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# 73

# Pathology of the Trachea and Main Bronchi

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The trachea and main bronchi are not a mere coupling device between the larynx and lungs proper. Their main function of transporting air in and out of the lungs is accomplished through remarkable and specific physiologic mechanisms.[1] They are also the seat of many pathologic processes to be presently discussed (Display 73-1).

## *PATHOPHYSIOLOGY*

Embryologically, the tracheobronchial tree arises as an outpouching of the primitive esophagus or foregut, and both structures are endowed with a rich muscular wall. However, in the esophagus the muscle is arranged in a circularly oriented inner coat and a longitudinal outer coat, whereas in the tracheobronchial tree the muscular wall is fundamentally circular. This elemental anatomic difference is reflected in diametrically opposed functions. The esophagus generates successive contraction or propulsion waves analogous to the peristaltic activity of the intestine. On the other hand, the trachea and bronchi contract as a whole and uniformly reduce the caliber of the airway in an all-or-none manner. This occurs throughout the ventilatory cycle and particularly during coughing, when a quick rise in pressure is created against a closed glottis.

As a corollary to the previous discussion, the tracheobronchial muscle has a relatively small role in the mobilization and elimination of secretions; the latter is mainly a function of the mucociliary apparatus of the mucosa (see Chaps. 1 and 11). It is only in the presence of large amounts of secretions that quick muscle contractions are elicited through the cough mechanism. Yet, a finely tuned contraction-dilation interplay of muscle is central to ventilatory aerodynamics throughout the respiratory cycle.

It is also clear that whereas muscle contraction is an active phenomenon resulting in a diminution of tracheobronchial caliber, dilatation results from the combination of muscle relaxation and the elastic recoil of the semirigid cartilaginous wall. Not surprisingly, diseases that affect the anatomic integrity of tracheobronchial cartilage will result in airflow limitation.

Clinical manifestations resulting from diseases of the trachea and main bronchi are fundamentally due to central airway obstruction (CAO), which frequently poses serious diagnostic challenges. As noted by Spivey and colleagues, the diameter of the trachea must be reduced by almost one half before symptoms such as dyspnea and wheezing appear, and before a reduction in exercise tolerance can be demonstrated.[2] Even in the presence of the previously described symptoms, there is a natural tendency to ascribe them to much more common clinical conditions, such as chronic bronchitis, asthma, and emphysema. To complicate matters, CAO frequently coexists with the previously described clinical processes. The presence of a normal chest x-ray film adds to the confusion, although this is less likely to happen with current imaging techniques. Therefore, it is not unusual to miss altogether or ignore the early stages in the development of CAO, thus forsaking a better chance for cure. Physiologic tests, however, are recognized as a most valuable, although not infallible, means to arrive at an early diagnosis of CAO.

The seven patients in the study by Spivey and associates exemplify some of the most common pathologic conditions that give rise to CAO[2]:

- benign recurrent subglottic obstruction due to fibrous webs
- benign fibrous strictures secondary to tracheostomy
- intermittent obstruction of the base of the tongue in an obese person, designated "sleep apnea"[3]
- primary and metastatic tumors of the trachea and bronchi
- compression of the airways by mediastinal masses, such as in a patient with Hodgkin disease.

**DISPLAY 73-1. PATHOLOGY OF THE TRACHEA AND MAIN BRONCHI**

**Malformations**
Tracheocele and diverticulosis
Saber-sheath trachea

**Iatrogenic Injury**
Postendotracheal and post-tracheostomy intubation
Tracheoarterial fistulae
Acquired tracheoesophageal fistulae

**Inflammatory and Infectious Conditions**
Infections intrinsic to the airways
Infections and inflammatory conditions of the mediastinum that secondarily affect the airways

**Tumors**
Primary
Metastatic

**Specific Entities**
Relapsing polychondritis
Tracheobronchopathia osteochondrodysplastica
Tracheobronchial amyloidosis

## *MALFORMATIONS OF THE TRACHEA*

Malformations of the trachea and main bronchi can be congenital or acquired, sometimes both. In Chapters 6 and 7, the congenital malformations of the airways are discussed; I wish to add the subject of tracheocele, a rare lesion that can be either congenital or acquired. In the report by Gronner and Trevino, the patient was a 59-year-old woman in whom a tracheocele had the features of an air goiter, which the patient could produce by increasing intrathoracic pressure.[4] It resembled closely a diffusely enlarged thyroid gland, but it was soft and disappeared with the release of the Valsalva maneuver. Collection of mucus in a tracheocele can overflow and produce aspiration pneumonia.

### *Diverticulosis of the Trachea*

Diverticulosis of the trachea may be localized or generalized and probably represents a slightly different manifestation of tracheocele. As discussed by Ettman and Keel, the diverticula may be secondary to congenital weakness of the trachea, to chronic inflammation, or to a combination of both.[5] The diverticula are usually small and multiple, although one or two may be large enough to be considered tracheoceles. In the case described by Dinner and colleagues, a tracheal diverticulum was the cause of ventilatory difficulty upon intubation.[6]

### *Saber-Sheath Trachea*

This deformity refers to a narrowing of the intrathoracic trachea in the coronal plane resulting in an anteroposterior lengthening of the organ (Fig. 73-1). The malformation is acquired and observed mainly in men older than 50 years of age. Although lateral collapse of the trachea suggests a weakening of the wall, the tracheal cartilage is usually thickened and densely calcified. Clinical manifestations are those of increased airway obstruction with resulting accumulation of inspissated and encrusted endotracheal secretions. The treatment of this anomaly consists of tracheal dilatation and cleansing, with some improvement.[7] In the patient reported by Hayakawa and colleagues, external fixation of the trachea and right main bronchus was accomplished with polypropylene mesh (Marlex, CR Bard, Billerica, MA) and additional application of lyophilized human cadaveric dura (Lyodura, Braun, Melsungen, AG).[8] The postoperative course of this patient was satisfactory, with functional and radiologic improvement.

The original description of "saber-sheath" trachea was by Simmonds in 1905.[9] In their postmortem study of 1967, Campbell and Liddelow drew attention to the marked variability in the cross-sectional shape of tracheas of older men.[10] Some of their cases had more or less round cross sections, whereas others showed flattening in either the coronal or sagittal diameters. In 3 of 53 cases (6%), they reported marked coronal narrowing similar to saber-sheath trachea.

Greene and Lechner collected 13 cases of saber-sheath trachea, which they defined radiologically as an intrathoracic trachea that was one half or less of the corresponding sagittal diameter.[11] They described in their cases an abrupt change to a rounded

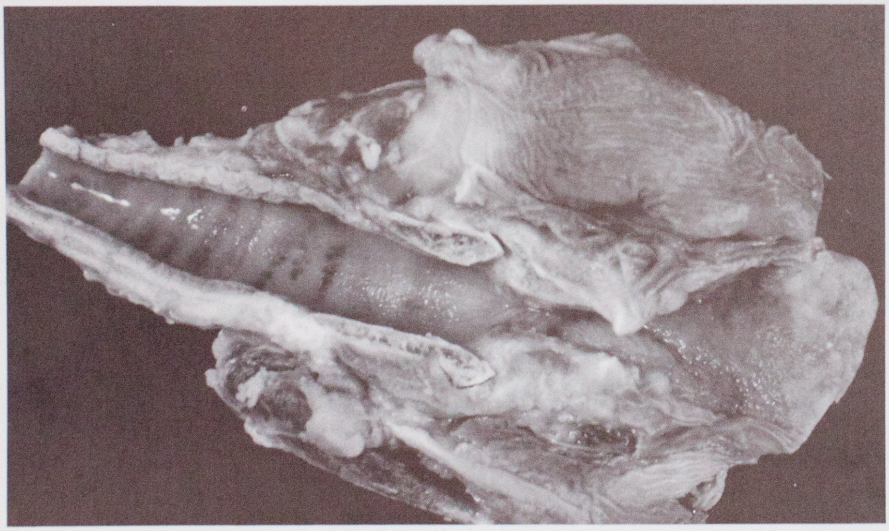


**FIGURE 73-1.** Saber-sheath trachea is seen in an adult alcoholic man who was admitted in respiratory failure and acidosis. Intubation of the patient was impossible; his condition deteriorated rapidly and he expired. At necropsy, the trachea measured 0.7 cm in transverse diameter in the coronal plane and 2.0 cm in the sagittal plane. (Courtesy of Ronald Wright, M.D., Ft. Lauderdale, FL.)

configuration at the thoracic outlet. The tracheal wall was described as thickened, showing evidence of calcification of the cartilaginous rings.

Recognition of saber-sheath trachea can avoid a mistaken diagnosis of mediastinal mass and may help to substantiate a diagnosis of chronic obstructive pulmonary disease. In the series by Greene and Lechner, the latter was present as a clinical diagnosis (11 of 13 patients), a functional abnormality (10 of 11), or both (8 of 11 patients).[11]

In their report, Hoskins and colleagues described two cases of saber-sheath trachea in association with mediastinal lipomatosis.[12] Both cases were initially interpreted as a mediastinal tumor compressing the trachea. The correct diagnosis was subsequently achieved by computed tomography.

## IATROGENIC INJURY

### Complications of Tracheal Intubation

The pathologic effects of cuff endotracheal and tracheostomy tubes have been well documented by Wylie,[13] Fields,[14] and Lewis and Swerdlow[15] (Fig. 73-2*A*, *B*). In 1984, Blanc and Tremblay classified the changes as occurring during the act of intubation, while the tube was in place, and after extubation.[16] Sequelae included manifestations such as vocal cord paralysis, laryngotracheal membranes and webs, laryngeal fibrosis, and tracheal stenosis (Color Fig. 73-1).

Rasche and Kuhns described the histopathologic changes in the airway mucosa of infants at times ranging from 15 minutes to 9 weeks after intubation.[17] They explained the focal necrosis of the larynx and the extensive necrosis of the trachea as due to mechanical trauma by endotracheal and tracheostomy tubes, respectively. As noted by Gould and Graham, acquired subglottic stenosis is the most serious long-term complication of endotracheal intubation in neonates.[18] The stenosis is due to granulation tissue progressing to dense scar formation as a response to endotracheal tube trauma. Comparable changes were described by Puhakka and colleagues[19] and by Smith and associates,[20] who also noted the presence of subglottic cysts.

In adults, use of the Carlens tube for differential spirometry can produce tracheal perforation, as noted by Massard and colleagues[21] and Evrard and associates.[22] Massive tracheal necrosis following elevated endotracheal tube cuff pressures was described by Abbey and colleagues.[23] In newborns, a lesion termed necrotizing tracheobronchitis has been described by Metlay and associates,[24] and the severity of the lesion is related to the duration of the ventilation. It consists of a characteristic basophilic necrosis of the tracheal mucosa followed by sloughing that may cause respiratory obstruction. Metlay and associates[24] believe that the process is due to airflow rather than the effects of the tube itself, because it is worse beyond the end of the tube and extends into major bronchi.

Of great interest for the pathologist are the stenotic lesions consisting of granulation tissue and fibrosis at the site of a prior tracheostomy. Geffin and colleagues stated that more typically the lesions consisted of circumferential stenosis at the level of the inflatable cuff.[25] At the tracheostomy site, the scarring resulted in a shelf or U-shaped obstruction. The pathogenesis of the lesions appears to be pressure necrosis caused by the rigidly inflated cuff followed by cicatrix formation. Other factors include infection (*e.g.*, *Staphylococcus aureus, Pseudomonas aeruginosa* ) and chemical irritation by the tube material, particularly following ethylene oxide sterilization, a toxic and irritant chemical. Resection and anastomosis of the trachea is the treatment of choice in the majority of cases. In patients with coexistent disease processes that contraindicate major tracheal surgery, endotracheal excision of fibrous tissue and dilatation with various types of stents is an alternative, as suggested by Bergström and colleagues.[26]

### Tracheoarterial Fistula

Tracheoarterial fistula, or delayed bleeding following tracheostomy, can result from erosion of a large vessel followed by massive aspiration of blood or exsanguination. In 115 such cases compiled by Schlaepfer, 83 demonstrated erosion of the innominate artery (Fig. 73-3), whereas the remaining cases involved the common carotid, inferior and superior thyroid arteries, aortic arch (Fig. 73-4), and innominate vein.[27] According to Lunding, this complication results from tracheostomies below the fifth cartilaginous ring of the trachea.[28] Infection and incorrect positioning and angulation of the tube are contributory factors.

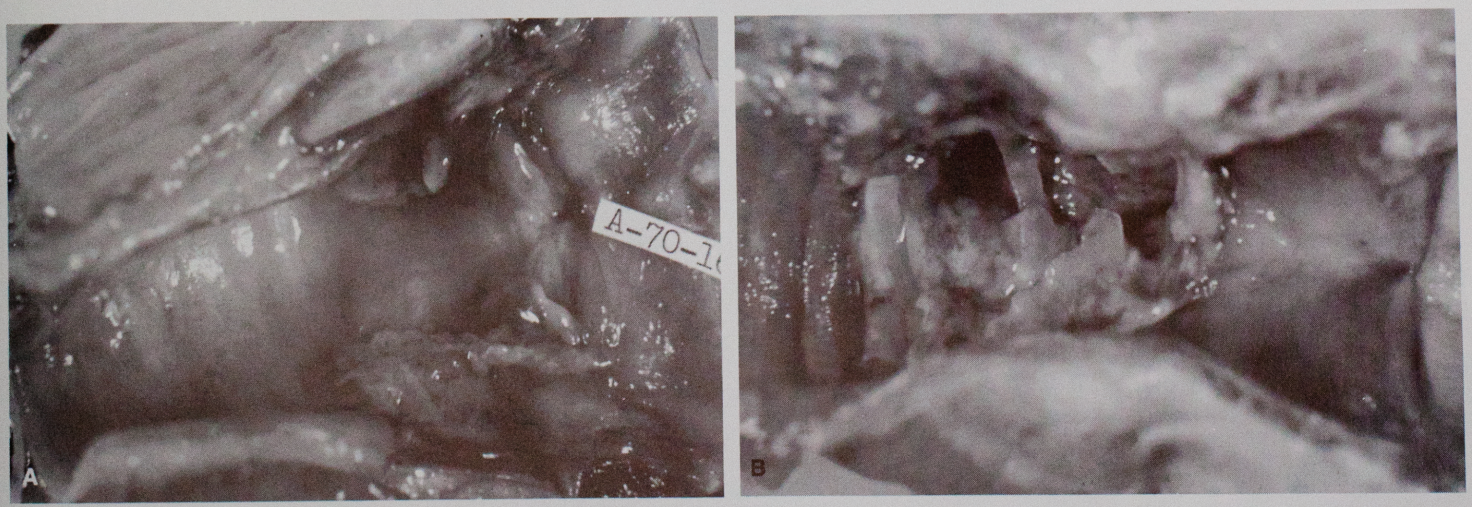



**FIGURE 73-2.** (**A**) Hemorrhagic necrosis and ulceration of the larynx occurred following endotracheal intubation. (**B**) Suppuration and chondromalacia took place at the site of the tracheostomy. (Courtesy of Bolivar Kunhardt, M.D., Miami, FL.)

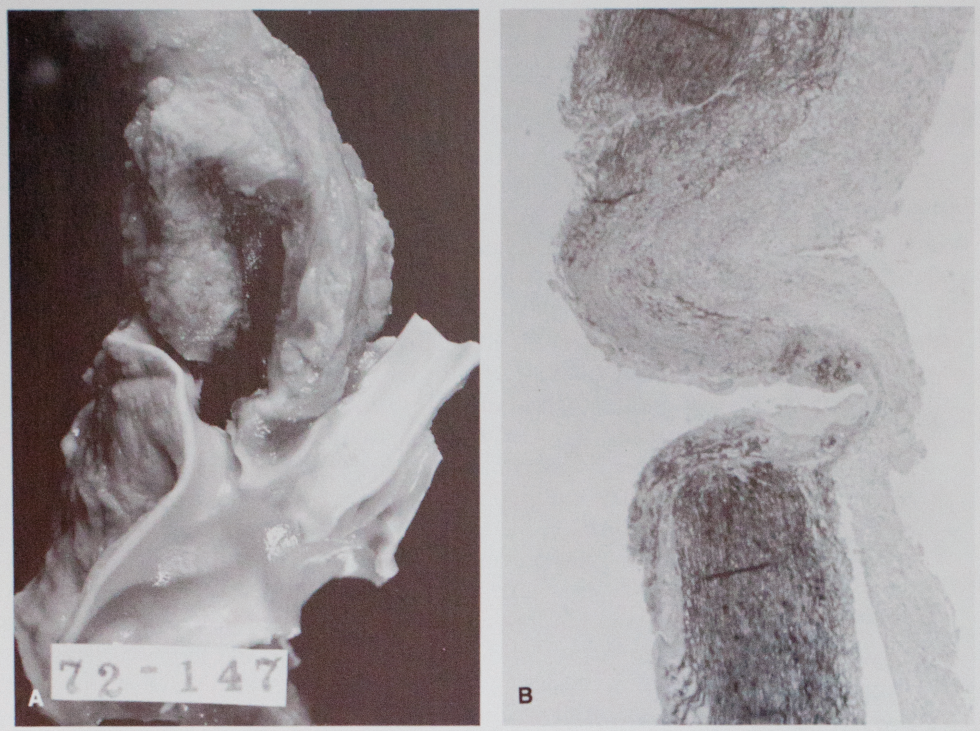



**FIGURE 73-3.** (**A**) A trachea–innominate artery fistula was produced by a tracheostomy tube. The patient died from massive exsanguination. (**B**) In a histologic section of the specimen shown in **A**, the innominate artery wall, recognizable by its rich content of elastic tissue, appears interrupted at the level of the fistula. (Elastic tissue stain; low magnification.)

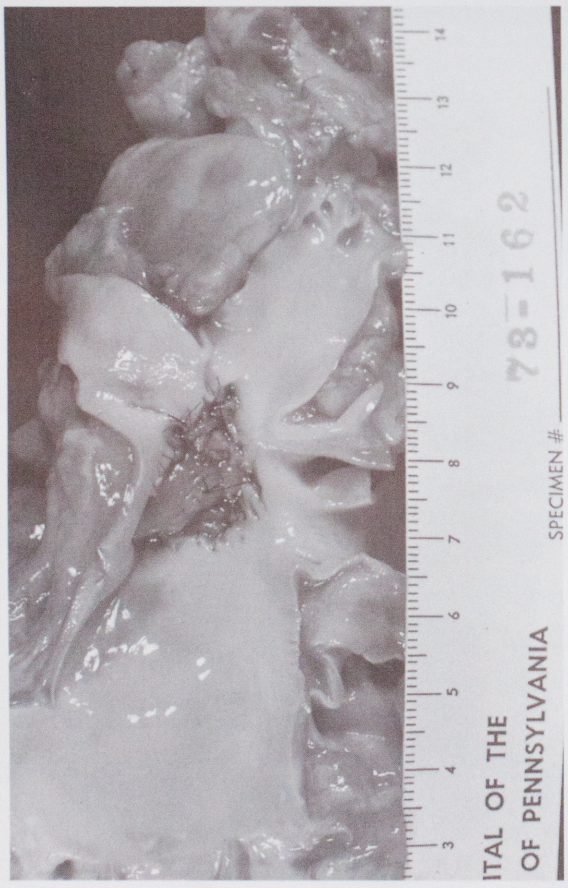



**FIGURE 73-4.** A tracheoaortic fistula was produced by a tracheostomy tube. As in the patient shown in Figure 73-3, there was massive hemorrhage, and the patient died.

### *Tracheoesophageal Fistula*

Acquired tracheoesophageal fistula (TEF) can develop following continuous respiratory assistance.[29–32] This is the result of ischemia caused by pressure of the tracheal cuff on the noncartilaginous membranous posterior trachea and the anterior esophagus. This potentially lethal complication is usually corrected immediately by surgical means. If this is not possible because of the patient's poor clinical condition, it is necessary to wait 8 to 10 weeks until healing and maturation of the fistula has occurred before definitive surgical correction can take place.

In the series of 27 patients with TE fistula described by Marzelle and associates, the lesion was produced by tracheostomy tube cuff (17 patients; Fig. 73-5), intubation tube cuff (8 patients; Fig. 73-6), and injury at the site of tracheostomy (2 patients).[33] The size of the fistulas ranged from 0.3 to 5.0 cm (mean, 2.0 cm).

## *INFLAMMATORY DISEASES OF THE TRACHEA*

### *Infectious Tracheitis*

Tracheal involvement is a common occurrence in many bacterial, viral, and fungal diseases of the respiratory tract described in Section VIII of this book. I wish to call attention to the occurrence of tracheitis in immunosuppressed patients, particularly that caused by herpes virus and cytomegalovirus (see Chaps. 42 and 45).

*Candida* pneumonia complicating acquired TEF was described by Klapholz and colleagues in a patient with AIDS.[34] In a case reported by Iacoviello and associates, protothecosis, a ubiquitous, aerobic, unicellular alga closely related to the green algae *Chlorella*, complicated prolonged endotracheal intubation and resulted in a nasopharyngeal ulceration with a soft-tissue mass.[35] Iacoviello and associates also reviewed 59 cases of this peculiar infection previously reported in the literature.[35] Tuberculosis of the trachea is uncom-

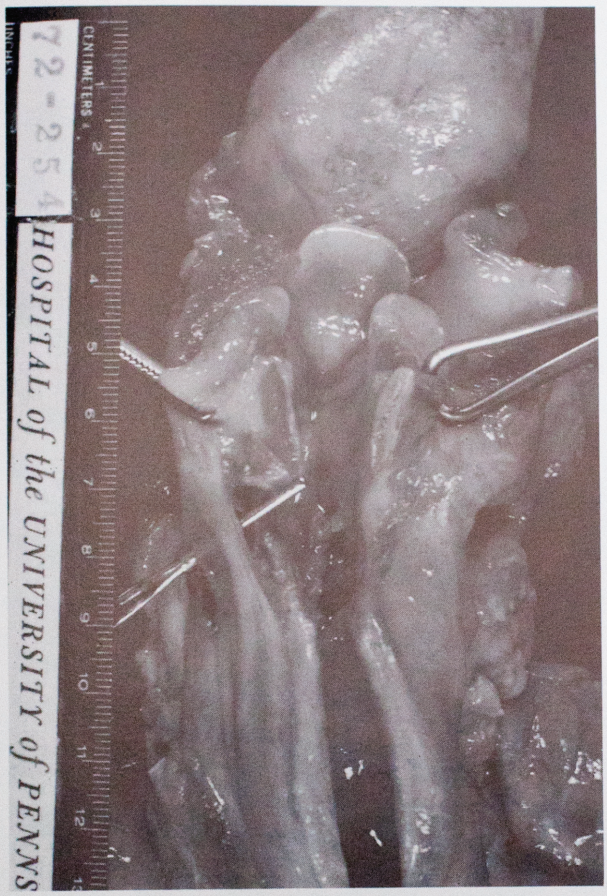



**FIGURE 73-5.** A tracheoesophageal fistula occurred secondary to a tracheostomy. A metal probe has been passed through the fistula.

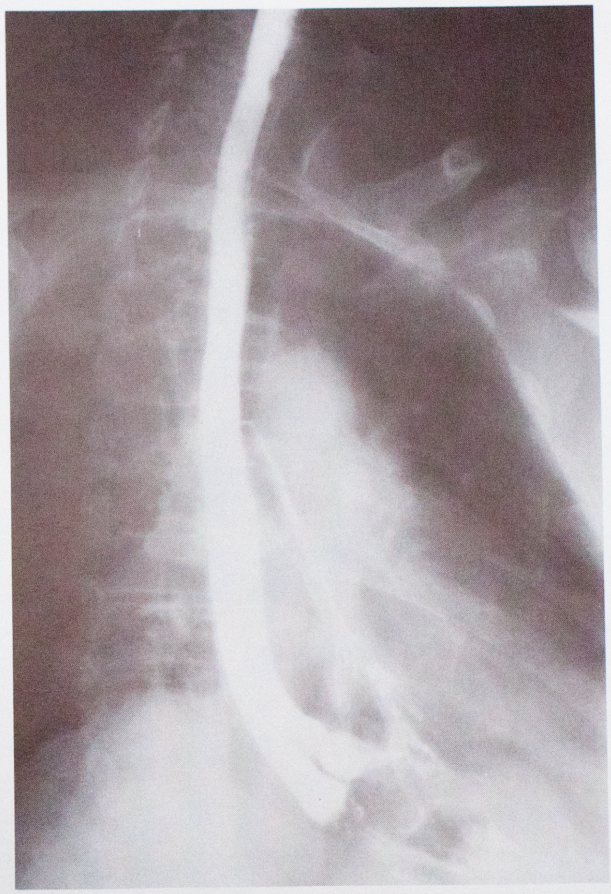


**FIGURE 73-6.** A tracheoesophageal fistula occurred following endotracheal intubation. The esophagram reveals massive passage of contrast medium to the left bronchial system and lung.

mon; in the case reported by Natkunam and colleagues, tuberculosis produced stenosis at the carina requiring surgical resection of the lesion.[36]

Infectious and other inflammatory processes of the mediastinum, including lymph node enlargement by granulomatous processes, can produce obstruction of major airways, particularly of bronchi. This subject, as well sclerosing mediastinitis, is discussed in Chapter 74.

## PRIMARY AND SECONDARY TUMORS OF THE TRACHEA

The first description of a tracheal tumor was made by Morgagni in 1762.[37,38] From that date to the late 1960s, only 37 cases had been reported.[39] In their paper of 1969, Houston and colleagues collated the Mayo Clinic experience from 1936 to 1965.[39] During this 30-year period, there were 53 primary cancers of the trachea, the majority of them squamous cell carcinoma (45%) and adenoid cystic carcinoma (35%). Small cell carcinoma accounted for 4% of the cases, there was one mucoepidermoid carcinoma (2%), and there was one adenocarcinoma (2%; Color Figs. 73-2 and 73-3; Figs. 73-7 through 73-9).

Among mesenchymal tumors of the trachea, leiomyosarcomas accounted for 6% of the cases in the same study.[39] Malignant lymphoma not further specified, Hodgkin disease, lymphocytic lymphoma, and plasma cell myeloma each represented 2% of the cases. Of the two more common tracheal tumors, extension beyond the trachea occurred three times more frequently with cylindromas (58%) than with squamous cell carcinomas (17%). This disparity is perhaps explained by the more prolonged periods of observation in the former tumor. Both malignancies are capable of extensive local invasion and spread to mediastinal lymph nodes, lung, pericardium, vena cava, nerves, and esophagus.[39]

In the study by Hadju and colleagues, 30 of 45 carcinomas of the trachea (73%) were of the squamous variety.[40] In a study by Webber and Grillo, of 30 malignant tracheal tumors, almost two thirds (19 cases) also had this histology.[41] Squamous cell carcinoma was also the most frequent histologic type in the study by Olmedo and associates, followed by adenoid cystic carcinomas (Color Fig. 73-3; see Fig. 73-9), carcinoid tumors (Color Fig. 73-4; Fig. 73-10), sarcomas, and plasmacytomas.[42]

In his recent review of seven series reporting surgically treated malignant tracheal tumors, Allen notes that the most common type of tracheal tumor is adenoid cystic carcinoma.[42a] However, if surgically treated and nonsurgically treated malignant tracheal tumors are included, squamous cell carcinoma is the most frequent.

A variety of benign and malignant papillary tumors occur in the trachea and major bronchi (see Chap. 53). Juvenile laryngotracheal papillomatosis (JLP) is a disease of younger individuals in which numerous papillomas extend from the larynx to the trachea and lung.

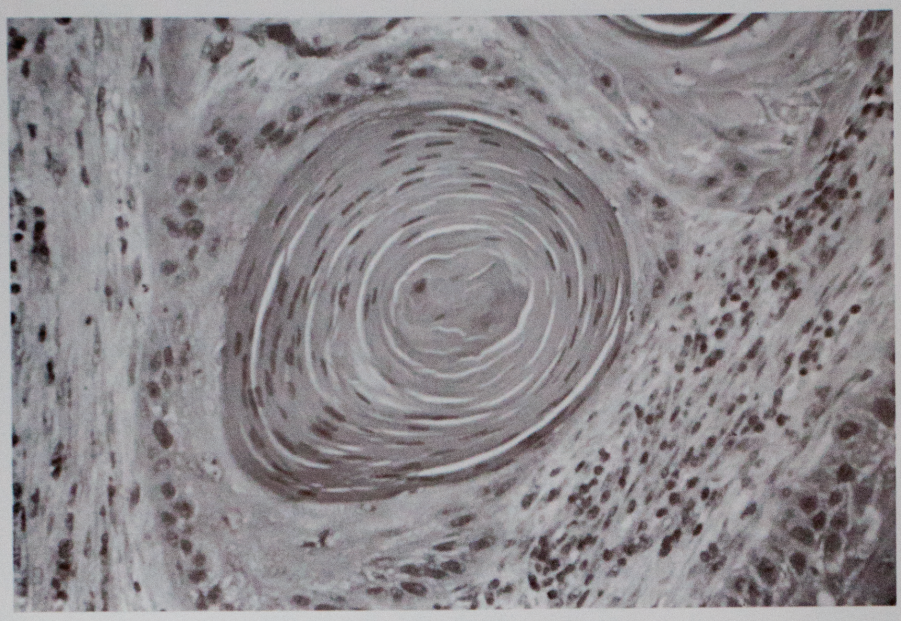
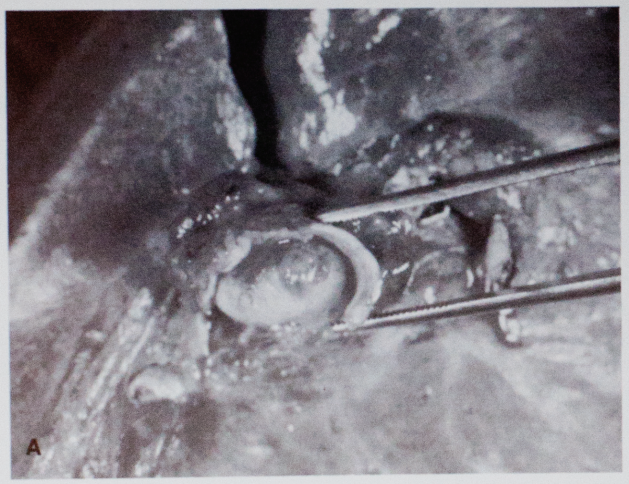
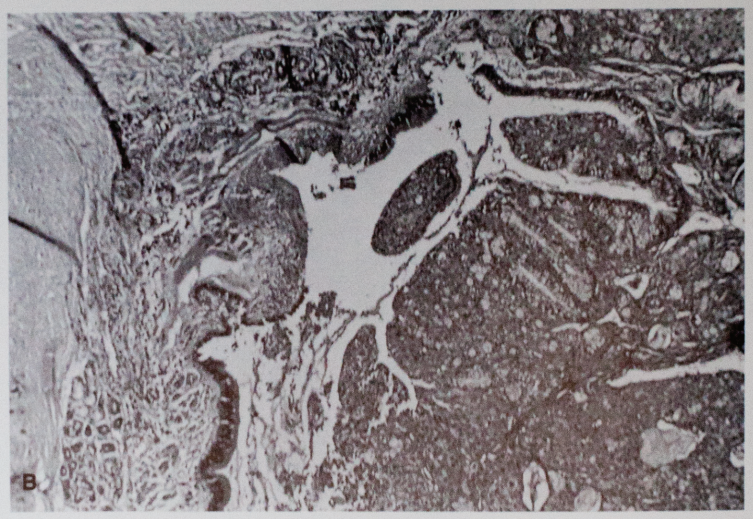


**FIGURE 73-7.** A histologic view of a tumor that produced marked narrowing of the lower one third of the trachea shows well-differentiated keratinizing squamous cell carcinoma infiltrating fibrous stoma (see Color Fig. 73-2). (H & E stain; intermediate magnification.)



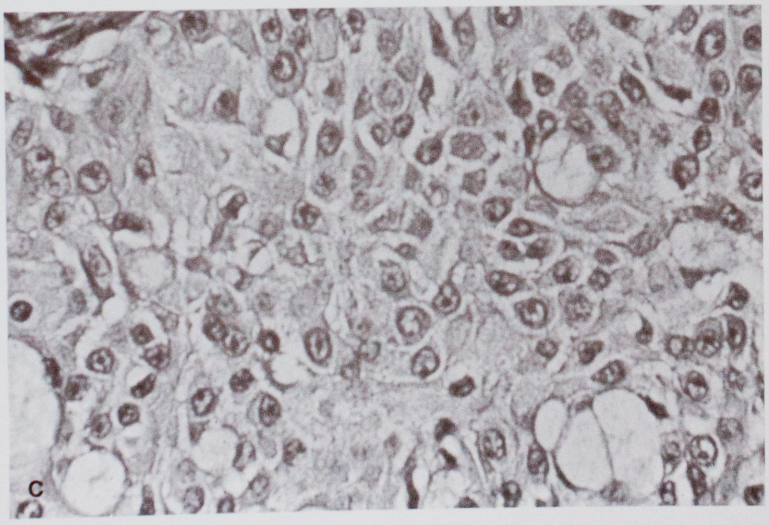




**FIGURE 73-8.** Mucoepidermoid carcinoma of the left main bronchus. (**A**) Marked obstruction by an endobronchial polypoid mass. (**B**) Masses and fronds of tumor cells occlude the bronchial lumen. (H & E stain; low magnification.) (**C**) Low-grade mucoepidermoid carcinoma with mucinous glandular spaces and a solid, well-differentiated squamous component. (H & E stain; intermediate magnification.)

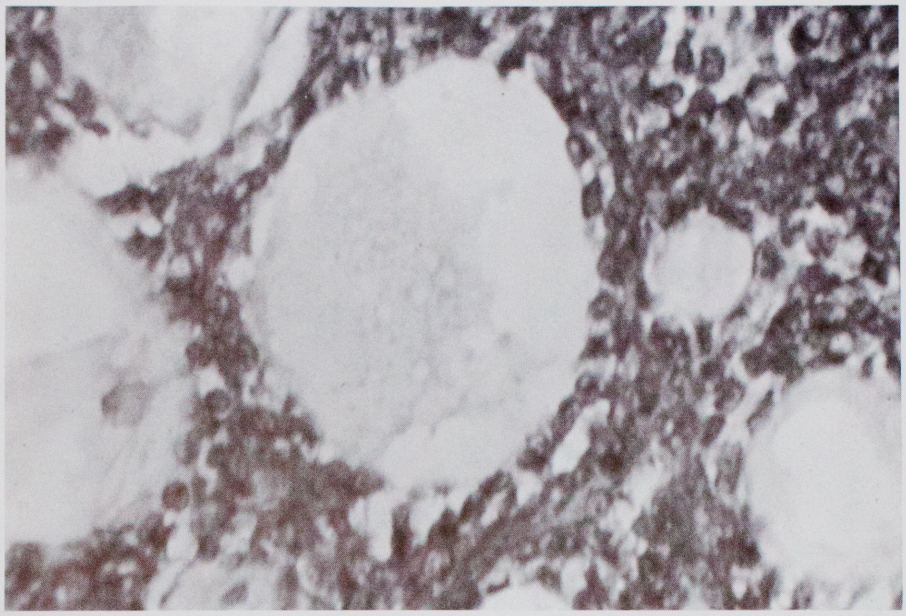


**FIGURE 73-9.** Characteristic histologic appearance of adenoid cystic carcinoma (see Color Fig. 73-3). (H & E stain; intermediate magnification; courtesy of Massachusetts General Hospital, Boston, MA; autopsy 69-13948.)

JLP has the potential to progress to squamous cell carcinoma, particularly following irradiation.

Metastatic lesions of the trachea and major bronchi are frequently the result of primary carcinomas in the breast and kidney (Fig. 73-11), and to malignant melanoma (see Chap. 60). Compression and frank invasion can also be seen in a variety of primary and metastatic tumors of the mediastinum (see Chap. 74).

## SPECIFIC DISORDERS

### Relapsing Polychondritis

The designation "relapsing polychondritis" (RP) was introduced by Pearson and colleagues in 1960[43] for a systemic condition consisting of recurrent lesions of cartilage resulting in collapse and distortion of the external ears, nose, tracheobronchial passages, and articular cartilages.[44–53] The association of the generalized cartilaginous disorder with inflammatory ocular lesions has also been noted.

RP was originally described in the European literature in 1923 by Jaksch-Wartenhorst,[54] and also by Altherr[55] and von Meyenburg.[56] Other terms for the disease include panchondritis, chronic atrophic polychondritis, and diffuse polychondritis (see Chap. 72).

The lesions of RP frequently affect the tracheobronchial tree, producing dissolution and destruction of the cartilage matrix progressing to tracheomalacia. Because of the loss of cartilaginous support, the airways collapse during expiration, producing air trapping. There is also mucosal edema, poor clearance of secretions, and obstructive pneumonia. The resulting respiratory failure is difficult to treat with mechanical ventilation.

The microscopic picture is that of loss of basophilic staining and metachromasia of the cartilage matrix associated with loss of acid mucopolysaccharides. In early stages of the process, loss of lacunae and the presence of neutrophils in the cartilage matrix have also been observed. Later stages of the process are characterized by an inflammatory cell infiltrate composed predominantly of lymphocytes. Still later stages exhibit dense collagenization with replacement of the cartilage and extensive areas of calcification.

It is thought that exposure of cartilage-matrix components to the immune system produces antibodies against cartilage, as detected in some patients with the disease. The clinical relevance of the Glynn and Holborrow study, which involved immunizing rabbits with chondroitin sulfates and producing polysynovitis with destruction of cartilaginous matrix, is yet to be ascertained.[48,57] Studies of T-cell immunity to cartilage-matrix components have also been confusing.[48,58] It is not clear yet if the immune responses in this disease are primary or secondary, and, furthermore, they cannot be demonstrated in every case. Nevertheless, enzymatic degradation of cartilaginous matrix appears to play a role in the genesis of RP.

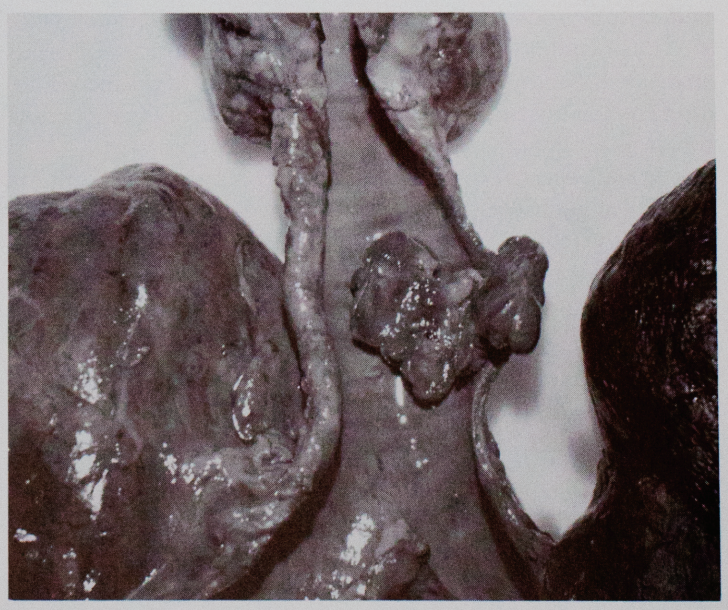


**FIGURE 73-10.** Ossifying carcinoid of the trachea. This pedunculated mushroomlike tumor arose from the trachea of a middle-aged woman. Portions of the tumor felt rock-hard on sectioning (see Color Fig. 73-4).

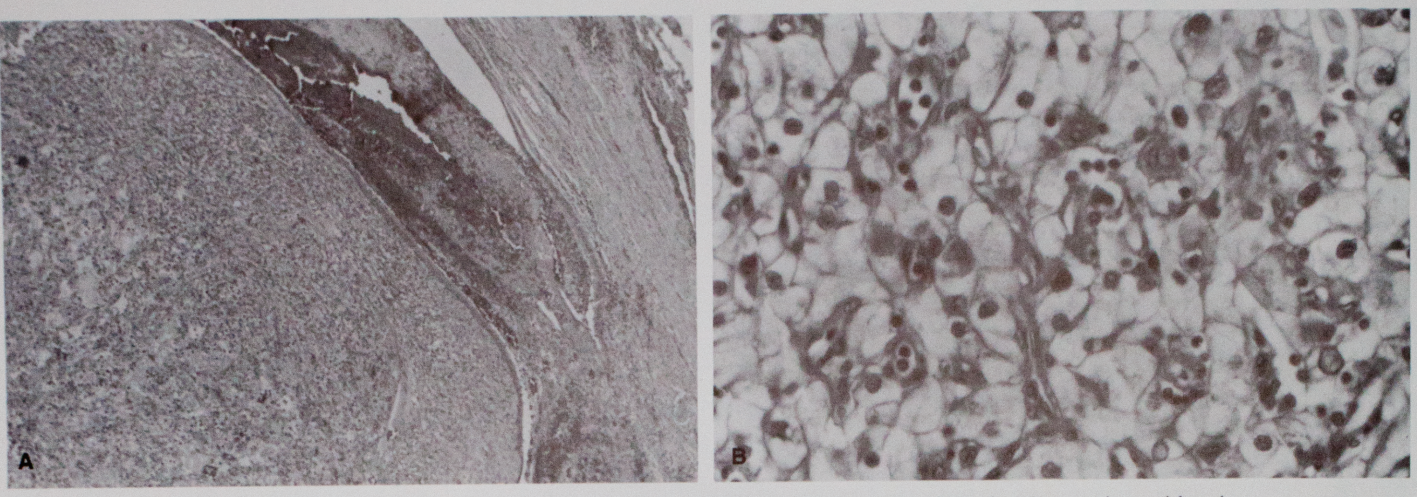



**FIGURE 73-11.** Renal cell carcinoma metastasized to the wall of the main bronchus in a patient with prior nephrectomy for this tumor. (**A**) There is marked dilatation and obstruction by tumor. (H & E stain; low magnification.) (**B**) Characteristic microscopic view of renal cell cancer shows clear cell features and delicate intervening vessels. (H & E stain; intermediate magnification.)

## *Tracheobronchopathia Osteochondrodysplastica*

Tracheobronchopathia osteochondrodysplastica (TBO) is characterized by variable numbers of sessile, irregular, bony, and cartilaginous excrescences of the tracheal mucosa, covered by normal epithelium.[59–61] The individual nodules usually range in size from 0.3 to 0.6 cm in diameter, but they can be considerably larger. When numerous nodules become confluent, they give the tracheobronchial mucosa a rock-garden or cobblestone appearance. The bronchoscope passing over these structures produces a grating and gritty sound.

TBO may involve the larynx or may be just below the larynx, but it is most commonly seen in the lower two thirds of the trachea and often extends to the initial portion of the main bronchi. The posterior membranous portion of the trachea is usually spared; when involved, it has a characteristic wrinkled appearance. In severe cases of the disease, the profusion of osteocartilaginous nodules can result in severe luminal narrowing.

Most commonly, the disease is asymptomatic and represents an incidental autopsy finding. When symptomatic, the most common complaints are dyspnea, hemoptysis, dry cough, dryness of throat, and changes in the quality of voice.

Wilks provided the first microscopic description of TBO in 1857, although Rokitansky, in 1855, saw a case he thought was "multiple osteomas," and Luschka published his observations on the same disease in 1856.[59–61] Pederson and Worsoe-Petersen, in 1969, compiled 29 cases of TBO reported since 1957 and added one case of their own, to bring the total number of documented cases to 217.[62] In her paper of 1974, Martin described two cases of TBO and reviewed the literature, to bring the total number of reported cases to 245.[61]

An atypical distribution of the lesions may occur in TBO, as in the case reported by Shuttleworth and colleagues in which the disease was restricted to the left main bronchus.[63] In one of the two cases reported by Martin, the cobblestone appearance of the mucosa extended to segmental bronchi. Her second case was apparently associated with squamous cell carcinoma, and TBO involved mainly the right middle and lower lobe bronchi. There were areas of eosinophilic transformation of the submucosal glands that appeared hyalinelike or amyloidlike. The association of TBO with bronchogenic carcinoma has also been further documented by Dalgaard[64] and by de Wall and colleagues,[65] but a relationship remains yet to be established on a statistical basis.

In their report, Nienhuis and colleagues reviewed clinical and radiologic findings in 15 patients with TBO, 8 of whom were female.[66] The mean age of their patients was 63.5 years. Although upper airway involvement by TBO had been thought uncommon, 40% of their patients disclosed involvement of the larynx and upper trachea. Two additional patients with TBO described by Hodges[5] and Israel[67] had right middle lobe collapse at presentation.

According to Lundgren and Stjernberg, TBO probably occurs more frequently than is thought.[68] During an 8-year period, nine patients with TBO were found among 2180 performed bronchoscopies. In 8 of their patients, spirometry showed an obstructive pattern.

Microscopically, TBO is confined to the submucosa of the airways, although attachment of the lesions to the cartilaginous rings occurs. Some of the bony excrescences contain a core of bone marrow tissue.[59–61] In the study by van Nierop and colleagues, four patients had TBO with significant obstruction of the airways.[69] Van Nierop and colleagues noted that endoscopic removal of the obstructing nodules is the treatment of choice, but treatment is usually not required, and the prognosis is good.

Many theories on the etiology of TBO have been advanced over the years, including infection, congenital malformation, degenerative processes, chemical irritation, and mechanical damage, and little has been done to clarify this problem.[60] Aschoff's theory of 1910 is most favored among students of this disease—the submucosal masses of elastic cartilage that are so characteristic of TBO result from metaplasia of elastic tissue of the bronchial submucosa, and the cartilage has the ability to calcify and ossify.[60,61] Dalgaard, in his scholarly review of 1947, also agrees with the metaplastic theory of elastic tissue as set forth by Aschoff.[59] A metaplastic process arising from a multipotential connective tissue cell is an alternative view offered by Smith and Dixon.[70]

## *Tracheobronchial Amyloidosis*

Amyloidosis is characterized by the presence of extracellular deposits of a fibrillar protein. The term "amyloidosis" was coined by

Virchow, because of a similarity in staining characteristic to cellulose.[71] Amyloid is usually diagnosed by its microscopic appearance and confirmed by special stains, including metachromasia with crystal violet, violaceous appearance with periodic acid-Schiff, and positive staining with Congo red. Congophilia with apple-green birefringency with polarized light is the most popular diagnostic test. Ultrastructurally, amyloid has a characteristic fibrillar structure and cross-B pattern on x-ray diffraction.

Formerly, amyloidosis was thought to represent a single disease entity. However, over the past two decades, numerous biochemical, histochemical, and immunohistochemical studies of the subunit proteins have established that amyloidosis encompasses a heterogeneous group of disorders (see Chap. 32).[71]

Tracheobronchial amyloidosis has been the subject of several studies, and more than 100 patients with this disease have been described in the literature.[71] The age of the patients ranges from 16 to 76 years (average, 53 years). It occurs equally often in men and women. The common presenting symptoms are dyspnea, cough, hemoptysis, and hoarseness. One fourth of the patients show a normal chest radiograph; abnormal findings in the remaining three fourths include atelectasis, pneumonia, and narrowing of the tracheobronchial tree, which can be unifocal, multifocal, or diffuse.

Histologically, the lesion is characterized by submucosal deposits of irregular nodules or diffuse sheets of amyloid. Frequently, there is an infiltrate of lymphocytes with numerous plasma cells and giant cells. Osseous metaplasia is observed in 14% of the cases. In occasional patients with diffuse involvement, the associated ossification was so severe and extensive that it led to a second diagnosis of TBO.[72,73]

Amyloidosis of the tracheobronchial tree is fatal in only 20% of the cases, usually those with diffuse or multifocal involvement. The usual causes of death are bleeding, infection, and respiratory failure. Hemorrhage can occur following bronchoscopic removal of amyloid deposits. Despite the perils of such a therapeutic approach, piecemeal extraction of amyloid deposits remains the treatment of choice.[74]

## REFERENCES


1. Toremalm NG. The function of the trachea. Laryngoscope 1972; 82:108.
2. Spivey CG, Walsh RE, Perez-Guerra F, Harkleroad LE. Central airway obstruction. Report of seven cases. JAMA 1973;226:1186.
3. Katz I, Stradling J, Slutsky AS, Zamel N, Hoffstein V. Do patients with obstructive apnea have thick necks? Am Rev Respir Dis 1990; 141:1228.
4. Gronner AT, Trevino RJ. Tracheocele. Br J Radiol 1971;44:979.
5. Ettman IK, Keel DT Jr. Tracheal diverticulosis. Radiology 1962; 78:187.
6. Dinner M, Ward R, Yum E. Ventilation difficulty secondary to a tracheal diverticulum. Anesthesiology 1992;77:386.
7. Callan E, Karandy EJ, Hilsinger RL Jr. "Saber-sheath" trachea. Ann Otol Rhinol Laryngol 1988;97:512.
8. Hayakawa M, Nakaoka K, Siono H, Kigizaki K, Satou S, Ihara K. A case of saber-sheath type tracheo-bronchomalasia. Nippon Kyobu Geka Gakkai Zasshi 1992;40:2095.
9. Simmonds M. Über Alterssäbelscheidentrachea. Virchows Arch [A] 1905;179:15.
10. Campbell AH, Liddelow AG. Significant variations in the shape of the trachea and main bronchi. Med J Aust 1967;1:1017.
11. Greene R, Lechner GL. "Saber-sheath" trachea: a clinical and functional study of marked coronal narrowing of the intrathoracic trachea. Radiology 1975;115:265.
12. Hoskins MC, Evans RA, King SJ, Gishen P. "Saber-sheet" trachea with mediastinal lipomatosis mimicking a mediastinal tumour. Clin Radiol 1991;44:417.
13. Wylie WD. Hazards of intubation. Anaesthesia 1950;5:143.
14. Fields JA. Injuries and sequelae associated with endotracheal anesthesia. Laryngoscope 1959;69:509.
15. Lewis RN, Swerdlow M. Hazards of endotracheal anaesthesia. Br J Anaesth 1964;36:504.
16. Blanc VF, Tremblay NAG. The complications of tracheal intubation. Anesth Analg 1984;53:202.
17. Rasche RFH, Kuhns LR. Histopathologic changes in airway mucosa of infants after endotracheal intubation. Pediatrics 1972;50:632.
18. Gould SJ, Graham J. Long term pathological sequelae of neonatal endotracheal intubation. J Laryngol Otol 1989;103:672.
19. Puhakka HJ, Kero P, Valli P, Iisalo, Erkinjuntti M. Subglottic stenosis in neonates and children. Clinical findings and therapy. Acta Paediatr Scand 1990;79:397.
20. Smith JD, Cotton R, Meyer CM III. Subglottic cysts in the premature infant. Arch Otolaryngol Head Neck Surg 1990;116:479.
21. Massard G, Wihlm JM, Roeslin N, et al. Iatrogenic tracheobronchial lesions during intubation. 5 cases and review of the literature. J Chir (Paris) 1992;126:297.
22. Evrard C, Pelouze GA, Quesnel J. Iatrogenic tracheal and left bronchial stenoses. Uncommon complication of Carlens tube. Apropos of a case surgically treated in a single stage. Ann Chir 1990;44:149.
23. Abbey NC, Green DE, Cicale MJ. Massive tracheal necrosis complicating endotracheal intubation. Chest 1989;95:459.
24. Metlay LA, Macpherson TA, Doshi N, Milley JR. Necrotizing tracheobronchitis in intubated newborns: a complication of assisted ventilation. Pediatr Pathol 1987;7:575.
25. Geffin B, Grillo HC, Cooper JD, Pontoppidan H. Stenosis following tracheostomy for respiratory care. JAMA 1971;21:1984.
26. Bergström B, Ollman B, Lindholm C-E. Endotracheal excision of fibrous tracheal stenosis and subsequent prolonged stenting. Chest 1977;1:1977.
27. Schlaepfer K. Fatal hemorrhage following tracheostomy for laryngeal diphtheria. JAMA 1924;82:1581.
28. Lunding M. The tracheostomy tube and postoperative tracheostomy complications. With special reference to severe arterial bleeding caused by erosion of the innominate artery. Acta Anaesthesiol Scand 1964;8;181.
29. Neale HW, Main FB. Acquired tracheoesophageal fistula: a formidable complication of continued respiratory assistance. South Med J 1974;67:1102.
30. Payne DK, Anderson WM, Romero MD, Wissing DR, Fowler M. Tracheoesophageal fistula formation in intubated patients. Risk factors and treatment with high-frequency jet ventilation. Chest 1990; 88:161.
31. Camilleri AE. Management of acquired trachea-oesophageal fistula following intubation. J Laryngol Otol 1990;104:267.
32. Mathisen DJ, Grillo HC, Wain JC, Hilgenberg AD. Management of acquired non-malignant tracheoesophageal fistula. Ann Thorac Surg 1991;52:759.
33. Marzelle J, Dartevelle P, Khalife J, Rojas-Miranda A, Chapelier A, Levasseur P. Surgical management of acquired post-intubation trachea-oesophageal fistulas: 27 patients. Eur J Cardio Thorac Surg 1989;3:499.
34. Klapholz A, Wasser L, Stein S, et al. *Candida* pneumonia secondary to acquired fistula in a patient with AIDS. N Y State J Med 1988; 88:279.
35. Iacoviello VR, DeGirolami PC, Lucarini J, Sutker K, Williams ME, Wanke CA. Protothecosis complicating prolonged endotracheal intubation: case report and review of the literature. Clin Infect Dis 1992;15:959.

36. Natkunam R, Tse CY, Ong BH, et al. Carinal resection for stenotic tuberculous tracheitis. Thorax 1988;43:492.
37. Morgagni GB. The seats and causes of diseases investigated by anatomy in five books. vol. 1. London: A Millar and T Cadell, 1769:367.
38. Houston HE. Primary malignant tumors of the trachea. Thesis, Mayo Graduate School of Medicine, University of Minnesota, Rochester MN, 1967:1.
39. Houston HE, Spencer Payne W, Harrison EG, Olsen AM. Primary cancers of the trachea. Arch Surg 1969;99:132.
40. Hadju SI, Huvos AG, Goodner JT, Foote FW Jr., Beattie EJ Jr.. Carcinoma of the trachea. Clinicopathologic study of 41 cases. Cancer 1970;25:1448.
41. Webber AL, Grillo HC. Tracheal tumors. A radiological, clinical, and pathological evaluation of 84 cases. Radiol Clin North Am 1978; 16:227.
42. Olmedo G, Rosenberg M, Fonseca R. Primary tumors of the trachea. Clinicopathologic features and surgical results. Chest 1982;81:701.

42a. Allen MS. Malignant tracheal tumors. Mayo Clin Proc 1993; 68:680.

43. Pearson CM, Kline HM, Newcomer VD. Relapsing polychondritis. N Engl J Med 1960;263:51.
44. Verity MA, Larson WM, Madden SC. Relapsing polychondritis. Report of two necropsied cases with histochemical investigation of the cartilage lesion. Am J Pathol 1963;42:251.
45. Dolan DL, Lemmon GB, Teitelbaum SL. Relapsing polychondritis. Analytical literature review and studies on pathogenesis. Am J Med 1966;41:285.
46. Hughes RAC, Berry CL, Sifert M, Lessof MH. Relapsing polychondritis: three cases with a clinico-pathological study and literature review. Q J Med 1972;41:363.
47. Arkin CR, Masi AT. Relapsing polychondritis: review of current status and case report. Semin Arthritis Rheum 1975;5:41.
48. Case Records of Massachusetts General Hospital (Case 50-1985). Relapsing polychondritis, involving trachea and ear. N Engl J Med 1985;313:1530.
49. Homma S, Matsumoto T, Abe H, et al. Relapsing polychondritis. Pathological and immunological finding in an autopsy case. Acta Pathol Jpn 1984;34:1137.
50. Rogerson ME, Higgins EM, Godfrey RC. Tracheal stenosis due to relapsing polychondritis in rheumatoid arthritis. Thorax 1987; 42:905.
51. Wallesch B, Kleinsasser O. Tracheal stenosis as initial symptom of a polychondropathy. Laryngorhinootologie 1990;69:561.
52. Goddar P, Cook P, Laszlo G, Glover SC. Relapsing polychondritis: report of an unusual case and a review of the literature. Br J Radiol 1991;64:1064.
53. Clark LJ, Wakeel RA, Ormerod AD. Relapsing polychondritis—two cases with tracheal stenosis and inner ear involvement. J Laryngol Otol 1992;106:841.
54. Jaksch-Wartenhorst R. Polychondropathia. Wien Ztschr Inn Med 1923;6:1923.
55. Altherr F. Über einen Fall von systematisierter Chondromalacie. Virchows Arch [A] 1936;297:445.
56. von Meyenburg R. Über Chondromalacie. Schweiz Med Wochenschr 1936;17:1239.
57. Glynn LE, Holborrow EJ. Conversion of tissue polysaccharides to autoantigens by group-A beta haemolytic streptococci. Lancet 1952; 2:449.
58. Rajapakse DA, Bywaters EGL. Cell-mediated immunity to cartilage proteoglycan in relapsing polychondritis. Clin Exp Immunol 1974; 16:497.
59. Dalgaard JB. Tracheopathia chondroosteoplastica. Case elucidating problems concerning development and ossification of elastic cartilage. Acta Pathol Microbiol Scand 1947;24:118.
60. Secrest PG, Kending TA, Beland AJ. Tracheobronchopathia osteochondroplastica. Am J Med 1964;36:815.
61. Martin CJ. Tracheobronchopathia osteochondroplastica. Arch Otolaryngol 1974;100:290.
62. Pederson MF, Worsoe-Petersen J. Tracheopathia osteoplastica. J Laryngol Otol 1969;83:883.
63. Shuttleworth JF, Self CL, Pershing HS. Tracheopathia osteoplastica. Ann Intern Med 1960;52:234.
64. Dalgaard JB. Lunge cancer ved tracheopathia condroosteoplastica. Nord Med 1955;53:572.
65. de Wall N, Roggenback C, Endres P, Hau T. Tracheobronchopathia osteochondroplastica and coexistent mucoepidermoid carcinoma of the lung: case report. Pneumologie 1992;46:74.
66. Nienhuis DM, Prakash UB, Edell ES. Tracheobronchopathia osteochondroplastica. Ann Otol Rhinol Laryngol 1990;99:689.
67. Hodges MK, Israel E. Tracheobronchopathia osteochondroplastica presenting as right middle lobe collapse. Chest 1988;94:842.
68. Lundgren R, Stjernberg NL. Tracheobronchopathia osteochondroplastica. A clinical bronchoscopic and spirometric study. Chest 1981;80:706.
69. van Nierop MA, Wagenaar SS, van den Biosch JM, Westerman CJ. Tracheobronchopathia osteochondroplastica. Report of four cases. Eur J Respir Dis 1983;64:129.
70. Smith CC, Dixon MF. Tracheopathia osteoplastica with pulmonary thromboembolic disease. Br J Dis Chest 1972;66:192.
71. Chen KT. Amyloidosis presenting in the respiratory tract. In: Rosen PP, Fechner RE, eds. Pathol Annu. Norwalk: Appleton-Century-Crofts, 1989;24(Part 1):253.
72. Jones AW, Chaterji N. Primary tracheobronchial amyloidosis with tracheobronchopathia osteoplastica. Br J Dis Chest 1977;71:268.
73. Loire R, Sangier J, Brune J, Gaby P. Bronchial amyloidosis and osteoplastic tracheobronchopathy. Lyon Med 1978;239:75.
74. Flemming AFS, Fairfax AJ, Arnold AGA, Lane DJ. Treatment of endobronchial amyloidosis by intermittent bronchoscopic resection. Br J Dis Chest 1980;74:183.