THREE

Pediatric Lung Pathology and Metabolic Disorders of the Lung

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6

Congenital Malformations of the Larynx and Trachea

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A diagram of the developing larynx (Fig. 6-1) helps to clarify the frequent association of abnormalities of the branchial arches and pouches and their derivatives with other malformations of the respiratory tract.

LARYNX

The developmental schedule of the larynx is important for understanding many of the anomalies of this structure.[1] At 4 weeks of gestational age, the arytenoid prominences, the epiglottic ridge, and the laryngotracheal groove in the pharyngeal floor appear, and the early stage of formation of the tracheoesophageal septum begins. The early stage of hyoid bone formation occurs at week 5 of gestation. At week 6 of gestation, cricoid and thyroid cartilages and the interarytenoid, cricothyroid, and posterior cricoarytenoid muscles appear. At week 8 of gestation, vocal cords and other laryngeal muscles appear. Laryngeal formation is relatively complete at 10 weeks of gestation.

Clinically, the most important laryngeal anomalies are laryngomalacia, laryngeal stenosis and atresia, and laryngotracheoesophageal cleft, but many others occur with lesser frequency. Aspects of their radiologic diagnosis by computed tomography scan are presented by Liu and Daneman[2] and Carpenter and Merten.[3] The frequent association of polyhydramnios with several laryngeal anomalies, including laryngeal stenosis and atresia and laryngotracheoesophageal cleft, is not fully explained, because it involves malformations that could interfere with inhalation of amniotic fluid or with outflow of airway secretions in fetal life.[4]

Epiglottis

Malformation, hypoplasia, or absence of the epiglottis have been associated with cri du chat syndrome (*i.e.*, 5p− syndrome), thoracolaryngopelvic dysplasia, and median mandibular cleft and are especially frequent with the Majewski short-rib polydactyly syndrome.[5] The association of bifid epiglottis and hand anomalies with the hypothalamic hamartoma syndrome (*i.e.*, Pallister-Hall syndrome) and with hypopituitarism is noteworthy; all features of the association apparently reflect a developmental disturbance during the fifth fetal week.[6] The most frequent cause of clinical laryngomalacia, with a narrow laterally curled epiglottis and abnormally short aryepiglottic folds, is presumably a malformation of the laryngopharyngeal junction, reflecting a disturbance very early in fetal life. Neurologic damage can produce a similar clinical picture of stridor, as can vallecular diverticulum, which causes inspiratory collapse of the posterior tongue into the laryngeal inlet with clinical stridor.[7,8]

Thyroid Cartilage and Hyoid Bone

Hypoplasia of the thyroid cartilage (*i.e.*, <72% of normal) with an increased anterior angle and short superior cornua is a feature of the more general laryngeal hypoplasia seen in the DiGeorge anomaly.[9] The ossification center of the hyoid bone is visible radiologically in about 75% of neonates. The incidence of visibility is reduced in DiGeorge anomaly and tetralogy of Fallot, suggesting that both result from developmental field defects, and increased in Down syndrome, complete transposition of the great arteries, and Ivemark asplenia syndrome.[10,11] The relatively high position of the larynx with abnormalities of the soft tissues of the palate and pharynx, large tongue, and short neck contributes to the frequent difficulty of laryngeal intubation of patients with mucopolysaccharidoses, including Hurler, Hunter, Sanfilippo, and Maroteaux-Lamy diseases.[12]

Laryngeal and Laryngotracheoesophageal Cleft

Laryngeal and laryngotracheoesophageal (LTE) lesions can be classified into five types[13,14]:

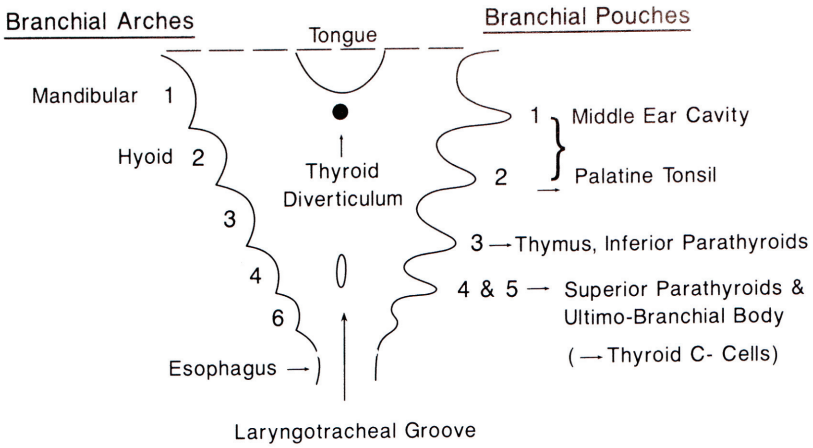

FIGURE 6-1. The embryonic oropharynx, showing the general locations of the ventral (*i.e.*, pharyngeal floor) derivatives, the thyroid diverticulum, and the laryngotracheal groove, which develops into the larynx, trachea, bronchi, and lungs, and of the branchial arches and pouches and their derivatives. These relations explain the frequent association between respiratory tract anomalies and abnormalities of branchial arch and pouch derivatives as a result of developmental embryonic field disturbances.

Type 1: the cleft involves the supraglottic larynx, but not the cricoid cartilage.
Type 2: the cleft extends through the cricoid cartilage.
Type 3: the cleft involves the upper trachea.
Type 4: the cleft involves the trachea to the carina.
Type 5: the cleft extends beyond the carina into the main stem bronchi.

The clinical picture of LTE clefts includes respiratory difficulty, stridor, choking with feedings, and dislodgement of an endotracheal tube into the esophagus.[15] Syndromic associations of LTE cleft include cleft lip and palate, esophageal atresia (EA) or tracheoesophageal fistula (TEF), the Pallister-Hall syndrome, the Opitz syndrome, connective tissue hamartoma arising in the region of the vocal cords and occluding the laryngeal inlet, and microgastria perhaps restricted to patients with type 4 or 5 LTE clefts.[16,17]

The surgical approaches recommended are anterior, with splitting of the thyroid, cricoid, and upper tracheal cartilages, or endoscopic repair for supraglottic clefts.[18–21] Recurrence of TEF is relatively frequent after either method.[19,21]

Opitz Syndrome

The Opitz syndrome (*i.e.*, G, BBB, BBBG, or Opitz-Frias syndrome) is an autosomal dominant condition with male preponderance (*i.e.*, partial male limitation). Features include distinctive facies, with ocular hypertelorism, low nasal bridge, low-set ears, prominent forehead and occiput, short lingual frenum, hypospadias, cryptorchidism, and LTE cleft. About one third of these patients also have cleft lip or palate. Dysphagia is an invariant feature, but stridor and hoarse cry are common.[22] Laryngeal hypoplasia, short trachea, tracheal or bronchial stenosis, tracheobronchomalacia, and pulmonary agenesis or hypoplasia have been described in some patients.[23,24] The condition was originally described as two different entities, but the term Opitz syndrome is used for the merged entity.[25,26] Occult posterior laryngeal cleft refers to a submucous defect in the posterior cricoid with a narrow and elongated laryngeal lumen; that such occult clefts are associated with polyhydramnios is puzzling.[27]

Laryngeal Atresia

After original formation of the larynx, its lumen is transiently occluded by growth of lateral epithelial and connective tissue masses, with persistence of a narrow posterior lumen called the pharyngotracheal duct. Different degrees of regression of the temporary laryngeal occlusion at different laryngeal levels during fetal weeks 8 to 10 can explain several versions of laryngeal stenosis and atresia; the least severe form is a congenital anterior interarytenoid web.[28] Onset of stridor during the first week of life is common, and tracheostomy at 3 to 5 years of age is necessary in most cases. Subglottic stenosis occurs in about 20% of patients with laryngeal web, and non-airway anomalies, often multiple, are also found in these patients.[29]

Antenatal ultrasonographic features of laryngeal atresia typically include markedly enlarged lungs, often with fetal hydrops and ascites and with thick echogenic and hydropic placenta. The lung images may resemble those of congenital cystic adenomatoid malformation of the lungs (CCAM), but the process is bilateral in laryngeal atresia and typically unilateral in CCAM.[30] The enlarged fluid-filled lungs of infants with laryngeal atresia are considered to be the result of retained lung and airway secretions, with resulting increased alveolar number and surface area, and the fetal and placental hydrops and polyhydramnios are the result of intrathoracic venous compression by the overdistended lungs.[31,32] Silver and colleagues found the alveolization of such lungs to be at the 3-month level at birth.[33] Nakayama and associates, studying the pulmonary function of a neonate with laryngeal atresia who also had the prune-belly deficient abdominal musculature syndrome, found the forced vital capacity in upper normal range but the maximal expiratory flow rate to be reduced.[34] Whether the latter value reflects air trapping by small airways or increased pulmonary connective tissue is not certain. Pulmonary hypoplasia can be associated with laryngeal atresia, with or without EA with TEF, which could permit drainage of respiratory tract secretions to the gastrointestinal tract.[35,36]

The clinical features of laryngeal atresia are respiratory distress, absence of cry, and an inability to pass an endotracheal tube beyond the larynx. Tracheostomy can permit survival, but the long-term course often depends on the patient's other anomalies.[37,38] Surgical treatment of cartilaginous laryngeal obstruction at the cricoid level by splitting the cartilage mass back to the pharyngotracheal duct, removing the excess cartilage, and covering the exposed surfaces with mucosa has been described.[39] A technique used for acquired laryngeal and tracheal atresia of covering the exposed surfaces with isolated autologous respiratory epithelial cells may be useful for congenital atresia of these structures.[40]

Cricopharyngeal Ring and Bar

Cricopharyngeal ring and bar refer to spasm or fibrosis of the cricopharyngeal muscle, the major muscle of the upper esophageal sphincter, not to structural anomalies of the respiratory tract.[41,42] The clinical picture is that of dysphagia.

Laryngocele

The ventricles of Morgagni are recesses of the laryngeal lumen between the true and false vocal cords. Enlarged saccules formed from small slitlike openings in the anterior roof of a ventricle are called laryngoceles.[43] Internal laryngoceles, which constitute about 33% of the total, lie behind the thyroid cartilage; external laryngoceles, which constitute about 25%, extend through the thyrohyoid membrane; and mixed laryngoceles, which constitute 42%, show dilatation in both loci. Laryngoceles are usually air filled, but they can show an air-fluid level or be filled with mucus (*i.e.*, saccular laryngoceles). They occur predominantly in boys (*i.e.*, 7 : 1 male-female ratio) and can present as cervical swellings or can cause airflow obstruction with hoarseness, stridor, or dysphagia.[44] Differential diagnosis in early infancy includes branchial cleft, thyroglossal duct cysts, and cystic hygroma.[45] Surgical and laser-endoscopic treatment can be used.[44,46]

Laryngomalacia

Isolated laryngomalacia typically presents within the first 4 months with audible stridor. The cause is an abnormality of the epiglottis and laryngeal inlet, with the epiglottis collapsing backward and the arytenoids forward on inspiration. Secondary laryngomalacia due to excessive negative inspiratory pressure because of airway obstruction occurs with adenoid hypertrophy, vocal cord paralysis, subglottic stenosis, and tracheal or bronchial stenosis; the inward collapse of the intrinsically normal laryngeal walls on inspiration is presumably caused by the Venturi effect.[47] Laryngeal stridor was the leading symptom of a patient with neurologic complications of biotinidase deficiency (*i.e.*, multiple carboxylase deficiency).[48]

TRACHEA

Tracheal Agenesis

Three anatomic forms of tracheal agenesis occur, and the classification used is that of Floyd and colleagues.[49] In type 1, the upper trachea is absent, and the lower trachea connects to the esophagus. In type 2, the upper and lower trachea are absent, with a common bronchus connecting the right and left main bronchi to the esophagus. In type 3, the upper and lower trachea are absent, with the right and left main bronchi connecting separately to the esophagus.

The basic features are respiratory distress, absence of cry, inability to intubate the airway below the larynx, inability to palpate the upper trachea, and radiologic demonstration of a lower tracheal air column or of abnormal carinal position and relations.[50] Maternal polyhydramnios, the explanation for which is unclear, is common. Ventilation of the lungs through the esophagus may permit survival long enough for attempted surgical therapy.[51] Other anomalies occur frequently in infants with tracheal agenesis, and a specific pattern, including cardiac anomalies, radial ray limb anomalies, and duodenal atresia, with or without gastric, splenic, and pancreatic anomalies, has been called the TACRD association.[52,53] Overlaps among the anomalies occur with EA and TEF.[54,55] Bray and Lamb listed 10 anomaly patterns associated with tracheal stenosis or agenesis[56]:

1. Subglottic tracheal stenosis with H or N pattern of TEF
2. Subglottic stenosis with the relatively frequent pattern of EA and TEF
3. Subglottic stenosis with EA and TEF to upper and lower esophageal segments
4. Central tracheal agenesis with the lower tracheal segment joining the esophagus (*i.e.*, Floyd type 1 pattern)
5. Lower tracheal agenesis, with the main bronchi arising separately from the esophagus (*i.e.*, Floyd type 3 pattern)
6. Lower tracheal agenesis with a TEF joining the carina to the esophagus (*i.e.*, Floyd type 2 pattern)
7. Lower tracheal agenesis, with a fistula from the upper tracheal segment to the esophagus and Floyd type 3 relation of the bronchi to the esophagus
8. Lower tracheal agenesis with the carina directly joining the esophagus (*i.e.*, Floyd type 2 pattern) with a short TEF
9. Lower tracheal agenesis with no esophageal connection
10. Central tracheal agenesis with EA and a fistula joining the upper esophageal segment to the lower trachea.

Ventilation of the lungs through the esophagus can be useful in the resuscitative management of infants with tracheal agenesis, but surgical correction of type 3 tracheal agenesis is not clearly practicable.[57,58] Lubinsky emphasized that association patterns of the type presented, with an overlapping spectrum of features, reflect the operation of causally nonspecific disruptive processes acting on developmental fields. The effects depend on the areas affected, the developmental status of the affected field or fields, the severity of the disruptive event, and susceptibility factors such as the genetic background of the affected fetus.[59]

Tracheoesophageal Fistula With and Without Esophageal Atresia

The literature on this frequent, important, and causally heterogeneous group of anomalies has shown a surprising dearth of pathogenetic explanations. The range of anomalies associated with TEF with and without EA is illustrated by acronyms used for the more frequent of these patterns:

- VATER association: vertebral, anal (especially imperforate anus), tracheal, esophageal, renal, and radial anomalies
- VACTEL association: vertebral, anal, cardiac, tracheal, esophageal, and limb (especially radial ray) anomalies
- VACTERL association: vertebral, anal, cardiac, tracheal, esophageal, renal, and limb anomalies
- ARTICLE association: anal, renal, tracheal, intestinal (especially duodenal), cardiac, limb, and esophageal anomalies
- ARTICLE-V association: anal, renal, tracheal, intestinal, cardiac, limb, esophageal, and vertebral anomalies.

Pattern overlaps among the anomalies associated with tracheal agenesis, tracheal stenosis, and unilateral pulmonary agenesis occur. Possibly deserving greater consideration as a cause of these anatomically widespread anomalies is a process or processes causing disseminated microvascular occlusion in early fetal life.

Figure 6-1 shows the embryonic derivatives of the pharynx, the branchial arches and pouches, the thyroid diverticulum, and the site of the laryngotracheal groove, which deepens and extends caudally anterior to the esophagus as the respiratory tract. A variety of anomaly associations can result from field defects involving this region.

There are various types of congenital TEF with and without EA (Fig. 6-2). The most frequent and important form is called type 3B in the Vogt categorization scheme and type A in the Stephens classification. An earlier concept that TEF and EA resulted from abnormal alignment or formation of the mesenchymal tracheoesophageal septum that forms between the developing respiratory tract and the esophagus was never fully satisfactory. It has been superseded by one that proposes that the tracheoesophageal septum is formed by upper and lower segments, with excessive angulation at higher, middle, or lower levels of the fetal cervical region leading to an abnormal course of the upper, lower, or both septal segments and to the TEF and EA patterns A through C of the Stephens scheme, with simple failure of septal segment fusion causing the H or N and K patterns of TEF (*i.e.*, types D and E; Fig. 6-3).[60]

Nakazato and associates described abnormal patterns of the Auerbach myenteric plexus of the esophagus and of the intrinsic tracheal nerve plexuses in TEF and EA.[61] These observations may explain the frequent persistent esophageal dysfunction of these patients after surgery, instead of or in addition to possible effects of disconnection from external nerve connections, ischemia of the neural plexuses or of the muscle of the esophagus, or scarring of the esophageal wall resulting from the surgical procedure. The frequent association of maternal polyhydramnios, hypertensive toxemia of pregnancy, and prematurity of the infant with EA with or without TEF applies to other types of congenital upper gastrointestinal obstruction, including duodenal and jejunal atresia. Wailoo and Emery showed that the tracheal cartilages are frequently relatively short and the tracheal pars membranacea relatively wide in patients with EA and TEF.[62] Application of the term tracheomalacia to this lesion appears misleading; a frequent cause of symptomatic tracheal stenosis in infants with EA and TEF is tracheal compression by the vascular pattern discussed later as common origin of the carotid arteries.[63,64] Emery and Haddadin found more extensive than normal lining of the upper trachea by squamous epithelium in patients with EA and TEF, and they proposed that deficient ciliary tracheal clearing could cause "retention lung" and pneumonia in these infants.[65]

Tracheal or Bronchial Stenosis With Unilateral Pulmonary Agenesis

Reported associations of unilateral pulmonary agenesis with tracheal stenosis and with EA and TEF support the earlier considerations about developmental errors, as does the report of unilateral pulmonary agenesis, lower tracheal stenosis, laryngotracheoesophageal cleft, hydrocephalus, and absence of the corpus callosum in an infant with oculoauriculovertebral dysplasia (*i.e.*, Goldenhar anomaly).[66–70] Goldenhar anomaly is a condition probably resulting from a first and second branchial arch field defect, other features of which include microtic and mandibular hypoplasia, epibulbar dermoids, and vertebral anomalies.[70] In addition to an intrinsic developmental anomaly, tracheal stenosis in unilateral pulmonary agenesis may be caused by compression of the trachea by the posteriorly shifted aortic arch, a mechanism similar to that of the right pneumonectomy syndrome; the problem can be alleviated by aortopexy.[71]

Midtracheal Stenosis With Ring Tracheal Cartilages in Down Syndrome

At least 10 patients with midtracheal stenosis with ring tracheal cartilages in Down syndrome have been reported.[72,73] Although uncommon, it appears to be several hundred times more frequent in patients with Down syndrome than in the general population and perhaps relatively more frequent in blacks.

Tracheal Stenosis From Common Origin of the Carotid Arteries

Tracheal stenosis from common origin of the carotid arteries (*i.e.*, anomalous origin of innominate or of left carotid arteries) is, in most pediatric surgical series, the most common cause of symptomatic tracheal compression by the great arteries. The basic anatomic pattern, with the right and left common carotid arteries arising from a short common trunk, with (*i.e.*, innominate trunk with the left carotid arising from it) or without (*i.e.*, bicarotid trunk) origin of the right subclavian artery from the trunk, is relatively frequent, occurring in approximately 11% of Caucasians and 20% of people of African origin.[64] Evidence that tracheal

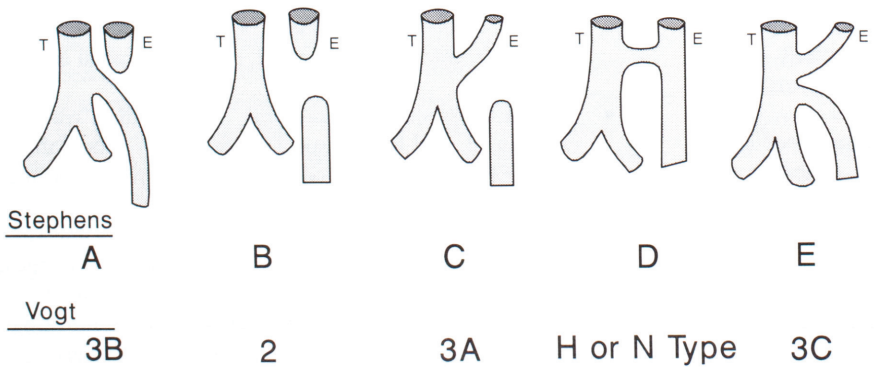

FIGURE 6-2. Patterns of congenital esophageal atresia and tracheoesophageal fistula, with their terms in older Vogt and more recent Stephens classifications. The most common pattern is atresia of the upper esophagus with fistulous connection of the lower esophageal segment to the trachea near the carina (*left*).

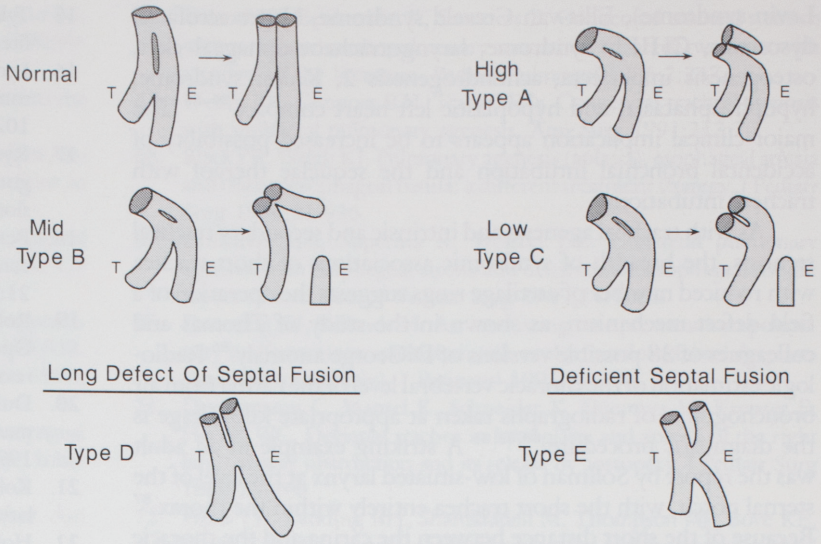

FIGURE 6-3. Embryonic mechanisms produce the various patterns of esophageal atresia and tracheoesophageal fistula. (E, esophagus; T, trachea.)

compression is more severe when the common trunk arises farthest to the left on the aortic arch, so that the innominate or right carotid arteries cross over the anterior face of the trachea, may explain the fact that most persons with the anatomic pattern do not have symptomatic tracheal stenosis. The pattern occurs more frequently in patients with anomalous origin of the left coronary artery from the pulmonary artery, EA and TEF, DiGeorge anomaly, trisomies 13, 18, and 21, congenital valvular disease, truncus arteriosus, aorticopulmonary window, Apert acrocephalosyndactyly syndrome (Fig. 6-4), tetralogy of Fallot, and clinical Noonan phenotype.[64,74] This breadth of associations suggests that the process is a heterogeneous field defect leading to arrest of division of the embryonic ventral aorta above the level of the fourth branchial arches.[59]

Diffuse Tracheal Stenoses and Tracheomalacia

The well-known association of diffuse tracheal stenosis with absence of the tracheal pars membranacea (*i.e.*, ring tracheal cartilages) and sling left pulmonary artery is discussed with the topic of bridging bronchus in Chapter 7. Diffuse narrowing of the tracheal lumen occurs in patients with lysosomal storage diseases, including Hurler mucopolysaccharidosis 1, I-cell disease (*i.e.*, mucolipidosis 2), and geleophysic dysplasia from thickening of the tracheal mucosa and submucosa.[75] Wood used the term localized tracheomalacia or bronchomalacia to describe local collapse of the lower trachea or right main bronchus in patients with deep brassy cough; the process is more likely the effect of excessive expiratory pressure on the airway than the result of cartilage abnormality.[76]

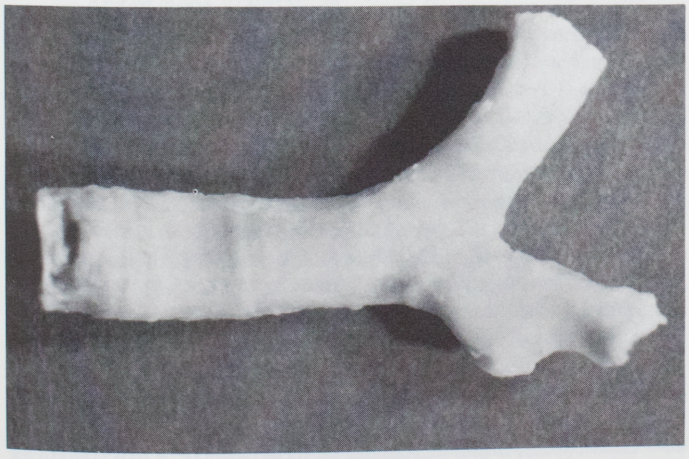

FIGURE 6-4. A dissected specimen of the lower trachea and main bronchi of a newborn boy with Apert syndrome shows a tracheal cartilaginous sleeve. The transverse groove on the trachea is caused by the anomaly called common origin of the carotid arteries or anomalous origin of the innominate artery.

Tracheal Cartilage Sleeve and Other Conditions of Tracheal Splint

The lack of separation of the tracheal cartilages to form a continuous or solid tracheal cartilage wall was originally called "completely cartilaginous trachea," but because this term could imply the trachea was a cartilaginous rod, the term "tracheal cartilaginous sleeve" has been employed.[77,78] An extreme degree of tracheal splint is highly associated with one or more of the acrocephalosyndactyly syndromes (see Fig. 6-4). Other patterns of tracheal cartilage fusion and tracheal splint have been described in Ellis-van Creveld chondroectodermal dysplasia and in partial chromosome 19 trisomy.[79] Because the tracheal pars membranacea occurs in patients with these several forms of tracheal splint, the physiologic effect is that the trachea cannot lengthen with inhalation, as it normally does, but it can dilate. Unpublished work by Ranganathan and Dyment, using ultrasonographic studies of a child with Ellis-van Creveld syndrome, confirms the reduced tracheal lengthening with inspiration and shows increased tracheal dilatation, with the implied increase in inspiratory force suggesting the mechanism of the respiratory difficulty described for patients with tracheal cartilage sleeve.[78]

Short Trachea With Reduced Numbers of Cartilage Rings

Short trachea with reduced number of cartilage rings has been reported especially for patients with DiGeorge anomaly and with neural tube defect, but there are several other syndromic associations, including brevicollis (*e.g.*, Klippel-Feil syndrome, Jarcho-

Levin syndrome), Ellis-van Creveld syndrome, Nager acrofacial dysostosis, CHILD syndrome, laryngotracheoesophageal cleft, osteogenesis imperfecta, achondrogenesis 2, Kniest syndrome, hypophosphatasia, and hypoplastic left heart complex.[79–85] The major clinical implication appears to be increased possibility of accidental bronchial intubation and the sequelae thereof with tracheal intubation.

As with tracheal agenesis and intrinsic and secondary tracheal stenosis, the breadth of syndromic associations of short trachea with reduced number of cartilage rings suggests the operation of a field defect mechanism, as shown in the study of Thomas and colleagues of 38 possible versions of DiGeorge anomaly.[86] Radiologic estimation of the thoracic vertebral level of the carina from air bronchograms of radiographs taken at appropriate kilovoltage is the diagnostic procedure.[80,82,84] A striking example in an adult was the report by Soliman of low-situated larynx at the level of the sternal notch, with the short trachea entirely within the thorax.[87] Because of the short distance between the carina and the thoracic vertebral column, the risk appears slight for an erroneous diagnosis of short trachea from the parallax effect of inappropriate angle of the x-ray beam in chest radiographs.[88]

REFERENCES

1. Smith RJ, Catlin FI. Congenital anomalies of the larynx. Am J Dis Child 1984;138:35.
2. Liu P, Daneman A. Computed tomography of intrinsic laryngeal and tracheal abnormalities in children. J Comput Assist Tomogr 1984; 8:662.
3. Carpenter BLM, Merten DF. Radiographic manifestations of congenital anomalies affecting the airway. Radiol Clin North Am 1991; 29:219.
4. Paes BA, deSa DJ, Hitch DA. Fatal malformations of the larynx and upper trachea. Laryngoscope 1984;94:1477.
5. Knapp CH Jr, Santin-Hodges A, Cole RR. Laryngeal findings in short rib polydactyly syndrome: case report and embryological correlations. Laryngoscope 1990;100:579.
6. Graham JM, Brown FE, Saunders RL, et al. Bifid epiglottis, hand anomalies and congenital hypopituitarism. Lancet 1985;2:443.
7. Peron DL, Graffino DB, Zenker DD. The redundant aryepiglottic fold: report of a new cause of stridor. Laryngoscope 1988;98:659.
8. Zalzal GH, Golden L. Diverticulum of the valleculae. Otolaryngol Head Neck Surg 1990;102:92.
9. Wells TR, Landing BH, Galliani CA, Thomas RA. Abnormal growth of the thyroid cartilage in the DiGeorge syndrome. Pediatr Pathol 1980;6:209.
10. Wells TR, Gilsanz V, Senac MO, Landing BH, Vachon L, Takahashi M. Ossification center of the hyoid bone in DiGeorge syndrome and tetralogy of Fallot. Br J Radiol 1986;59:1065.
11. Wells TR, Landing BH, Senac MO, Gilsanz V. Ossification center of the hyoid bone in complete transposition of great vessels, Ivemark asplenia syndrome and Down's syndrome with congenital heart disease: correlation with the humeral capital epiphysis. Br J Radiol 1986;59:1069.
12. Kempthorne PM, Brown TCK. Anesthesia and the mucopolysaccharidoses: a survey of techniques and problems. Anaesth Intensive Care 1983;11:203.
13. Wilkinson AG, MacKenzie S, Hendry GM. Complete laryngotracheoesophageal cleft: CT diagnosis and associated abnormalities. Clin Radiol 1990;41:437.
14. Ogawa T, Morita T, Tsuchiya H, Kohno S, Hamazaki Y. A new type of laryngotracheoesophageal cleft with extended bronchoesophageal cleft. J Pediatr Surg 1985;20:164.
15. Tyler DC. Laryngeal cleft: report of eight patients and a review of the literature. Am J Med Genet 1985;21:61.
16. Lyons TJ, Varicud S. Posterior cleft larynx associated with hamartoma: a case report and literature review. J Laryngol Otol 1988; 102:471.
17. Ryan DP, Meehrcke DD, Doody DP, Kim SH, Donohoe PK. Laryngotracheoesophageal cleft (type IV): management and repair of lesions beyond the carina. J Pediatr Surg 1991;26:962.
18. Berkovits RNP, Bax NMA, vander Schaus EJ. Surgical treatment of congenital laryngotracheo-oesophageal cleft. Prog Pediatr Surg 1987; 21:36.
19. Robie DK, Pearl RH, Gonsales C, Restuccia RD, Hoffman MA. Operative strategy for recurrent laryngeal cleft: a case report and review of the literature. J Pediatr Surg 1991;26:971.
20. DuBois JJ, Pokozny WJ, Harberg FJ, Smith RJ. Current management of laryngeal laryngotracheoesophageal clefts. J Pediatr Surg 1990;25:855.
21. Koltai PJ, Morgan D, Evans JNG. Endoscopic repair of supraglottic laryngeal clefts. Arch Otolaryngol Head Neck Surg 1991;117:273.
22. Howell L, Smith JD. G syndrome and its otolaryngologic manifestations. Ann Otol Rhinol Laryngol 1989;98:185.
23. Buckley JG, Hinton AE, Penter G, Farndon PA. Total laryngotracheal hypoplasia in a case of G syndrome. J Laryngol Otol 1988;102:1056.
24. Mitchell DB, Koltai P, Matthew D, Bailey CM, Evans JM. Severe tracheobronchomalacia associated with laryngeal cleft. Int J Pediatr Otorhinolaryngol 1989;18:181.
25. Secano HO, Gorbin RJ. Opitz oculo-genital-laryngeal syndrome (Opitz BBB/G compound syndrome). Am J Med Genet 1988;30:847.
26. Verloes A, LeMeeres M, Briand ML. BBBG or Opitz syndrome: new family. Am J Med Genet 1989;34:313.
27. Tucker GF Jr, Maddalozzo J. "Occult" posterior laryngeal cleft. Laryngoscope 1987;97:701.
28. Benjamin B, Mair EA. Congenital interarytenoid web. Arch Otolaryngol Head Neck Surg 1991;117:1118.
29. Miller RH, Cagle PT, Pitcock TK, McGavran M. Laryngeal atresia: a detailed histologic study. Int J Pediatr Otorhinolaryngol 1984;7:273.
30. Watson WJ, Thorp JM, Miller RC, Chercheir NC, Katz VL, Seeds JW. Prenatal diagnosis of laryngeal atresia. Am J Obstet Gynecol 1990;163:1456.
31. Wigglesworth JP, Desai JS, Hislop AA. Fetal lung growth in laryngeal atresia. Pediatr Pathol 1987;7:515.
32. Machin GA, Popkin JS, Zachs D, Newbigging J, Walther G, Bell D. Fetus with asymmetric parietal encephalocele and hydrops secondary to laryngeal atresia. Am J Med Genet 1987;3:311.
33. Silver MM, Thurston WA, Patrick JE. Perinatal pulmonary hyperplasia due to laryngeal atresia. Hum Pathol 1988;19:110.
34. Nakayama DK, Killian A, McBride T, Mutick R, Motoyama EK. Pulmonary function studies in a newborn with congenital laryngeal atresia. J Pediatr Surg 1991;26:210.
35. Walton JC, Silver MM, Chance GW, Vilos GF. Laryngeal atresia, pleurodesis and diaphragmatic hypertrophy in a newborn infant with findings relevant to fetal lung development. Pediatr Pathol 1985;4:1.
36. Lyon AJ. Congenital atresia of the larynx in association with prune belly syndrome. J R Army Med Corps 1983;129:118.
37. Farg SH, Ocejo R, Sin M, Fines NN, Wood BP. Radiological cases of the month. Congenital laryngeal atresia. Am J Dis Child 1989;143:625.
38. Leiberman A, Bar-Ziv J, Karplus M, Mares A, Weiss-Shmidek Z. Subglottic laryngeal atresia associated with tracheoesophageal fistula: long-term survival. Clin Pediatr 1985;24:523.
39. Berkovits RNP, van der Schaus EJ, Molenaar JC. Treatment of congenital cricoid stenosis. Prog Pediatr Surg 1987;21:20.
40. Gerhardt HJ, Böhm K, Kaschke O, Biedermann F. A new concept for reconstruction of atresias of larynx and trachea: lining of wound surfaces with autologous isolated respiratory epithelial cells. Acta Otolaryngol 1991;111:410.
41. Cumming WA, Akhtar M, Ferentzi C, Feteih W. Cricopharyngeal ring. A case report. Pediatr Radiol 1986;16:152.

42. Dantas RO, Cook IJ, Dodds WJ, Kern MK, Lang IM, Brasseur JG. Biomechanics of cricopharyngeal bars. Gastroenterology 1990;99: 1269.
43. Hubbard C. Laryngocele: a study of five cases with reference to the radiological features. Clin Radiol 1987;38:639.
44. Banks J, Davis BR, Monie RDH. Laryngocele causing airflow obstruction—a case report and summary of clinical manifestations in five other patients. Postgrad Med J 1984;60:290.
45. Lewis CA, Castillo M, Patrick E, Sybers R. Symptomatic external laryngocele in a newborn: findings on plain radiographs and CT scans. AJNR Am J Neuroradiol 1990;11:1002.
46. Myssiorek D, Persky M. Laser endoscopic treatment of laryngoceles and laryngeal cysts. Otolaryngol Head Neck Surg 1989;100:538.
47. Nussbaum E, Maggi JC. Laryngomalacia in children. Chest 1990; 98:942.
48. Dionisi-Vici C, Bachmann C, Graziami MC, Sabetta G. Laryngeal stridor as a leading symptom in a biotinidase-deficient patient. J Inherit Metab Dis 1988;11:312.
49. Floyd J, Campbell DC, Downing DE. Agenesis of the trachea. Am Rev Respir Dis 1962;86:517.
50. Chin T, Cuevas D, Cuevas L, Monteiso C. Tracheal agenesis. South Med J 1990;83:925.
51. Statz T, Lynch J, Ortmann M, Roth B. Tracheal agenesis: a case report. Eur J Pediatr 1989;149:203.
52. Diaz EM, Adams JM, Hawkins HK, Smith RJH. Tracheal agenesis. A case report and literature review. Arch Otolaryngol Head Neck Surg 1989;115:741.
53. Evans JA, Reggin J, Greenberg C. Tracheal agenesis and associated malformations: a comparison with tracheoesophageal fistula and the VACTERL association. Am J Med Genet 1985;21:21.
54. Nakada K, Kitagawa H, Enami T, Yamate N, Tsukada K, Seki I. Tracheal agenesis with bronchoesophageal fistulas—a case report. Jpn J Surg 1989;19:494.
55. Milstein JM, Lau M, Bickers RG. Tracheal agenesis in infants with VATER association. Am J Dis Child 1985;139:77.
56. Bray RJ, Lamb WH. Tracheal stenosis or agenesis in association with tracheo-oesophageal fistula and oesophageal atresia. Anaesthesia 1988;43:654.
57. McDonald SM, Oriol NE. Tracheal agenesis: resuscitative management. Anesthesiology 1990;73:1279.
58. Lopez L, Serrano A, Varela A, Freixinet J, Santana R, Beltra R. Tracheal agenesis. An unresolved problem. Thorac Cardiovasc Surg 1991;39:99.
59. Lubinsky M. Associations in clinical genetics with a comment on the paper by Evans et al. on tracheal agenesis (invited editorial comment). Am J Med Genet 1985;21:35.
60. Piekarski DH, Stephens FD. The association and embryogenesis of tracheo-oesophageal and anorectal anomalies. Prog Pediatr Surg 1976;9:63.
61. Nakazato Y, Landing BH, Wells TR. Abnormal Auerbach plexus in the esophagus and stomach of patients with esophageal atresia and tracheoesophageal fistula. J Pediatr Surg 1986;21:831.
62. Wailoo MP, Emery JL. The trachea in children with tracheo-oesophageal fistula. Histopathology 1979;3:329.
63. Emery JL, Nannayakhara CF, Wailoo MP. Tracheomalacia—lethal factor in a 17-month-old child. Pediatr Pathol 1984;2:259.
64. Landing BH, Wells TR, Dixon LG. Pathogenetic considerations of respiratory tract malformations in humans. In: Persaud TVN, Persaud MP, eds. Cardiovascular, respiratory, gastrointestinal and genitourinary malformations. Advances in the study of birth defects. vol. 6. New York: Alan R Liss, 1982;7.
65. Emery JL, Haddadin AJ. Squamous epithelium in respiratory tract of children with tracheoesophageal fistula. Arch Dis Child 1971; 46:236.
66. Voland JR, Benirschke K, Saunders B. Congenital tracheal stenosis with associated cardiopulmonary anomalies: report of two cases with a review of the literature. Pediatr Pulmonol 1986;2:247.
67. Weber TR, Connors RH, Tracy TF Jr. Congenital tracheal stenosis with unilateral pulmonary agenesis. Ann Surg 1991;213:70.
68. Black PR, Welch KJ. Pulmonary agenesis (aplasia), esophageal atresia and tracheoesophageal fistula: a different treatment strategy. J Pediatr Surg 1986;21:936.
69. Hoffman MA, Superina R, Wesson DE. Unilateral pulmonary agenesis with esophageal atresia and distal tracheoesophageal fistula: report of two cases. J Pediatr Surg 1989;24:1084.
70. Downing GJ, Kilbride H. An interesting case presentation: pulmonary malformations associated with oculoauriculovertebral dysplasia (Goldenhar anomaly). J Perinatol 1991;11:190.
71. Doehlemaun C, Mantel K, Schneider K, Guentver M, Kreuzer E, Hecker WC. Deviated trachea in hypoplasia and aplasia of the right lung: airway obstruction and its release by aortopexy. J Pediatr Surg 1990;25:290.
72. Wells TR, Landing BH, Shamszadeh M, Thompson JW, Bove KE, Caron KH. Association of Down syndrome and segmental tracheal stenosis with "ring" tracheal cartilages. Review of 9 cases. Pediatr Pathol 1992;12:673.
73. Devine WA, Debich DE, Taylor SR. Symmetrical bronchial pattern with normal atrial morphology. Int J Cardiol 1988;20:395.
74. Wells TR, Landing BH, Shankle WR. Additional syndromal associations of common origin of the carotid arteries. Pediatr Pathol 1993;13:203.
75. Peters ME, Arya S, Langer LO, Gilbert EF, Carlson R, Adkins W. Narrow trachea in mucopolysaccharidoses. Pediatr Radiol 1985; 15:225.
76. Wood RE. Localized tracheomalacia or bronchomalacia in children with intractable cough. J Pediatr 1990;116:404.
77. Devine P, Bhan I, Feingold M, Levnidos JC, Wolpert SM. Completely cartilaginous trachea in a child with Crouzon syndrome. Am J Dis Child 1984;138:40.
78. Davis S, Bove KE, Wells TR, Hartsell B, Weinberg A, Gilbert E. Tracheal cartilaginous sleeve. Pediatr Pathol 1992;349:12.
79. Landing BH, Wells TR. Tracheobronchial anomalies in children. Perspect Pediatr Pathol 1973;1:1.
80. Wells TR, Jacobs RA, Senac MO, Landing BH. Incidence of short trachea in patients with myelomeningocele. Pediatr Neurol 1990;6:444.
81. Sein K, Wells TR, Landing BH, Chow CR. Short trachea, with reduced number of cartilage rings—a hitherto unrecognized feature of DiGeorge syndrome. Pediatr Pathol 1985;4:81.
82. Landing BH, Dixon LG. Congenital malformations and genetic disorders of the respiratory tract (larynx, trachea, bronchi, and lungs). Am Rev Respir Dis 1979;120:151.
83. Wells AL, Wells TR, Landing BH, Cruz B, Galvis DA. "Short trachea"—a hazard in tracheal intubation of neonates and infants: syndromal associations. Anesthesiology 1989;71:367.
84. Marks F, Hernanz-Schulman M, Horii S, et al. Spondylothoracic dysplasia. Clinical and sonographic diagnosis. J Ultrasound Med 1989;8:1.
85. Wells TR, Wells AL, Galvis DA, Senac MO, Landing BH, Vachon LA. Diagnostic aspects and syndromal associations of short trachea with bronchial intubation. Am J Dis Child 1990;144:1369.
86. Thomas RA, Landing BH, Wells TR. Embryologic and other developmental considerations of thirty-eight possible variants of the DiGeorge anomaly. Am J Med Genet 1987;(Suppl 3):43.
87. Soliman SM. Thyroid cartilage at the suprasternal notch with low situated thyroid. J Laryngol Otol 1988;102:476.
88. Wells TR, Landing BH, Padua EM. The question of parallax-effect on radiographic assessment of short trachea in infants and children. Pediatr Radiol 1991;21:490.