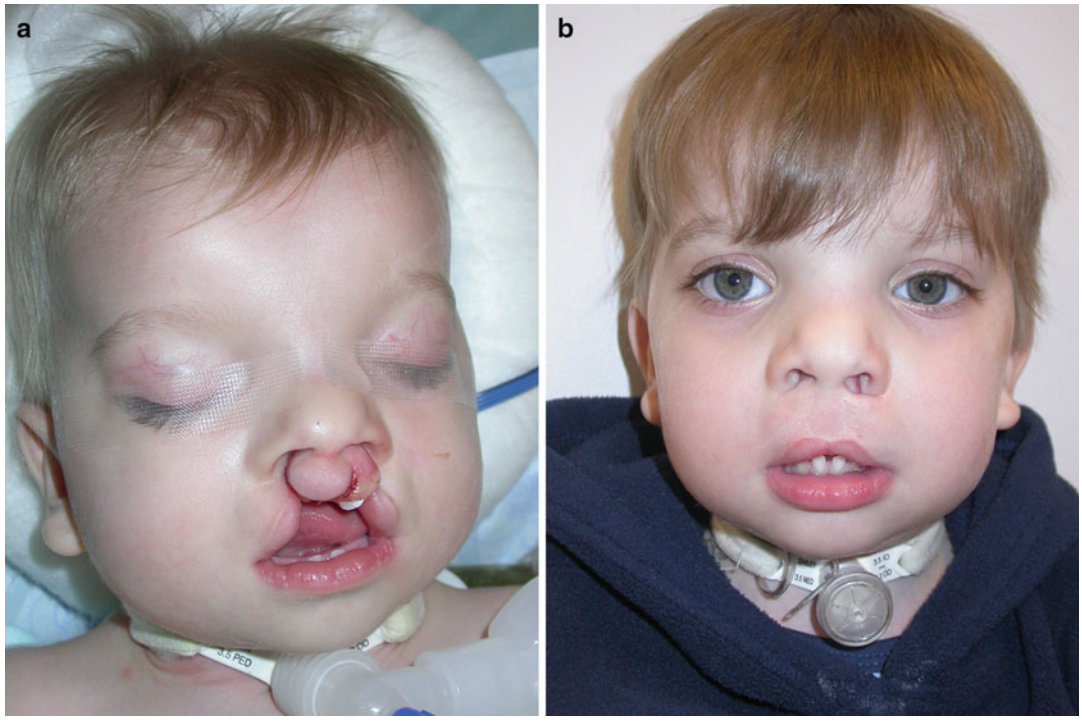

Fig. 5.20 (**a** and **b**) Bilateral complete cleft lip repair

of eliminating donor site morbidity, its long-term efficacy and reliability remain to be established.

Cleft palate repair is typically performed between 9 and12 months of age. Mucoperiosteal flaps from the hard palate are mobilized utilizing lateral releasing incisions and sutured to the midline. The levator veli palatini muscles are detached from the posterior hard palate and reoriented in the posterior velum to reconstruct the levator sling. The soft palate and levator can be repaired by either an intravelar veloplasty or Furlow double opposing z-plasty technique. Submucosal clefts of the palate need only be repaired if they are associated with velopharyngeal dysfunction and are therefore repaired later in childhood. To date, there have been no well-controlled, randomized studies to establish the optimal timing and technique of palate repair (refer to Figs. 5.7 and 5.8 for palatal repairs.)

Secondary surgical procedures are commonly required in children with cleft lip and/or cleft palate. Lip revision and tip rhinoplasty are commonly performed in the school-aged child. Operations to improve velopharyngeal function (posterior pharyngeal flap or sphincter pharyngoplasty) may be necessary in 10–25 % of cleft palate patients and can be completed once the child has achieved sufficient phonologic development and diagnostic studies can be performed (typically 4–6 years of age). Orthognathic surgery can be accomplished upon the completion of facial growth if jaw and occlusal discrepancies exist, and septorhinoplasty can be carried out upon in the teenage years for cleft patients with persistent cleft nasal deformities.

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