Series of Laryngomalacia, Tracheomalacia, and Bronchomalacia Disorders and Their Associations With Other Conditions in Children

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Summary. Laryngomalacia, bronchomalacia, and tracheomalacia are commonly seen in pediatric respiratory medicine, yet their patterns and associations with other conditions are not well-understood. We prospectively video-recorded bronchoscopic data and clinical information from referred patients over a 10-year period and defined aspects of interrelationships and associations.

Two hundred and ninety-nine cases of malacia disorders (34%) were observed in 885 bronchoscopic procedures. Cough, wheeze, stridor, and radiological changes were the most common symptoms and signs. The lesions were most often found in males (2:1) and on the left side (1.6:1). Concomitant malacia lesions ranged from 24%forlaryngotracheobronchomalaciato 47% for tracheobronchomalacia. The lesions were found in association with other disorders such as congenital heart disorders (13.7%), tracheo-esophageal fistula (9.6%), and various syndromes (8%).

Even though the understanding of these disorders is in its infancy, pediatricians should maintain a level of awareness for malacia lesions and consider the possibility of multiple lesions being present, even when one symptom predominates or occurs alone. Pediatr Pulmonol **Pediatr Pulmonol. 2002; 34:189-195.** © 2002 wiiey-Liss. inc.

Key words: laryngomalacia; tracheomalacia; bronchomalacia; malacia disorders; syndromes.

INTRODUCTION

Tracheomalacia, bronchomalacia, and laryngomalacia disorders are commonly seen in tertiary pediatric respiratory practice. These disorders of the large airways are associated with cough, wheeze, and stridor, covering most of the common respiratory symptoms seen in children. The importance of diagnosing tracheomalacia, bronchomalacia, and laryngomalacia ranges from life-threatening disease requiring major diagnostic and surgical interventions to parental reassurance and withdrawal of drugs often used to treat these disorders unnecessarily.[1~7] In our collective experience, many children are only referred for assessment after repeated failures of trials of asthma drug therapies and antibiotics.

However, with the symptoms involved often overlapping other respiratory disorders, it is not surprising that the management of these disorders could be viewed as suboptimal. In addition, the prevalence of these disorders is not known, and just what relationships exist between these disorders and vascular and cardiovascular disorders, immunological disorders, recurrent bronchitis, bronchiolitis, asthma, chronic suppurative lung disease and pneumonia are also not known, making decisions of management even more difficult in terms of diagnostic precision, drug therapies, and long-term prognostication,

The aim of this report is to describe an extensive experience of various forms of laryngomalacia, tracheomalacia, and bronchomalacia and explore some of the interrelationships that exist between these conditions with respect to their anatomical sites and associations,

METHODS

A detailed review of the prospectively recorded clinical features and videotaped bronchoscopic lesions of the airways from children referred to the authors over a 10-year period was undertaken. The children were referred to the Royal Children's Hospital and Mater

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Children's Hospital, Brisbane, from throughout the state of Queensland, Australia, where the total population is approximately 3 million, of whom 500,000 are children. These referral centers handle almost all complex pediatric respiratory medicine for the state.

Children with the endoscopic diagnosis of laryngomalacia, bronchomalacia, or tracheomalacia were selected from all bronchoscopic procedures performed.

The endoscopic diagnostic features are outlined below, and examples are given in Figures 1-10. For the purposes of this report, we introduce the term "malacia disorders" to cover the lesions as a group.

Definition 1

Laryngomalacia is a long, curved epiglottis, short aryepiglottic folds (false cords), prominent and or bulky arytenoids and degrees of prolapse of the arytenoids, and changes in epiglottic appearance and position seen during inspiration and returning to the original position during expiration.

Definition 2

Tracheomalacia is a membranosa deformity in the trachea, maintained during spontaneous respiration but which could be altered by the passage of the bronchoscope or positive airway pressure changes. The descriptive appearances accepted as tracheomalacia are as follows: triangular (Fig. 1), oval/flattening (Fig. 2a-c), localized extrathoracic raised and dynamically bulging pars membranosa (tracheal dyskinesia) (Fig. 3a,b), and an "Eifel Tower" appearance (Fig. 4a,b).

Pericarinal tracheobronchomalacia was defined as a flattening in the anterior/posterior plane of the trachea, extending into the left and right main-stem bronchi (Figs. 5a,b, 6a-c). Tracheomalacia associated with tracheo-esophageal fistula is usually seen as a combination of a dynamically bulging pars membranosa and anterior flattening or triangular appearances (Figs. 7a-d, 8a-c).

Definition 3

Bronchomalacia is an appearance of deformity in the large right or left main-stem bronchi, and/or their respective divisions at the lobar or segmental level. The appearance of deformity could be altered by a passage of the bronchoscope or applied positive airway pressures. The usual appearance of malacia in the left main stem was that of an "inverted teardrop," with partial or complete apposition of the mucosal superior and inferior surfaces producing a slit-like opening (Fig. 9a,b). Lobar or segmental lesions usually had slit-like or "lunar crescent appearances" (Fig. 10a,b).

ABBREVIATIONS

CLE	Congenital lobar emphysema
CT	Cono-truncal
LMS	Left main .stem
RMS	Right main stem
SYN	Syndrome
TEF	Tracheo-esophageal lislula

Materials and Bronchoscopic Procedure

All diagnostic information was obtained during flexible bronchoscopic procedures performed during spontaneous breathing under gaseous general anesthesia. The anesthetic agents used were halothane and or sevoflurane. The vocal cords and trachea were sprayed with lignocaine from a Cass needle or direct spray. Generally, the children breathed spontaneously throughout the procedure, and positive end expiratory pressure was not usually applied except during periods of assessment of malacia. The bronchoscope was passed into the airway through a port in the connector to the facemask. The same four anesthetists were involved in all procedures. All cases were videotaped for later perusal. Anatomical sites and type of lesion were detailed in each case. All bronchoscopic procedures were performed when the children were clinically well or stable. A Pentax FB10X 3.5 mm or Olympus BF 3C40 3.6 mm bronchoscope was used in each case.

Statistics

All data were expressed as simple percentages, medians, and ranges.

RESULTS

Two hundred and ninety-nine cases of laryngomalacia, tracheomalacia, bronchomalacia, and/or combinations of the three were defined from a total of 885 bronchoscopies performed over a 10-year period. This represents 34% of the procedures being defined a "malacia disorder."

Malacia disorders were defined in 205 males and 94 females, i.e., a male to female ratio of 2:1. In recognized syndromes and related disorders, the male predominance ranged from 1.6:1 to 8:1. The ratios and associated conditions are shown in Tables 1 and 2.

The median age of this cohort was 9 months (range, 1 day to 240 months), with the median age of males being 9 months, and that of females being 9.6 months.

Stridor was reported in 127 (42.5%), and of these, 58 (19.4%) reported stridor alone. Wheeze and cough symptomatology was reported in 130 (43.4%) and 212 (71%), respectively, while 34 (11.7%) reported all three symptoms. These signs were not usually present in very sick patients, particularly cardiac patients, where unex-

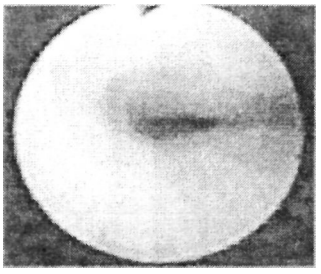

Fig. 1. Triangular appearance of tracheomalacia.

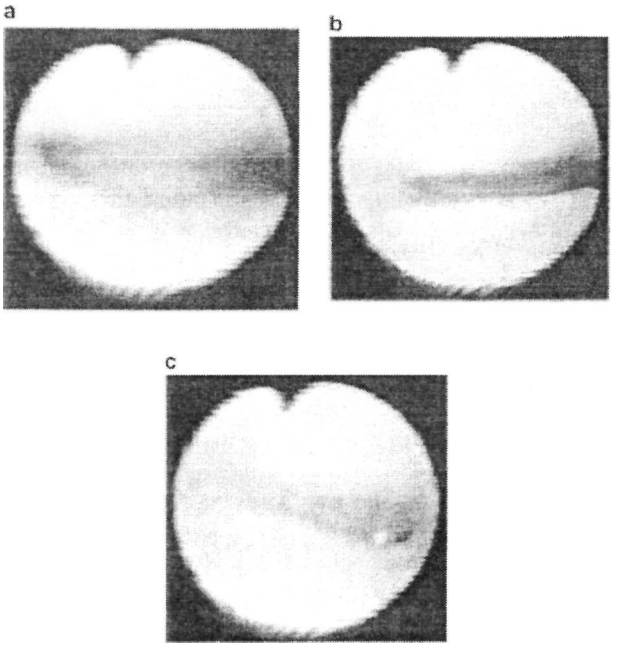

Fig. 2. Pericarinal and right and left main-stem malacia. Oval shape (a) and progressive flattening on expiration of pericarinal and right and left main-stem bronchi (b), and complete closure of L main stem bronchi (c).

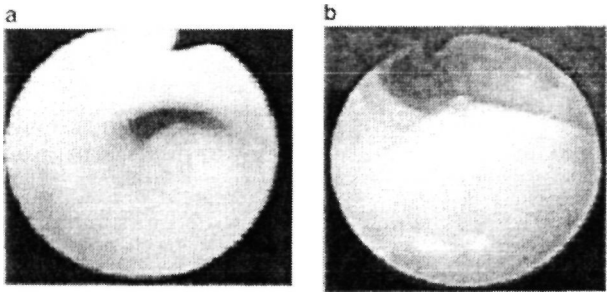

Fig. 3. Bulging pars membranosa: subglottis and proximal trachea: "posterior tracheomalacia." Dynamically bulging pars starting in the subglottis (a), and progressing to less prominent bulge lower in the trachea (b).

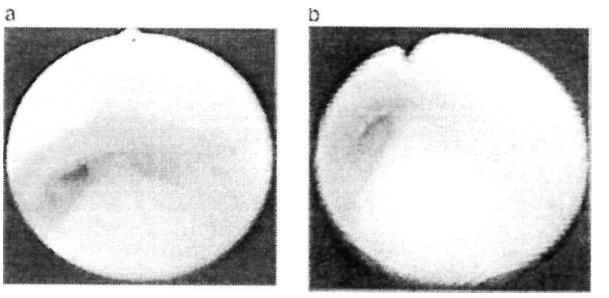

Fig. 4. "Eifel tower" appearance of tracheomalacia (a), and progressive expiratory closure with mucosal surfaces apposed (b).

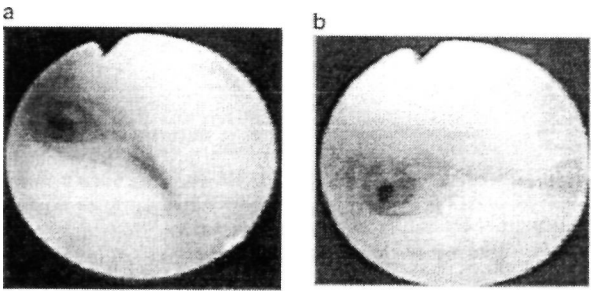

Fig. 5. Pericarinal right main-stem malacia (a), and progressive closure of right main stem on expiration (b).

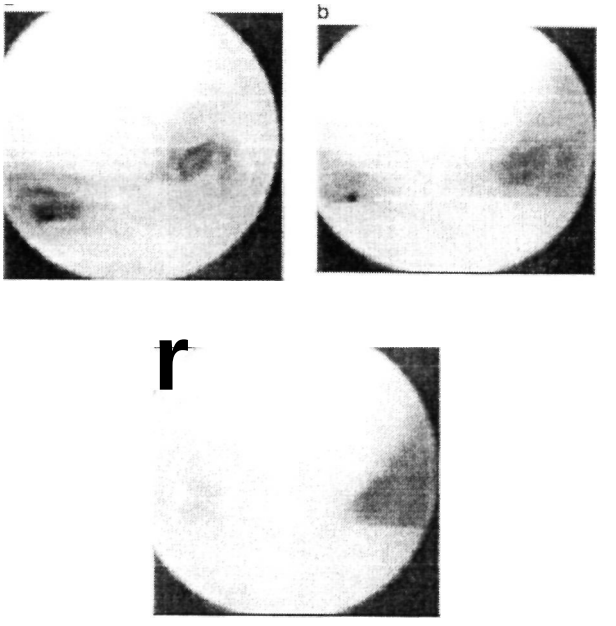

Fig. 6. Pericarinal and left main-stem malacia (a),and progressive closure of left main stem on expiration (b) to complete closure and mucus extrusion (c).

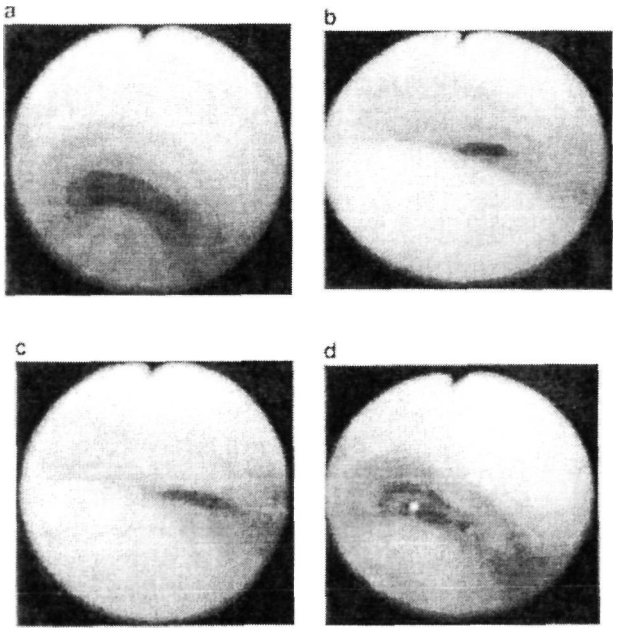

Fig. 7. Tracheo-esophageal fistula malacia. Progressive closure with pars bulging forwards (a) and flattened anterior cartilage (b), proximal to fistula site and progressing from right-to-left triangle (c) to left-to-right triangle appearance (d) lower in the trachea.

plained oxygen requirements and radiographic signs were the predominant reason for referral.

One hundred and twelve (37%) had radiographic abnormalities in the form of parenchymal abnormalities consistent with any of the following changes of collapse, consolidation, and radio-lucency.

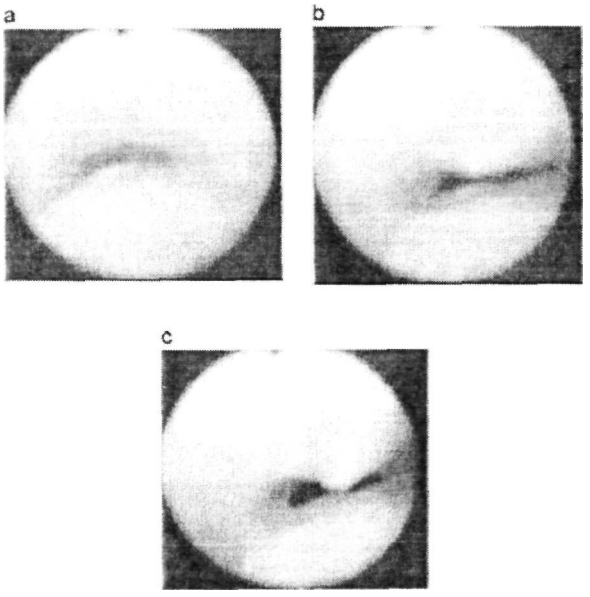

Fig. 8. Tracheo-esophageal fistula malacia with residual pit visible (a), triangular appearance, and an associated anterior granuloma (b, c).

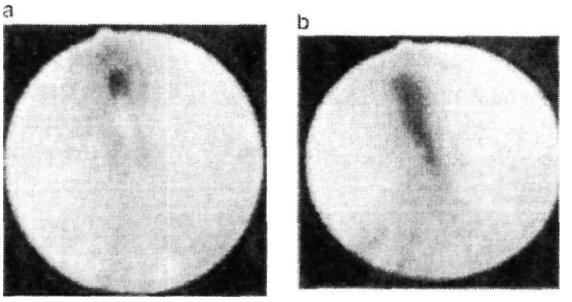

Fig. 9. Left main-stem bronchomalacia. Left main-stem "inverted teardrop" malacia with (a) and without (b) retained secretions.

Of the 59 children diagnosed with laryngomalacia, 14 (24%) had combined lesions, i.e., laryngotracheobronchomalacia. Eighty children (26.7%) had tracheomalacia alone, 103 (34.4%) had bronchomalacia alone, and 146 (48%) had some combination of tracheobronchomalacia. There was a male predominance for all of these lesions (Tables 1 and 2).

Congenital cardiac disorders and/or cardiovascular anomalies were present in 41 (13.7%) patients, of whom 11 had a vascular ring anomaly, including 3 with a double aortic arch and 2 with a pulmonary artery sling. Of the 3 patients with a double aortic arch, one had a surgical division of the ring because of respiratory failure in the neonatal period. This produced a marked improvement in function, but the appearance changed little over the first 12 months of life. The two cases of pulmonary artery sling were left unoperated; the associated appearance of saber-shaped tracheal stenosis and RMS malacia remained unchanged but functionally less important over time. Cono-truncal cardiac disorders were present in 19 cases, with the malacia appearance being universally found in the trachea and/or the left main-stem bronchus. Most had had surgery at the point of assessment, but such lesions were also present in those in whom an operation had not been performed.

Tracheomalacia was associated with the primary diagnosis of tracheo-esophageal fistula (TEF) in 29 patients (9.7%), and congenital lobar emphysema (CLE)

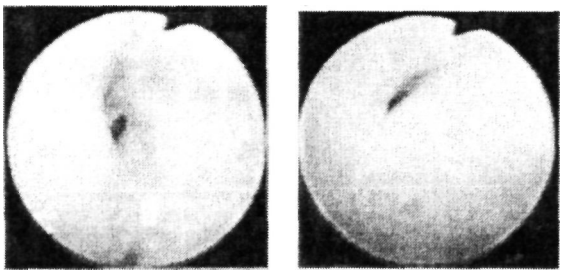

Fig. 10. Left upper lobe lobar and segmental bronchomalacia. Left upper lobe malacia (a) and segmental malacia (b).

TABLE 1 — Age and Gender Distribution of the "Malacia Disorders"

	Lm (n = 88)	Lm** (n = 59)	T (n= 163)	T** (n = 80)	B (n=143)	LTB (n=14)
Male	57	35	118	55	103	9
Female	31	24	45	25	43	5
M:F	1.54:1	1.45:1	2.6:1	2.2:1	2.4:1	1.8:1
Median age	4Mths	4Mths	15 Mths	15 Mths	9.6 Mths	5 Mths

Lm, laryngijmalacia in combination; Lm**, laryngomalacia alone; T, tracheomalacia; T*[1]:, tracheomalacia alone; B, bronchomalacia; LTB, laryn gotracheobronchomalacia; Mths, months.

was found in 9 patients. In the former group with TEF, 6 required aortopexy/tracheopexy because of severe airway obstruction requiring mechanical ventilation. All procedures were carried out with bronchoscopic guidance, all patients were extubated successfully, and none required further ventilation. The endoscopic appearances were markedly changed at the end of the procedure, with either a near-normal appearance or a peaked triangular appearance sustained across the respiratory cycle. In this latter group of children, the bronchomalacia was at the lobar site of the CLE. There was a male predominance for both of these disorders (Table 2).

Twenty-four children (8%) had defined syndromes, associations, and/or chromosomal abnormalities including Down's syndrome, cri du chat syndrome, Rubinstein-Taybi syndrome, Ehlers-Danlos syndrome, Smith's syndrome, Opitz syndrome, Goldenhaar syndrome, Costello's syndrome, neurofibromatosis syndrome, Allagille's syndrome, Hunter's syndrome, VATER association, CHARGE association, and arthrogryposis.

Laryngomalacia cases exhibited a variety of functional appearances, with varying degrees of prolapse of the arytenoids and supraglottic rima structures generally. The mucosal appearance in terms of color and apparent bulkiness of the arytenoids varied, as did the extent of airway closure, with some cases actually displaying complete luminal closure with inspiration.

Tracheomalacia was usually located in the middle and lower thirds of the trachea, but 4 cases were localized to the upper airway, where localized sections of the pars membranosa protruded into the lumen and bulged further forwards dynamically with inspiration. The degree of airway closure associated with these lesions varied, as did the mucosal appearances and associated presence of mucus.

TABLE 2—Gender Distribution of Malacia Disorders Associated With Various Disorders

	TEF	CT	CLE	SYN
n	29	19	9	23
Male	IS	13	8	17
Female	11	6	1	6
Ratio M:F	1.6:1	2:1	8:1	2.8:1

TEF, tracheoesophageal fistula; CT, cono-truncal lesions; CLE, congenital lobar emphysema; SYN, syndrome.

Bronchomalacia was predominantly seen on the left side, with 107 (35.7%) left-sided lesions and 66 (22%) right-sided lesions, the ratio of left:right lesions being 1.6:1. The malacia was most commonly seen in the left main-stem (LMS) bronchus (73 cases), followed by the left upper lobe bronchus, right middle lobe bronchus, and right main-stem (RMS) bronchus, with 37, 33, and 31 cases, respectively. Males again predominated, accounting for 74 (71.8%) of the left-sided lesions and 52 (78.7%) of the right-sided lesions.

DISCUSSION

This is the largest series of large airway lesions diagnosed by flexible bronchoscopy in children reported to date. We showed that malacia changes are common in children referred for persistent respiratory symptoms and signs; that combined or multiple lesions commonly overlap the upper and lower airway compartments either serially or concomitantly; and that left-sided lesions are more common than right-sided bronchomalacia lesions. These data also suggest that there is a predilection for males to have all forms of malacia disorders. Males are thought to have more respiratory disorders early in life than females, but what the relative risks of such differences are is not known. Therefore, it is possible that the male predominance in this study merely reflects these differences. However, as there was no separation of age ranges between males and females, it is likely that this gender effect is real.

What role these lesions have in the development of symptoms such as wheeze may be readily accepted in the cases of main-stem lesions, but in segmental lesions it appears to be beyond simple mechanical arguments, unless there is significant peripheral gas-trapping associated. Nevertheless, persistent respiratory symptoms in association with lobar and/or segmental airway lesions have been well-described.[8-] ' Exactly why this occurs is unknown, but the possibility of a subtle and generalized etiological process that involves functional abnormalities in the development of the neurovascular and airway immunological, smooth muscle, and epithelial

cell lines would be biologically possible. It is also well-known that signs or symptoms may persist after surgical interventions, such as tracheopexy/aortopexy on airway lesions. Follow-up endoscopy often reveals incomplete anatomical correction, but concomitant lesions as seen in this series should always be considered.

It should also be remembered that the loss of signs, radiographic changes, and unexplained oxygen requirements may be presenting features, particularly in sick cardiac patients.

The finding of multiple-lesion bronchomalacia in conjunction with tracheomalacia has not been universally described, despite relatively large numbers in the previous series.[8,12] It is well-recognized that positioning of the bronchoscope, state change, and the application of lignocaine may result in changes in the functional appearance of laryngomalacia lesions.[13,14] In this study, we carried out the procedures under a general anesthetic, with a local anesthetic agent applied to the glottic and tracheal structures. With respect to airway lesions involving the trachea and bronchi, we do not believe that such appearances could be totally explained by local/general anesthetic effects or artificially induced by pressure dynamics[15] across a shared airway, as the segmental orifices distal to the malacic orifice are often normal. Airway closure during suction is common, and while suction appears to amplify airway closure in malacic areas, the effect is usually transient. Whatever the effect of anesthesia, we believe that the bronchoscopic appearances must always be considered in conjunction with the clinical features when defining severity or the need for interventional therapy.

This series revealed left main-stem lesions to be the most common. Defining this "inverted teardrop" appearance is a controversial diagnostic issue.[16,17] While this appearance is common at entry into the left main stem, closer inspection often reveals the appearance to be due to the curvature of the left main stem without any apparent real reduction in cross-sectional area. While such cases were not included or diagnosed as malacia in this series, the lack of objective measurements necessary to define the normal and observed changes remains a difficulty in assessing minor changes of the left main-stem bronchus.[18]

Tracheomalacia and bronchomalacia are associated with congenital heart lesions,[19] especially cono-truncal lesions.[20] Cono-truncal lesions may be associated with 22ql 1 — chromosomal defects. Vascular ring lesions have also been described in association with 22ql 1— chromosomal defects,[21,22] albeit at low rates, thus serving to highlight the need to consider investigation for this genetic defect and associated immunological anomalies in cases of tracheomalacia and bronchomalacia.

The male predominance of malacia lesions and the left-side predominance of bronchomalacia lesions raise questions about the importance of gender, laterality in the development of the lung and airways, and the interrelationships of the airway, heart, and blood vessels in the development of lesions. Similarly, the association of tracheo-esophageal fistula (TEF) with malacia is interesting, but the variable position of the malacia in relation to the fistula and the fact that the malacia may postdate the TEF surgery again raise concerns about the embryonic origins of these lesions.[1-23~2:'] Indeed, the sonic hedgehog gene (SHH) has been shown to be important in the generation of tracheo-esophageal fistulas in mice and humans.[26]

The understanding of the etiological or genetic factors that contribute to the development of malacia disorders is in its infancy. Also, there are minimal data on how malacia disorders contribute to respiratory symptoms in children. From the data presented, we suggest that pediatricians should have an awareness of the possibility of malacia lesions in a child with persistent or recurrent respiratory symptoms, and we feel the need to be cognizant of the possibility of multiple lesions being present, even when one symptom predominates or occurs alone. In doing so, pediatricians should also be cognizant of the need not to overtreat these disorders with asthma medications. While developments in gene technologies raise interesting questions as to the etiology and development of these lesions, the need for strict definitions utilizing objective measures should not be underestimated, particularly if further research in this area is contemplated.

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