An additional layer of airway complexity exists with a congenital syndrome associated with difficult airway.
The etiology of the difficult airway (DA) in the pediatric patient may be a congenital syndrome or an acquired defect. The majority of DAs in these two groups of patients can be identified before the induction of anesthesia. That said, the basis for predicting a DA in a child is somewhat limited.1

First, it is important to have an understanding of which characteristics of the normal pediatric airway may result in DA management. Second, clinicians should be cognizant of the key features of the congenital syndrome, particularly as they relate to overall airway management. Finally, congenital syndromes with a DA presentation necessitate an increase in the level of preparedness by the anesthesiologist.

The airway management of a pediatric patient can present various challenges, even for the most experienced anesthesiologist. There are several anatomic differences between the neonate, infant and child airway.2 A thorough understanding of these differences is critical to ensure safe management of the pediatric airway. Several of these anatomic differences are summarized in Table 1.

A number of physiologic differences exist between pediatric (in particular, neonate and infant) and adult airways. A detailed discussion of lung mechanics and function is beyond the scope of this article. However, it is important to note that there are differences in chest wall compliance, oxygen consumption, and composition of muscle fibers of the diaphragm that result in a greater incidence of airway resistance in neonates and infants. Ultimately, an increase in airway resistance causes an increase in the work of breathing that will lead to hypoventilation, hypoxemia and hypercapnia.

Based on the various anatomic and physiologic differences in the airway, particularly in the neonate and infant, it would appear that pediatric patients are at a higher risk for an adverse airway event than adult patients. The Closed Claims database revealed that respiratory events were observed more frequently in the pediatric population than in adults.3 An additional layer of airway complexity exists with a congenital syndrome associated with DA. It is impossible to discuss all of the syndromes that present a DA as one of its features. This article will review some of the more commonly encountered congenital syndromes.

### Selected Pediatric Congenital Syndromes

#### Apert Syndrome

Apert syndrome is an autosomal dominant disorder caused by fibroblast growth factor receptor-2 (FGFR2) gene mutations. It is characterized by midfacial hypoplasia, craniosynostosis, a high-arched and narrow palate with or without a cleft, high forehead, flat occiput, and syndactyly. Occasionally, there may be choanal stenosis or atresia and cervical spine fusion. Intellectual and developmental disabilities may be present. The upper airway difficulties occurring in this disorder are primarily due to the small nasopharynx, reduced patency of the choanae, and anomalies of tracheal cartilage. The presence of abnormal tracheal cartilage increases the risk for injury during suctioning and reduces the ability to clear secretions.4

#### Beckwith-Wiedemann Syndrome

Most cases of Beckwith-Wiedemann syndrome are sporadic. Whereas other cases are known to be inherited in an autosomal dominant fashion, this disorder is caused by the insulin-like growth factor-2 (IGF-2) gene, which plays a role in somatic overgrowth. Beckwith-Wiedemann syndrome consists of macroglossia, macrosomia, omphalocele, visceromegaly and exophthalmos. Additional features of this syndrome include malocclusion with mandibular prognathism and maxillary underdevelopment. The macroglossia can lead to upper airway obstruction, especially during the induction phase of anesthesia. These children can benefit from lying on their side or face down to improve respiration. In more severe cases, a partial glossectomy may be beneficial.5

#### Cri du Chat Syndrome

Cri du chat syndrome is the result of a partial deletion of variable size in the short arm of chromosome 5. The phenotypic changes are linked to the absence of the telomerase reverse transcriptase (TERT) gene.5 This chromosomal disorder is characterized by microcephaly, hypotonia, micrognathia, short neck, low-set ears, facial asymmetry, intellectual disability and a rather unique crying sound. Quite often during infancy the cry will sound similar to that of a cat mewing. For the

### Table 1. Neonate/Infant/Child Airway Differences Compared With Adult Airway

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Neonate/Infant/Child</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head (occiput)</td>
<td>Relatively large</td>
<td></td>
</tr>
<tr>
<td>Nares</td>
<td>Small</td>
<td></td>
</tr>
<tr>
<td>Neck</td>
<td>Short</td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>Large relative to mouth size</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>More cephalad in the infant at C2 until it approaches that of the adult at C4</td>
<td></td>
</tr>
<tr>
<td>Epiglottis</td>
<td>Long and angled, projecting above the glottic opening</td>
<td></td>
</tr>
<tr>
<td>Vocal cords</td>
<td>Slanted anteriorly and rostrally</td>
<td></td>
</tr>
<tr>
<td>Narrowest part</td>
<td>Recent studies suggest the glottis instead of the larynx cricoid cartilage</td>
<td></td>
</tr>
</tbody>
</table>
most part, the characteristic cry is the result of laryngeal deformity. The head/neck and upper airway abnormalities that may contribute to the difficult airway are mainly caused by micrognathia, short neck, a long and floppy epiglottis, and a small narrow-shaped larynx.9

**Crouzon Syndrome**

Crouzon syndrome, similar to Apert syndrome, is inherited in an autosomal dominant manner. Also like Apert syndrome, this craniofacial dysmorphic disorder results from FGFR2 gene mutations. However, different mutations are responsible for Crouzon syndrome. The anomalies found in Crouzon syndrome are limited to the craniofacial region, and include premature craniosynostosis of the coronal, sagittal and lambdoid sutures. Maxillary hypoplasia, hypertelorism and shallow orbits are present. Occasionally, these patients have cleft lip and palate and tracheobronchomalacia. There have been reports of tracheal cartilaginous sleeves.10 Hearing loss is present. Upper airway obstruction is commonly manifested as obstructive sleep apnea, but acute respiratory distress is not often observed.

**Down Syndrome**

Typical airway findings in patients with Down syndrome include macroglossia, pharyngeal muscle hypotonia, narrowed nasopharynx, short neck, high-arched palate and lax cervical vertebral ligaments. Adenoidal and tonsillar hypertrophy may be present. It is not unusual for children with Down syndrome to require a smaller than predicted endotracheal tube size because their trachea may be small.11 The presence of a large protuberant tongue and pharyngeal muscle hypotonia also put these patients at increased risk for difficult intubation and postoperative airway obstruction. One possible solution for postoperative respiratory complications is administration of nasal continuous positive airway pressure to maintain airway patency.12

**Goldenhar Syndrome**

Most cases of Goldenhar syndrome are sporadic, but some inheritance may be autosomal dominant or autosomal recessive. Many of the features that are observed in Goldenhar syndrome are the result of anomalies of the first and second branchial arches, and primarily the result of a vascular accident in utero. Goldenhar syndrome involves hypoplasia of the malar, maxillary and mandibular regions. In addition, hypoplasia of facial musculature, lateral cleft-like extension of the corner of the mouth, anomalies of the tongue, microtia, and occasionally cleft lip and palate may be present. Cervical spine and temporomandibular joint fusion also have been reported.13 These anomalies collectively can result in restricted mouth opening, limitation of neck flexion and extension, and poor mask seal due to asymmetry, all of which progressively worsen with age.

**Klippel-Feil Sequence**

The majority of cases of Klippel-Feil sequence are sporadic, but some inheritance is autosomal dominant. Some features of Klippel-Feil sequence include a short neck, limited head movement and a low hairline, and the syndrome may be primarily the result of intrauterine disruption of the subclavian or vertebral arteries and failure of normal segmentation of the cervical spine.13 The airway can be managed by mask fairly easily, but intubation remains difficult due to limitation of neck movement.

**Nager Syndrome**

Nager syndrome is an acrofacial dysostosis disorder that is associated with an inheritance pattern that can be autosomal dominant or recessive.14 It is characterized by craniofacial anomalies, non-sensory hearing loss and preaxial upper extremity abnormalities. Nager syndrome has similar craniofacial dysmorphic features as seen in Treacher Collins syndrome (see page 47). Several of these common facial features are downward angulated palpebral fissures, lower lid coloboma, low-set positioned ears and absence of an external auditory canal. An endotracheal tube intubation is challenging, mainly due to micrognathia, small mouth opening, mandibular hypoplasia and laryngeal anomalies.15 The presence of cleft lip and/or cleft palate may result in further difficulty in airway management.

**Pfeiffer Syndrome**

Pfeiffer syndrome consists of three clinical subtypes. Type 1 is an autosomal dominant disorder, whereas types 2 and 3 occur sporadically. The majority of cases are the result of mutations in the genes that encode FGFR1 or FGFR2. The main features of Pfeiffer syndrome are craniosynostosis, mild syndactyly, and broad thumbs and great toes. In addition, maxillary hypoplasia, proptosis and shallow orbits are present. Occasionally, laryngomalacia, tracheomalacia and bronchomalacia may be observed. Vertebral fusion can occur, usually of the upper cervical spine, which may limit mobility and make laryngoscopy more difficult. Patients with Pfeiffer syndrome, similar to those with Crouzon syndrome, can have a tracheal cartilaginous sleeve.16

**Pierre Robin Sequence**

The classic features of Pierre Robin sequence include micrognathia, glossoptosis and cleft soft palate that have long been known to complicate intubation in affected children.17 Hypoplasia of the mandible occurs before nine weeks’ gestation, causing the tongue to be posteriorly displaced. Mechanical constraint in utero also has been proposed as a possible mechanism. Neuromuscular dysfunction of lingual and pharyngeal musculature is another manifestation of this disorder. In some patients with Pierre Robin sequence, intubation becomes less difficult with increasing age due to catch-up mandibular growth,
but in others the mandible remains proportionately small. For anesthetic management, these patients may require prone positioning, a nasopharyngeal airway or glossolabiopexy.

**Russell-Silver Syndrome**
Most cases of Russell-Silver syndrome are sporadic and are linked to genetic defects in specific areas of chromosomes 7 and 11.\(^{18}\) The facial features of Russell-Silver syndrome consists of a wide forehead, while the lower jaw is remarkable for micrognathia and downward slanting of the corners of the mouth.\(^{19}\) Additional features of this syndrome that can affect airway management include short stature/small size and gastroesophageal reflux disease (GERD). Face-mask ventilation and endotracheal tube intubation may be difficult primarily due to facial anomalies. Children with Russell-Silver syndrome may benefit from a smaller than predicted endotracheal tube size because of their small size, and closely check the depth of the tube placement. GERD is not uncommon and therefore the risk for aspiration must be considered.\(^{20}\)

### Table 2. Clinical Features of Selected Congenital Syndromes\(^a\)

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Autosomal Dominant Inheritance</th>
<th>Cervical Spine Fusion</th>
<th>Craniosynostosis</th>
<th>Cleft Palate</th>
<th>Hearing Loss</th>
<th>High-arched Palate</th>
<th>Macrognathia</th>
<th>Micrognathia</th>
<th>Obstructive Sleep Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beckwith-Wiedemann syndrome</td>
<td>![✔️]/sporadic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>![✔️]</td>
</tr>
<tr>
<td>Nager syndrome</td>
<td>![✔️]/recessive</td>
<td></td>
<td></td>
<td>![✔️]</td>
<td>![✔️]</td>
<td>![✔️]</td>
<td>![✔️]</td>
<td>![✔️]</td>
<td>![✔️]</td>
</tr>
</tbody>
</table>

\(^a\) Highlighted clinical features may not always be present.
Treacher Collins Syndrome

Treacher Collins syndrome is an autosomal dominant disorder and most likely involves a gene (TCOF1) that encodes a protein involved in embryonic craniofacial development. The main features of this disorder include malar hypoplasia with down-slanting palpebral fissures, zygomatic hypoplasia, mandibular hypoplasia, malformation of the external ear, and lower eyelid colobomas. A small mouth opening, high-arched palate, cleft lip or palate, and pharyngeal hypoplasia also may be present. Mask ventilation and intubation can be nearly impossible to perform. The procedure of choice in the past has been either sedated fiber-optic intubation or placement of a supraglottic airway.17

Conclusion

Airway management of the pediatric patient with a syndrome associated with DA is an ongoing challenge for the anesthesiologist. The skill set required in the airway-related care of these patients is similar to that for any pediatric patient with DA. However, an understanding of the unique clinical features of these syndromes remains crucial to the anesthesia care (Table 2).

References