Pediatric Thoracic Surgery

Mario Lima
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Preface

Pediatric thoracic surgery is becoming increasingly important in clinical practice; moreover, recent anesthetic and technological achievements have made it safer and more reliable.

This awareness brought about the idea to organize a conference assessing the state of the art of this discipline, and in November 2010 the "Symposium on Pediatric Thoracic Surgery" took place in Bologna. This event involved some of the most expert thoracic pediatric surgeons.

The idea to write this monograph was the outcome of this fruitful experience; our wish was to create a starting point for future studies, research and technical developments, with the aim of offering both young and experienced pediatric surgeons a comprehensive textbook and an updated review on this rapidly changing field. We hope that the result will achieve such high goals.

The text is divided into 37 chapters, grouped in 9 parts. Thoracic pathologies (congenital or acquired) are discussed in a comprehensive and systematic way; the surgical techniques are described in detail, including mini-invasive procedures, which are gaining importance, mostly in the thoracic field.

I take the occasion to thank all my colleagues, who contribute to improve the quality of care and innovative surgical techniques with their daily work. Special thanks go to Giovanni Ruggeri for the constant and precious help he always offers me during our daily clinical practice. Giovanni cowrote many chapters and well coordinated the work of many authoritative foreign colleagues.

When one finishes writing a book, there is always a bit of regret and fear of not having said everything, especially when describing innovative techniques.

In conclusion, I would like to recall a quote from Marcel Proust: "The real voyage of discovery does not consist of finding new landscapes, but of having new eyes".

Bologna, December 2012 Mario Lima

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Part I

General Aspects

Anatomy of the Thorax

1

Giovanni Ruggeri, Francesco Fascetti-Leon, Giulio Gregori and Mario Lima

1.1 Introduction

Typing "anatomy" or "interactive anatomy" into the search-window of any web browser elicits information on hundreds of potentially useful websites. Most are very helpful in learning what is needed to pass an examination or to prepare a surgical intervention accurately. However, accurate anatomical descriptions for any one approaching thoracic pediatric surgery are needed, and which are the basis of this chapter.

1.2 Superficial Muscles of the Chest Wall

The pectoralis major muscle is immediately below the clavicle. It originates from clavicular, sternal and costal attachments that converge toward the axilla, forming a tendon that attaches to the lateral lip of the inter-tubercular sulcus at the humerus. The lower and lateral parts of this muscle form the anterior fold of the axilla. Medial and lateral pectoral nerves from the brachial plexus provide innervation. This muscle elevates the upper ribs during forced inspiration.

The pectoralis minor muscle is deep to the pectoralis major. It originates from the second to fifth rib and converges upward to form a tendon that inserts on the coracoid process. The pectoralis minor muscle receives the same innervation as the major pectoralis muscle.

The serratus anterior muscle originates from the upper eighth rib, passes close to the thoracic cage, and attaches to the anterior and medial border of the scapula. The long thoracic nerve provides innervation for the serratus anterior muscle: it passes down the mid-axillary line on the external surface of the muscle. This muscle holds the scapula toward the thoracic cage. Lesions of the nerves that supply this muscle during thoracotomy can lead to a winged scapula [1].

The trapezius muscle originates from a large medial insertion (occipital bone; ligamentum nuchae; spine of the seventh cervical vertebra; spine and supraspinosus ligaments of all the thoracic vertebrae). It attaches to the lateral third of the clavicle, to the spine, and to the acromion of the scapula. This muscle is innervated by the spinal accessory nerve as well as from C3 and C4.

The latissimus dorsi muscle covers the lower and lateral part of the back of the thorax. Insertion arises from the iliac crest, lumbodorsal fascia, and spines of lower thoracic

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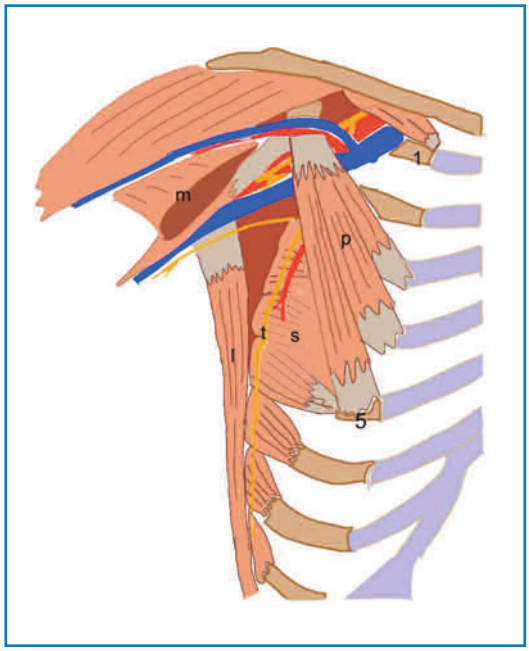

Fig. 1.1 Superficial muscles of the chest wall (schematic). Anteroposterior view of the right hemitorax. *1*, first rib; *5*, fifth rib; *p*, pectoralis major muscle; *m*, pectoralis major muscle; *l*, latissimus dorsi muscle; *s*, serratus anterior muscle; *t*, long thoracic nerve

vertebrae. Additional sections arise also from the outer surfaces of the lower third or fourth ribs. Fibers converge as a tendon up to the intertubercular groove of the humerus. The muscle forms the posterior fold of the axilla. It is supplied by the thoracodorsal nerve from the brachial plexus. It is considered to be the accessory muscle of respiration due to the rib attachments. Retracting backwards the latissimus dorsi muscle and forward and downward the serratus anterior muscle, the fourth and fifth intercostal spaces are readily exposed. This allows muscle-sparing thoracotomy, which is widely used in neonatal thoracic surgery [1–4].

The **levator scapulae** muscle extends from the transverse processes of the first three or four cervical vertebrae and attaches at the superior angle of the scapula. The rhomboid minor muscle (sometimes fused with rhomboid major muscle) extends from the spine of the seventh cervical and first thoracic vertebrae to the medial border of the scapula. The rhomboid major arises from the spines of the second to fifth thoracic vertebrae and attaches to the medial border of the scapula.

The arrangements of the superficial muscles of the chest wall are shown in Figure 1.1.

1.3 Thoracic Cage

The thoracic cage is formed by the sternum and costal cartilages in front, the vertebral column behind, and the ribs and intercostal spaces laterally. It is separated from the abdominal cavity by the diaphragm and communicates superiorly with the root of the neck through the thoracic inlet (anteriorly, sternal manubrium; posteriorly, T1 vertebra; laterally, the first rib).

1.3.1 Ribs

The first seven ribs articulate with the vertebrae posteriorly and with the sternum anteriorly by way of the costal cartilages ("true ribs"). The eighth, ninth and tenth ribs articulate by their cartilages with the cartilages of the ribs above ("false ribs"). The eleventh and twelfth ribs do not articulate anteriorly ("floating false ribs").

Ribs have a: head (which bears two demifacets for articulation with the bodies of the numerically corresponding vertebra, and the vertebra above); tubercle (which comprises a rough non-articulating lateral facet as well as a smooth medial facet, with the latter articulating with the transverse process of the corresponding vertebra); subcostal groove (which accommodates the intercostal neurovascular structures).

The first rib is short, flat and sharply curved. The head bears a single facet for articulation. A prominent tubercle (scalene tubercle) on the inner border of the upper surface represents the insertion site for the scalenus anterior muscle. The subclavian vein passes over the first rib anterior to this tubercle, whereas the subclavian artery and lowest

trunk of the brachial plexus pass posteriorly.

The cervical rib is a rare "extra" rib which articulates with C7 posteriorly and the first rib anteriorly. The cervical rib is involved in the inlet syndrome, a rare (but well described) condition in the pediatric population [5]. The second rib is less curved and longer than the first rib. The tenth rib has only one articular face to the head. The eleventh and twelfth ribs articulate posteriorly with the vertebrae by way of a single facet on the head. They are devoid of a tubercle and a subcostal groove. Rib anomalies are described in 14% of healthy subjects (cervical rib, 6%; aplasia of the twelfth rib in 6% and of lumbar ribs in 0.9%) [6].

1.3.2 Sternum

The three parts of the sternum are the manubrium, body and xiphoid process. The manubrium has facets for articulation with the clavicles, first costal cartilage and upper part of the second costal cartilage. It articulates inferiorly with the body of the sternum at the manubriosternal joint. The body is composed of four parts (sternebrae) which fuse usually between the age of 15 years and 25 years. It has facets for articulation with the lower part of the second and third to seventh costal cartilages. The xiphoid articulates with the body above at the xiphisternal joint. The xiphoid usually remains cartilaginous well into adult life.

1.3.3 Costal Cartilage

Costal cartilage refers to bars of hyaline cartilage which connect the upper seven ribs directly to the sternum and the eighth, ninth and tenth ribs to the cartilage immediately above.

1.3.3.1 Joints of the Thoracic Cage

The manubriosternal and xiphisternal joints are secondary cartilaginous joints (symphysis). The manubriosternal joint usually ossifies after the age of 30 years. The first sternocostal joint is a primary cartilaginous joint. The remainder (second to seventh) are synovial joints. The costochondral joints (between the ribs and costal cartilages) are primary cartilaginous joints. The interchondral joints (between the costal cartilages of the eighth, ninth and tenth ribs) are synovial joints. The costovertebral joints comprise two synovial joints formed by the articulations of the demifacets on the head of each rib with the bodies of its corresponding vertebra together with that of the vertebra above. The first and tenth to twelfth ribs have a single synovial joint with their corresponding vertebral bodies. The costotransverse joints are synovial joints formed by the articulations between the facets on the rib tubercle and the transverse process of its corresponding vertebra [7].

1.4 Intercostal Space

Each intercostal space contains three muscles layers.

- The external intercostal muscle fills the intercostal space from the vertebra posteriorly to the costochondral junction anteriorly, where it becomes the thin anterior intercostal membrane. The fibers run downwards and forwards from the rib above to the rib below.
- The internal intercostal muscle fills the intercostal space from the sternum anteriorly to the angles of the ribs posteriorly, where it becomes the posterior intercostal membrane (which reaches as far back as the vertebral bodies). The fibers run downwards and backwards.
- The innermost intercostals muscle group comprises the subcostal muscles posteriorly, the intercostales intimi laterally, and the transversus thoracis anteriorly. The fibers of these muscles span more than one intercostal space.

The neurovascular space is the plane in which the neurovascular bundle (intercostal vein, intercostal artery and intercostal nerve) courses. It lies between the layers of the internal intercostal and innermost intercostal muscles.

The intercostal structures pass under cover of the subcostal groove. Pleural aspiration should be carried out close to the upper border of a rib to minimize the risk of injury [8].

1.5 Arterial Supply and Venous Drainage of the Chest Wall

The intercostal spaces receive their arterial supply from the anterior and posterior intercostal arteries. The anterior intercostal arteries are branches of the internal thoracic artery and its terminal branch, the musculophrenic artery. The lowest two spaces have no anterior intercostal supply. The first 2–3 posterior intercostal arteries arise from the superior intercostal branch of the costocervical trunk, a branch of the second part of the subclavian artery. The lower nine posterior intercostal arteries are branches of the thoracic aorta. The posterior intercostal arteries are much longer than the anterior intercostal arteries. The anterior intercostal veins drain anteriorly into the internal thoracic and musculophrenic veins. The posterior intercostal veins drain into the azygos and hemiazygos systems [9].

1.6 Lymphatic Drainage of the Chest Wall

Lymphatic drainage of the chest wall can be summarized thus:

- anterior chest wall: to the anterior axillary nodes;
- posterior chest wall: to the posterior axillary nodes;
- anterior intercostal spaces: to the internal thoracic nodes;
- posterior intercostal spaces: to the paraaortic nodes.

1.7 Nerves of the Chest Wall

The intercostal nerves are the anterior primary branches of the thoracic segmental nerves. Only the upper six intercostal nerves run in their intercostal spaces: the remainder gain access to the anterior abdominal wall.

Branches of the intercostal nerves include: the cutaneous anterior and lateral branches; a collateral branch which supplies the muscles of the intercostal space (also supplied by the main intercostal nerve); and sensory branches from the pleura (upper nerves) and peritoneum (lower nerves). As an exception, the first intercostal nerve is joined to the brachial plexus and has no anterior cutaneous branch. The second intercostal nerve is joined to the medial cutaneous nerve of the arm by a branch of the intercostobrachial nerve, and innervates the skin of the axilla and medial side of the arm.

1.8 Fascial Structures

There are two important fascial structures internal to the thoracic cage: the supra-pleural fascia and the endothoracic fascia. The supra-pleural fascia is the roof of the thoracic inlet; subclavian vessels lie on this fascia. The endothoracic fascia is a soft fascia interposed between the parietal pleura and thoracic wall. The endothoracic fascia represents the plane of dissection if an extrapleural approach is chosen for the repair of esophageal atresia [10].

1.9 Diaphragm

The diaphragm (Fig. 1.2) separates the thoracic and abdominal cavities. It comprises a peripheral muscular portion that converges into a central aponeurosis or central tendon. The muscular part has three attachments: vertebral (crura and arcuate ligaments), costal and sternal. The right crus arises from the anterior aspect of the L1–3 vertebral bodies and intervertebral disks. Some fibers from the right crus pass around the lower esophagus, so only fibers from the right crus form an esophageal hiatus. These two parts of the right

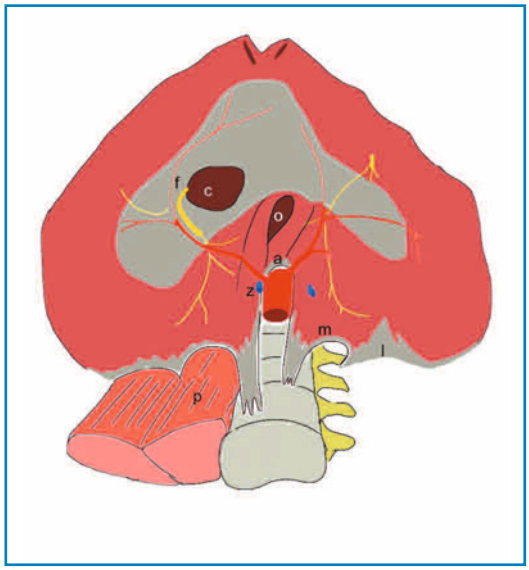

Fig. 1.2 The diaphragm (schematic). Abdominal view of the diaphragmatic dome. *c*, caval opening; *f*, right phrenic nerve; o, esophageal opening; a, aortic opening; *z*, azygos vein; *p*, psoas muscle; *m*, medial arcuate ligament; *l*, lateral arcuate ligament.

crus must be approximated during hiatal hernia repair. The left crus originates from L1 and L2 only. The medial arcuate ligament comprises thickened fascia that overlies the psoas major muscle and is attached medially to the body of L1 and laterally to the transverse process of L1. The lateral arcuate ligament overlies quadratus lumborum muscle from the transverse process of L1 medially to the twelfth rib laterally. The median arcuate ligament is a fibrous arch that connects anteriorly left and right crura to form the anterior edge of the aortic opening. The costal part involves the inner aspects of the lower six ribs. The sternal part consists of two small bundles arising from the deep surface of the xiphoid process. The space between each part of this bundle and the costal part of the diaphragmatic muscle is the site of an anterior diaphragmatic hernia (Morgagni–Larrey hernias) [11]. Structures traverse the diaphragm at different levels to reach the abdominal cavities (Table 1.1). The left phrenic nerve passes into the diaphragm as a solitary structure. The diaphragm receives its motor nerve supply through phrenic nerves (C3–C5) and its sensory supply from the lower intercostal nerves (periphery of the diaphragm) and phrenic nerves (central part) [12].

Table 1.1 Diaphragmatic openings and passing structures

Opening	Level	Passing structure
Esophageal hiatus	T10	Esophagus, vagi and branches of the left gastric artery and vein
Aortic hiatus	T12	Aorta, thoracic duct and azygos vein
Caval hiatus	T8	Inferior vena cava, right phrenic nerve

1.10 Mediastinum

The mediastinum (Fig. 1.3) is the space between the two pleural sacs. Superior and inferior mediastinal regions are separated by a horizontal line drawn backwards from the angle of Louis (manubriosternal joint) to the T4/5 intervertebral disk. The inferior mediastinum is subdivided further into the:

- anterior (the region in front of the pericardium);
- middle (comprises the pericardium and heart);
- posterior (the region between the pericardium and vertebrae).

1.11 Esophagus

The esophagus commences at the level of the cricoid cartilage at C6 in the neck. In the thorax, the esophagus passes initially through the superior and then the posterior mediastinum. Having deviated slightly to the left in the neck, the esophagus returns to the midline in the thorax at the level of T5. From here it passes downwards and forwards to reach the esophageal opening in the diaphragm (T10).

The esophagus comprises four layers: an inner mucosa of stratified squamous epitheli-

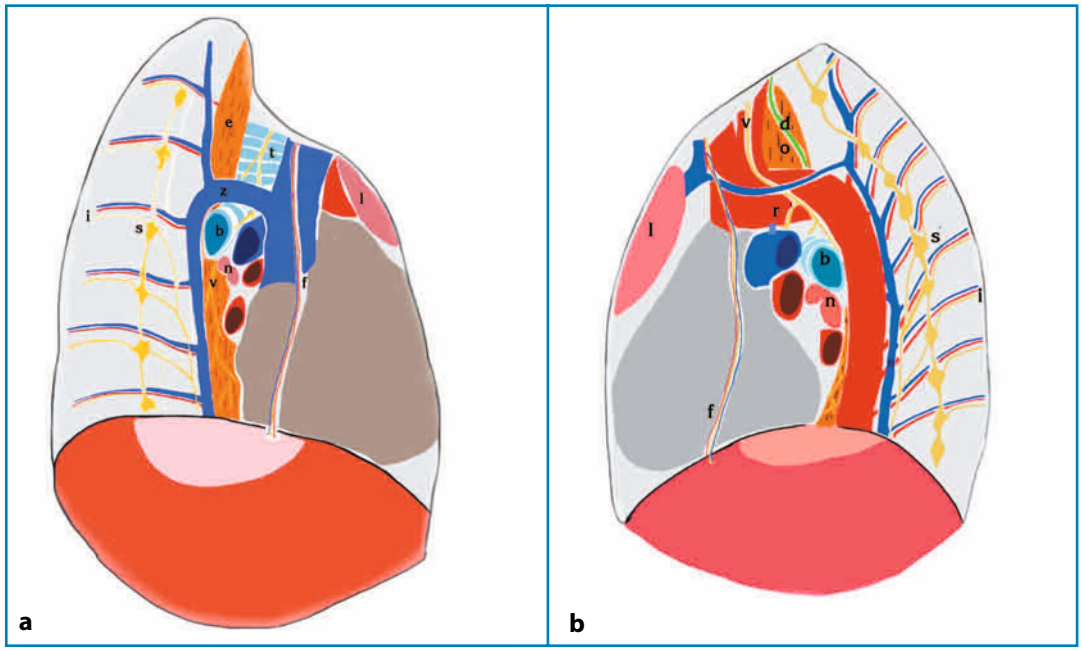

Fig. 1.3 The mediastinum (schematic). **a** Right view of the mediastinum, **b** left view of the mediastinum. *z*, azygos vein; *e*, emi-azygos vein; *s*, sympathetic chain; *i*, intercostal nerve, artery and vein; *o*, esophagus; *t*, trachea; *b*, main bronchi; *l*, thymus; *d*, thoracic duct; *n*, lymph nodes; *v*, vagus nerve; *r*, recurrent laryngeal nerve; *f*, phrenic nerve, artery and vein.

um; a submucosal layer in which lies the strength of the esophagus (the mucosa must be included in the suture during esophageal repair); a double muscular layer (longitudinal outer layer and circular inner layer, striated in the upper two-thirds and smooth in the lower third); and an outer layer of loose connective tissue.

With respect to relations, the azygos vein and right vagus nerve cross the esophagus on the right side only. In the intrathoracic part, the esophagus is impressed by the aortic arch on the left side. The thoracic duct is on the posterior aspect of the esophagus except for the proximal part, which lies on the left side.

The arterial blood supply for the esophagus is through the inferior thyroid artery (upper third); esophageal branches of thoracic aorta (middle third); and the left gastric branch of the celiac artery (lower third).

Venous drainage is represented by the: inferior thyroid veins for the upper third; azygos system for the middle third; azygos (systemic system) and left gastric veins (portal system) for the lower third. Dual drainage of the lower third forms a site of portosystemic anastomosis. In the case of portal hypertension, back-pressure on the left gastric tributaries at the lower esophagus is observed. These veins become fragile esophageal varices.

Lymphatic drainage is to a peri-esophageal lymph plexus and then to the posterior mediastinal nodes. From here lymph drains into the supraclavicular nodes. The lower esophagus also drains into the nodes around the left gastric vessels.

The nerve supply is autonomic from the vagus nerve and sympathetic chain. In the neck and superior mediastinum, the esophagus is innervated by the recurrent laryngeal nerve and from sympathetic fibers that follow the inferior thyroid arteries. In the posterior mediastinum, the vagus nerve ramifies in a plexus that receives fibers from the sympathetic trunk. The anterior and posterior trunk reform as fibers pass the esophageal hiatus.

1.12 Main Lymphatic Vessels

The cisterna chyli is a lymphatic sac that receives lymph from the abdomen and the lower half of the body. It is situated between the abdominal aorta and the right crus of the diaphragm. It is missing in 2% of cases. The thoracic duct carries lymph from the cisterna chyli through the thorax to drain into the left brachiocephalic vein. The thoracic duct passes along the esophagus on its posterior aspect until the aortic arch level, where it moves on the left aspect of the esophagus before reaching the brachiocephalic vein [13]. It usually receives tributaries from the left jugular, subclavian and mediastinal lymph trunks (although they may open into the large neck veins directly). On the right side, the main lymph trunks from the right upper body usually join and drain directly through a common tributary (right lymph duct) into the right brachiocephalic vein. Anatomical variations of the thoracic duct are common. Duplication, triplication or other anatomical variations are present in nearly 35–50% of the population. There is also an extensive lymphatic network of collaterals. This richness of collaterals is such that the thoracic duct can be ligated at any point during its thoracic or cervical course without stasis [14–15].

1.13 Thymus Gland

The thymus gland is an important component of the lymphatic system. It usually lies behind the manubrium (in the superior mediastinum) but can extend to the fourth costal cartilage in the anterior mediastinum. After puberty, the thymus is gradually replaced by fat. The arterial supply arises from small branches of the internal mammary arteries. Venous drainage is through a short vein into the left brachicephalic vein.

1.14 Thoracic Aorta

The ascending aorta arises from the aortic vestibule behind the infundibulum of the right ventricle and the pulmonary trunk. It is continuous with the aortic arch. The arch lies posterior to the lower half of the manubrium and arches from front to back over the left main bronchus. The descending thoracic aorta is continuous with the arch and begins at the lower border of the body of T4. It initially lies slightly to the left of the midline and then passes medially to gain access to the abdomen by passing beneath the median arcuate ligament of the diaphragm at the level of T12. From here it continues as the abdominal aorta.

The branches rising from the ascending aorta are the right and left coronary arteries. The branches of the aortic arch are the brachiocephalic artery (which arises behind the manubrium and passes upwards to divide into right subclavian and right common carotid branches at the level of the right sternoclavicular joint), left common carotid artery, left subclavian artery, and the thyroidea ima artery. The branches of the descending thoracic aorta include the esophageal, bronchial, mediastinal, posterior intercostal and subcostal arteries.

The subclavian arteries become the axillary arteries at the outer border of the first rib. Each artery is divided into three parts by the scalenus anterior muscle: the first part lies medial to the medial border of scalenus anterior muscle and gives rise to three branches, vertebral artery, thyrocervical trunk and internal thoracic (mammary) artery. The thoracic artery passes the posterior surface of the anterior chest wall one fingerbreadth from the lateral border of the sternum. Along its passage it gives off anterior intercostal, thymic and perforating branches. These “perforators” pass through the anterior chest wall to supply the breast. The internal thoracic artery divides behind the sixth costal cartilage into superior epigastric and musculophrenic branches. The thyrocervical trunk terminates as the inferior thyroid artery. The second part (which is behind the scalenus anterior muscle) gives rise to the costocervical trunk. The third part lateral to the lateral border of scalenus gives rise to the dorsal scapular artery.

1.15 Great Veins

The brachiocephalic veins are formed by confluence of the subclavian and internal jugular veins behind the sternoclavicular joints. The left brachiocephalic vein traverses diagonally behind the manubrium to join the right brachiocephalic vein behind the first costal cartilage, thereby forming the superior vena cava.

1.16 Azygos System

The azygos vein is the only tributary of the superior vena cava. It commences as the union of the right subcostal vein and one or more veins from the abdomen. It passes through the aortic opening in the diaphragm, ascends to the posterior chest wall to the level of T4, and then arches over the right lung root to enter the superior vena cava. It receives tributaries from the lower eight posterior inter-costal veins, right superior intercostal vein, and hemiazygos veins.

The hemiazygos vein arises on the left side (similar to the azygos vein). It passes through the aortic opening in the diaphragm and up to the level of T9 from where it passes diagonally behind the aorta and thoracic duct to drain into the azygos vein at the level of T8. It receives venous blood from the lower four left posterior intercostal veins. The accessory hemiazygos vein drains blood from the middle posterior intercostal veins (as well as some bronchial and mid-esophageal veins). The accessory hemiazygos crosses to the right to drain into the azygos vein at the level of T7. The upper four left intercostal veins drain into the left brachiocephalic vein.

The azygos system has several normal variants. For example, in 1–2% of individuals, the accessory hemiazygos vein drains into the brachiocephalic vein; in 3.6% of subjects, the hemiazygos and accessory hemiazygos veins form common channels ventral to the aorta called the “interazygos veins”. As an anatomical variation, the arch can be displaced laterally, thereby creating a pleural septum delimitating part of the upper lobe (azygos lobe) of the right lung. This anomaly has been reported in 0.5–1% of normal subjects, but has been reported to be associated with cardiac malformation, lobar emphysema, extralobar sequestration and esophageal atresia [16–19]. A hypertrophic azygos vein could be due to a congenitally interrupted inferior vena cava. This fact should be taken into consideration before ligating the azygos vein during thoracic neonatal surgery.

1.17 Phrenic Nerves

The phrenic nerves arise from the C3, C4 and C5 nerve roots in the neck. The right phrenic nerve descends along a near-vertical path, anterior to the lung root, and lies sequentially on the right brachiocephalic vein, the superior vena cava, and the right atrium before passing to the opening to the inferior vena cava in the diaphragm (T8). Here, the right phrenic nerve enters the caval opening and immediately penetrates the diaphragm (which it supplies).

The left phrenic nerve descends alongside the left subclavian artery. On the arch of the aorta it passes over the left superior intercostal vein to descend in front of the left lung root onto the pericardium overlying the left ventricle. The left phrenic nerve then pierces the muscular diaphragm as a solitary structure. The phrenic nerves do not pass beyond the under-surface of the diaphragm.

The phrenic nerves are composed mostly of motor fibers, which supply the diaphragm. However, they also transmit fibers which are sensory to the fibrous pericardium, mediastinal pleura and the peritoneum, as well as the central part of the diaphragm [12]. Irritation of the diaphragmatic peritoneum is usually referred to the C4 dermatome. Hence, insufflation of carbon dioxide during laparoscopy often causes pain felt at the shoulder [20].

1.18 Vagi

The vagi are the tenth cranial nerves. The right vagus nerve descends adherent to the thoracic trachea before passing behind the lung root to form the posterior pulmonary plexus. It finally reaches the lower esophagus, where it forms an esophageal plexus with the left vagus nerve. From this plexus, anterior and posterior vagal trunks descend (carrying fiber from left and right vagi) on the esophagus to pass into the abdomen through the esophageal opening in the diaphragm at the level of T10. The left vagus nerve crosses the arch of the aorta and its branches. It is itself crossed here by the left superior intercostal vein. Below, it descends behind the lung root to reach the esophagus, where it contributes to the esophageal plexus mentioned above [21].

With respect to vagal branches, the left recurrent laryngeal nerve arises from the left vagus nerve below the arch of the aorta. It hooks around the ligamentum arteriosum and ascends in the groove between the trachea and the esophagus to reach the larynx. The right recurrent laryngeal nerve arises from the right vagus nerve in the neck and hooks around the right subclavian artery before ascending in the groove between the trachea and the esophagus before finally reaching the larynx. The recurrent laryngeal nerves supply the mucosa of the upper trachea and esophagus as well as providing a motor supply to all of the muscles of the larynx (except the cricothyroid muscles) and sensory fibers to the lower larynx. The vagi contribute to cardiac and pulmonary plexuses [21].

1.19 Thoracic Sympathetic Chain

The sympathetic chain passes the necks of the ribs, behind the pleura, immediately lateral to the vertebral bodies crossing the intercostal vessels and nerves. It passes under the medial arcuate ligament of the diaphragm to continue as the lumbar sympathetic trunk. The first thoracic ganglion fuses with the last cervical ganglion to form the stellate ganglion in 80% of subjects. Their fibers innervate the head and neck. Horner's syndrome derives from lesions of the stellate ganglion. The second and third thoracic ganglia give fibers to the hand, and the fourth thoracic ganglion supplies the axilla. The upper four thoracic ganglia give fibers to the esophagus and lung. These structures receive parasympathetic fibers from the vagi nerves. The lower eight ganglia give origin to the greater and lesser splanchnic nerves; the lowest splanchnic nerve derives from the twelfth ganglion, then pierces the crus of the diaphragm. The anatomy of the sympathetic thoracic chain is extremely variable and symmetrical in only 16% of cases [22].

1.20 Trachea

The trachea initiates at the level of the cricoid cartilage in the neck (C6). It terminates at the level of the angle of Louis (T4/5), where it bifurcates into the right and left main bronchi. It is a rigid fibroelastic structure. Incomplete rings of hyaline cartilage continuously maintain the patency of the lumen. The trachea is lined internally with ciliated columnar epithelium. Behind the trachea lies the esophagus. The second, third and fourth tracheal rings are crossed anteriorly by the thyroid isthmus. The trachea receives its blood supply from branches of the inferior thyroid and bronchial arteries.

1.22 Lungs: General Points

In adults, the lungs provide an alveolar surface area of approximately >40 m^2 for gaseous exchange. Each lung has: an apex that reaches above the sternal end of the first rib; a costovertebral surface that underlies the chest wall; a base overlying the diaphragm; and a mediastinal surface that is molded to adjacent mediastinal structures.

The right lung is divided into upper, middle and lower lobes by oblique (or major) and

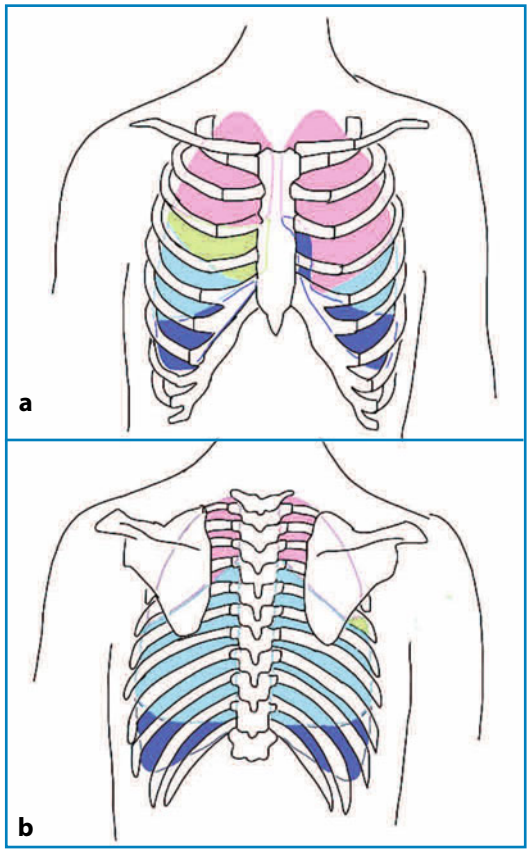

Fig. 1.4 Projection of the lobes and fissures on the thoracic cage. **a** Anterior view, **b** posterior view. Note the extent of the costodiaphragmatic recesses (shown in *blue*)

horizontal (or minor) fissures. The lower lobe is commonly incomplete and completely absent in 10–50% of the population. The left lung has only an oblique fissure (incomplete in 18% of cases) and no middle lobe [23]. The lingular segment (anatomical part of the upper lobe) represents the left-sided equivalent of the right middle lobe.

Structures enter or leave the lungs by the lung hilum, which is wrapped in a loose pleural coat. Bronchial arteries, branches of the descending thoracic aorta, supply the bronchi and parenchymal tissue of the lungs. The proximal right bronchus receives blood supply from the right superior intercostal artery in 90% of cases [13]. Bronchial veins, which also communicate with pulmonary veins, drain into the azygos and hemiazygos veins. The alveoli receive deoxygenated blood from the terminal branches of the pulmonary artery, and oxygenated blood returns *via* tributaries of the pulmonary veins. Two pulmonary veins return blood from each lung to the left atrium. Lymph returns from the periphery towards the hilar tracheobronchial groups of nodes and from there to the mediastinal lymph trunks.

A pulmonary plexus is located at the root of each lung. The plexus comprises sympathetic fibers (from the sympathetic trunk) and parasympathetic fibers (from the vagus nerve). Efferent fibers from the plexus supply the bronchial musculature, and afferents are received from the mucous membranes of bronchioles and from the alveoli. The projection of the lobes and fissures on the thoracic cage are depicted in Figure 1.4.

1.23 Bronchi and Bronchopulmonary Segments

The right main bronchus is shorter, wider and takes a more vertical course than the left main bronchus, and has an angle with the axis of the trachea of 30° in children (20° in adults) *versus* 47° (40° in adults). These features account for the tendency for inhaled foreign bodies to impact preferentially in the right-middle and lower-lobe bronchi [24]. The bronchus to the upper lobe originates from the right main bronchus before the hilum. Once into the hilum, the right main bronchus divides into middle and inferior lobar bronchi. The left main bronchus enters the hilum and divides into a superior and inferior lobar bronchus. Each lobar bronchus divides within the lobe into segmental bronchi (Fig. 1.5). Each segmental bronchus enters a bronchopulmonary segment. Each bronchopulmonary segment has a pyramidal shape with its apex directed towards the hilum. It is a structural unit of a lobe that has its own segmental bronchus, artery and lymphatic system. If one bronchopulmonary segment is diseased it may be resected with preservation of the rest of the lobe. The veins draining each segment are

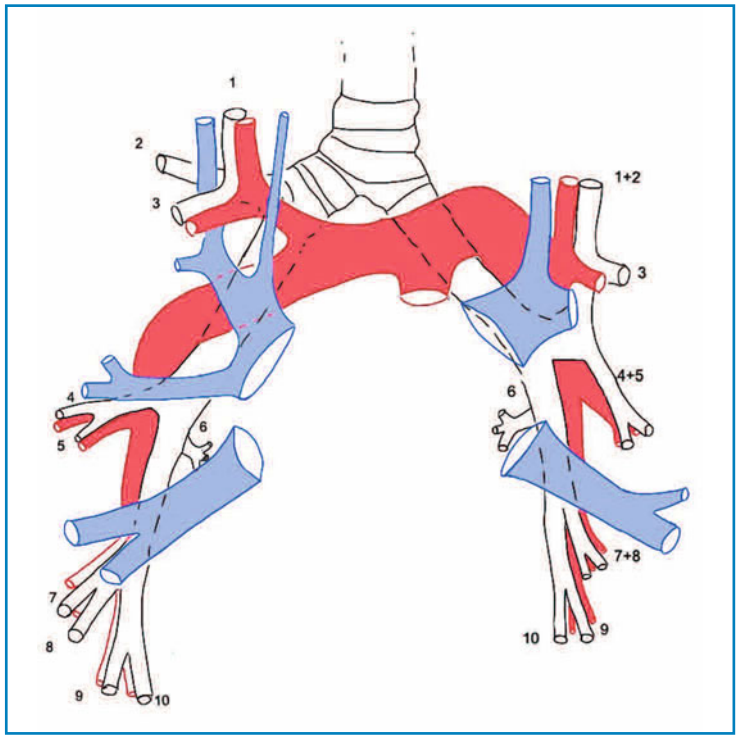

Fig. 1.5 Relations between the segmental bronchi and main vascular divisions of the lung

intersegmental (however, in the right upper lobe, the pulmonary veins are generally anterior to the pulmonary arteries). These segmental subdivisions are shown in Table 1.2.

1.23.1 Right Upper Lobe

Anomalies of the right upper lobe bronchus have been described in 3% of subjects (i.e., segmental bronchi arising directly from the main bronchus or from the middle lobe bronchus; apical segmental bronchus arising directly from the trachea). Anomalies of the arterial supply of the upper lobe have been described in 10% of the population. Furthermore, in 90% of subjects, the posterior segment receives blood from the inferior trunk of the right pulmonary artery by a variable number of branches. Superior pulmonary veins drain the upper and middle lobes. The anatomy of the venous drainage is constant.

1.23.2 Right Middle Lobe

After the origin of the upper lobe bronchus, the main right bronchus continues as the bronchus intermedius. The middle lobe bronchus arises from the bronchus intermedius. The inferior trunk of the right pulmonary artery lies down the anterior surface

Table 1.2 Segmental subdivision of lung lobes

	Right lung segments	Left lung segments
Upper lobe	1 apical, 2 posterior, 3 anterior	1–2 apical-posterior, 3 anterior
Middle/lingular lobe	4 lateral, 5 medial	4 superior, 5 inferior (lingular)
Lower lobe	6 apical, 7 medial-basal, 8 anterior-basal, 9 lateral-basal, 10 posterior-basal	6 apical, 7–8 antero-medial-basal, 9 lateral-basal, 10 posterior-basal

of the bronchus intermedius, and can be seen with its trunks in the middle lobe (in the major fissure). The two segmental veins from the middle lobe drain into the superior pulmonary vein.

1.23.3 Right Lower Lobe

The segmental bronchus for the apical segment of the lower lobe arises at the same level of the middle bronchus. For resection of the lower right lobe, one must consider the risk of lesions of the middle lobe bronchus. One (or rarely) two arteries supply the apical segment of the lower lobe. Another variant of the arterial supply for the sixth segment derives from the posterior upper lobe segmental artery. The superior segmental vein and common basal vein drain into the inferior pulmonary vein.

1.23.4 Left Upper Lobe

The main left bronchus divides in the upper and lower left bronchi immediately after passing under the aorta arch. The upper bronchus bifurcates in the lingular lobe bronchus and common bronchus for the apical-posterior and anterior segments. The arterial supply for the upper lobe varies, having from one to eight branches of the left pulmonary artery (more commonly three). Two-to-three major branches form the superior pulmonary vein.

1.23.5 Left Lower Lobe

The arteries for the lower left lobe segments arise from the left artery in the major fissure. The most proximal branch is for the superior segment, and originates from the posterior surface of the left pulmonary artery. In one-quarter of cases, the superior segment receives two arteries. A common origin of the superior segment artery and posterior upper lobe segmental artery is possible. On the opposite surface is the origin of the lingular segmental vessel. Venous drainage is similar to that seen for the right lower lobe [9, 13, 25].

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Further Reading

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Prenatal Diagnosis of Thoracic Anomalies

2

Gianluigi Pilu

2.1 Introduction

Congenital thoracic anomalies are not common. The overall incidence is unknown, but is probably in the region of 1 per 2,000 live births. The most relevant entity is probably diaphragmatic hernia because it usually presents as a perinatal emergency, and it has been postulated that *in utero* transfer to tertiary care centers and prompt neonatal treatment may increase the likelihood of survival. Although this has not been demonstrated thus far, there is also the hope that antenatal treatment may be beneficial for selected cases [1–3]. There is, however, increased interest also in the prenatal detection of primary lung lesions such as congenital cystic adenomatoid malformations (CCAMs) and lung sequestration (LS). These anomalies are usually asymptomatic at birth and therefore invariably escape clinical diagnosis. Many authorities believe that identification with prenatal ultrasonography may be important because surgical treatment prior to onset of complications may improve the long-term prognosis [4–10].

An ultrasound examination at mid-gestation to evaluate fetal anatomy and detect possible malformations is now the standard of care in most industrialized countries [11]. The examination is carried out after a well-established protocol, and includes a view of the fetal thorax demonstrating the heart and lungs (Fig. 2.1). A prenatal diagnosis of thoracic anomalies is now common and has originated large clinical series. The most common conditions that are encountered include cystic and echogenic malformations of the lungs, pleural effusion and diaphragmatic hernia.

2.2 Hyperechogenic and Cystic Lungs

The typical finding for hyperechogenic and cystic lungs is that of enlarged, brightly echogenic lungs displacing the mediastinum and causing an inversion of the diaphragm [4–5]. The pathophysiology is related to obstruction of the respiratory tree, which causes accumulation of secretions into the lungs. Different entities are responsible for this phenomenon, and they may be difficult to differentiate antenatally. Although these entities were originally described as "separate", there is recent evidence suggesting that there is much pathological and clinical overlapping between the different entities. This includes CCAMs, LS, congenital segmental emphysema (CSE) and congenital high airway obstruction syndrome (CHAOS).

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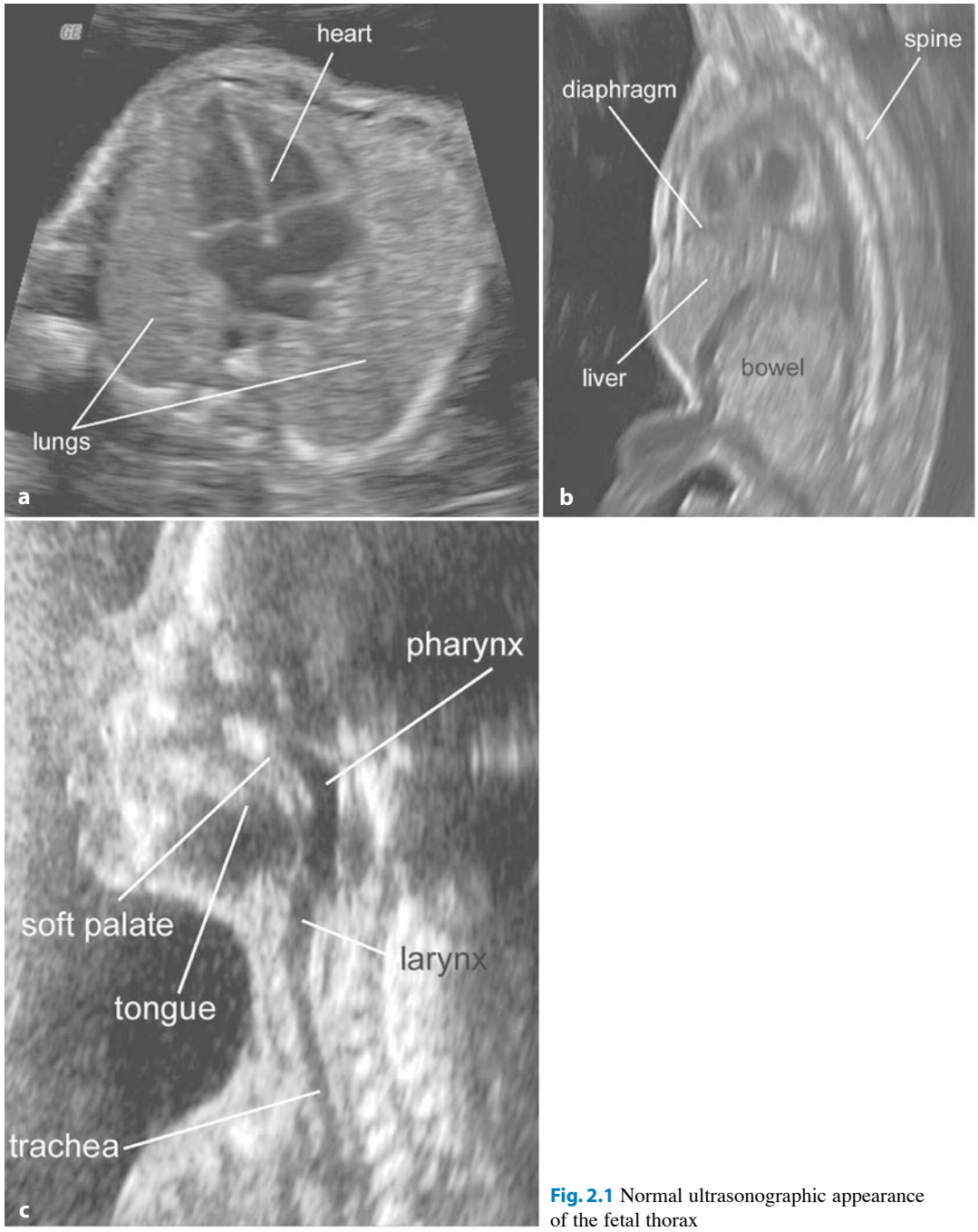

Fig. 2.1 Normal ultrasonographic appearance of the fetal thorax

2.2.1 CCAMs

A CCAM of the lung is a hamartoma. It is characterized by overgrowth of the terminal bronchioles (adenomatoid) at the expense of saccular spaces. The term "hamartoma" refers to a benign tumor-like malformation which reproduces (in a disorderly manner) the mature structure of the organ from which it is derived. Early and long-standing obstruction

of a major bronchus is probably responsible for this condition. Obstruction may result from primary atresia, or be the consequence of a mucus plug. Although in pediatric studies CCAMs are considered to be a rare malformation, they represent 50–75% of all lung lesions detected antenatally. Prenatal studies suggest an overall incidence of 1:4,000–6,000 [4, 5, 7]. The lesion is almost always unilateral with no preference of right or left lung. Only a few cases of bilateral involvement have been reported. The disease generally affects one lobe, and the tumor appears as a mass of variable size that deforms the lung. It is often large enough to cause a shift of the mediastinal structures and to compress the contralateral lung. Although different classifications have been proposed, the most relevant classification from a prenatal perspective distinguishes macrocystic tumors with cysts of ≥5 mm in diameter and microcystic lesions with cysts <5 mm in diameter that appear sonographically as solid, bright lesions [5, 6, 8, 9].

Polyhydramnios and non-immune hydrops may be present in cases detected antenatally (although this is rare). Fetal hydrops can result from decreased venous return due to vascular compression by the pulmonary mass or decreased myocardial contractility. Polyhydramnios in the absence of hydrops is probably related to esophageal compression.

In most reports, CCAMs are not associated with other anomalies. However, renal abnormalities, congenital heart disease, intestinal obstructions and diaphragmatic hernia have been reported occasionally.

The diagnosis of CCAMs is reliant on the demonstration of overgrowth of one lung that may be bright and echogenic without evidence of acoustic shadowing (microcystic variety) or contain multiple cysts of variable size (macrocystic variety) (Fig. 2.2). The former is by far the more common. A shift in the mediastinum and diaphragmatic inversion are commonly encountered. The diagnosis is typically made around mid-gestation. The differential diagnoses include other thoracic lesions such as diaphragmatic hernia, pulmonary sequestration and CHAOS. Differentiation from diaphragmatic hernia is usually easy. In CCAMs, the diaphragm is readily demonstrated in longitudinal scans. In diaphragmatic hernia, the diaphragmatic line is disrupted and crossed by abdominal organs such as bowel loops and/or the liver. Distinguishing CCAMs from intrathoracic lobar sequestrations may be difficult. The two conditions have a similar prognosis and the same obstetric management. Demonstration with color Doppler ultrasound of a vascular peduncle crossing the diaphragm and connecting the lung mass to the abdominal aorta may be difficult but allows a specific diagnosis of sequestration [4]. In CCAMs, the vasculature of the lung mass is seen to derive from the pulmonary vessels. CHAOS is a bilateral condition: both lungs are enlarged and echogenic, the trachea and main bronchi are markedly dilated, and fetal hydrops is the rule [12]. CSE is a subtype of CCAMs that cannot be identified specifically antenatally and evolves after birth [10]. Magnetic resonance imaging (MRI) clearly demonstrates the lung lesions (Fig. 2.3) but is rarely needed because ultrasonography is usually effective in the diagnosis.

The prognosis of CCAMs diagnosed *in utero* is excellent [6, 7, 9, 10]. Survival is >90% of cases, with the exception of the rare cases associated with intrauterine hydrops. The lung mass may appear disproportionately large at mid-gestation, but tends to decrease in size by the third trimester. Vaginal delivery at term is not contraindicated, and the infants are usually asymptomatic at birth. Post-natal diagnostic imaging and close surveillance of the neonates are required because in a minority of cases CSE will develop and result in respiratory insufficiency [10]. Even in asymptomatic infants resection is recommended by most authorities, and this is usually delayed until a few months after birth [6, 9]. The management of cases complicated by fetal hydrops is uncertain. Prior to viability, termination of pregnancy can be offered. Macrocystic lesions may be drained with fine needles or by thoraco–amniotic shunting [13].

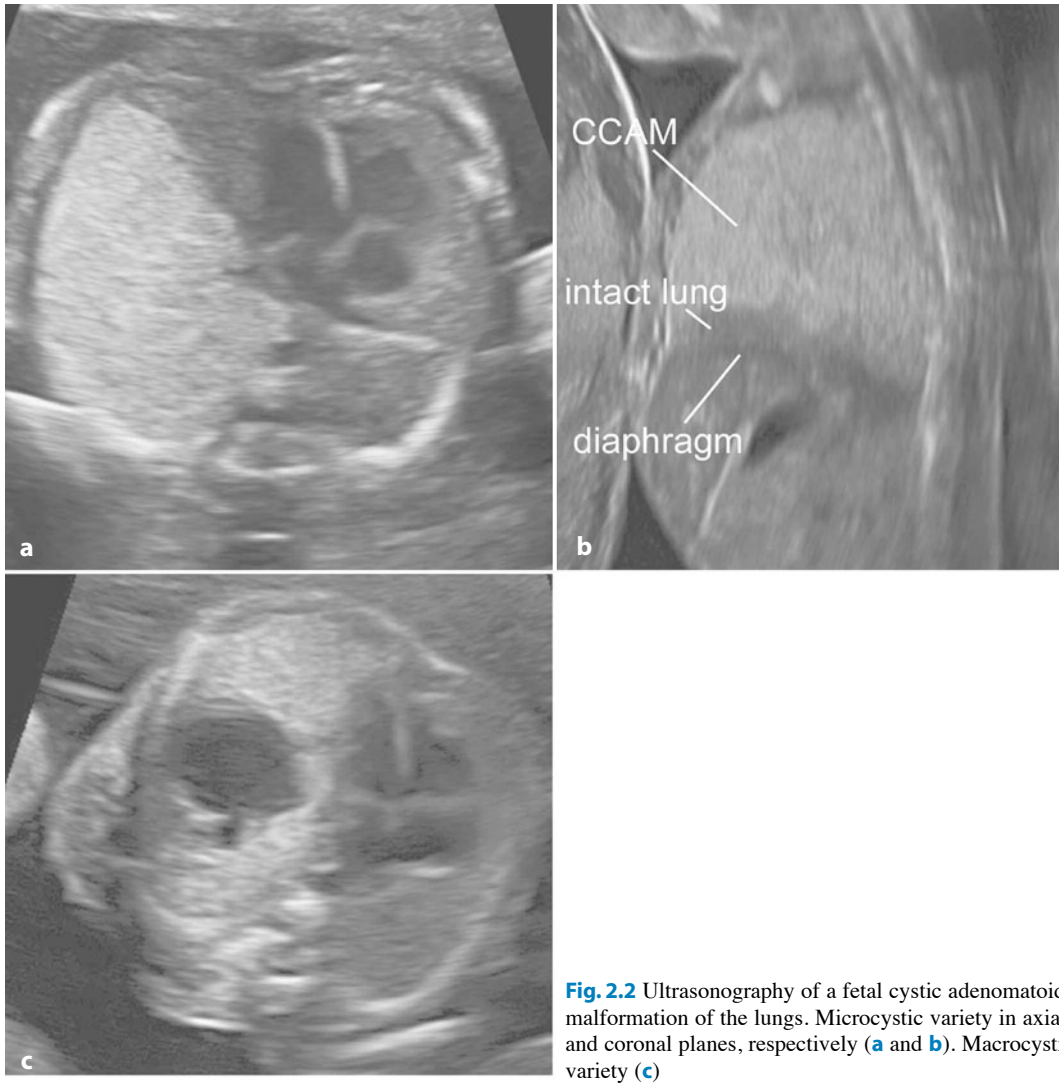

Fig. 2.2 Ultrasonography of a fetal cystic adenomatoid malformation of the lungs. Microcystic variety in axial and coronal planes, respectively (**a** and **b**). Macrocystic variety (**c**)

In microcystic lesions, benefit has been suggested by maternal administration of corticosteroids [14].

2.2.2 LS

LS is a congenital anomaly in which a mass of pulmonary parenchyma is separated from the normal lung. It usually does not communicate with the airways and receives its blood supply from the systemic circulation. The normal tracheobronchial tree derives from an outpouching of the foregut. A sequestered lung originates from a separate outpouching of the foregut or is a segment of developing lung that has lost its connection with the rest of the tracheobronchial tree. The timing of the separation is critical. If the accessory lung bud arises before the formation of the pleura, the sequestered lung will be adjacent to the normal lung and surrounded by the same pleura ("intralobar sequestration"). If the accessory lung bud arises after formation of the pleura, the sequestered lung will have its own pleura ("extralobar sequestration"). LS is a "bron-

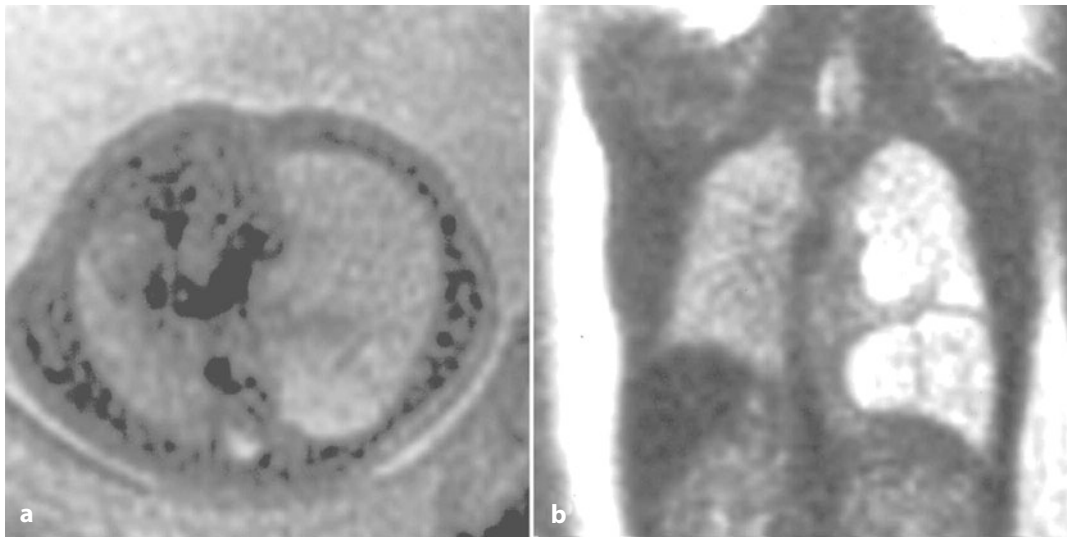

Fig. 2.3 MRI of fetal cystic adenomatoid malformation of the lungs

chopulmonary foregut malformation", a term that refers to a group of anomalies of the respiratory and gastrointestinal tracts that originate from the embryonic foregut. Besides LS, these anomalies include tracheoesophageal fistulas, esophageal duplications, neurenteric cysts, esophageal diverticula, esophageal cysts, and bronchogenic cysts. In some cases, the sequestered lung connects to the gastrointestinal tract. This occurs if the pedicle of the accessory lung bud does not involute. If a segment of the pedicle containing bronchial epithelium does not involute but loses its connection with the foregut, a bronchogenic cyst will result. The circulatory supply of the sequestered lung derives from the aorta rather than the usual pulmonary artery. Extralobar LS is virtually the only type that has been diagnosed *in utero* and in general is the most frequent in newborns. It is usually located between the lower lobe and diaphragm (>70% of cases). The other locations include infradiaphragmatic and abdominal sites. The size of the sequestered lung is variable. The arterial supply is usually from the thoracic or abdominal aorta, and venous drainage terminates in the pulmonary veins. Macroscopically, the sectioned areas may show a wide spectrum of appearances, ranging from the most frequent cystic pattern (with a solitary cyst or polycysts) to the rare pseudotumorous form.

Extrapulmonary anomalies occur in 10% of patients with intralobar LSs and include skeletal deformities (funnel chest, polydactyly), diaphragmatic hernias, congenital heart disease (tricuspid atresia, transposition of great vessels, subvalvular aortic stenosis), and renal and cerebral anomalies (hydrocephalus). In contrast, the prevalence of extrapulmonary anomalies in the extralobar variety is ≈50%, including diaphragmatic hernia, heart anomalies (atrial and ventricular septal defects, congenital absence of pericardium, truncus arteriosus), funnel chest, vertebral defects, and megacolon. Often, several anomalies are present in the same patient. The anomalous blood supply to the sequestered lung can cause a left-to-right shunt leading, in some patients, to cardiac failure *in utero* or after birth. LS has been associated with nonimmune hydrops.

Sonographically, fetal extralobar sequestration has the same appearance as CCAMs: an echogenic lung mass that frequently displaces the mediastinum (Fig. 2.4). A specific diagnosis is difficult, and is reliant upon the demonstration (with color Doppler) that the blood supply to the mass does not derive from

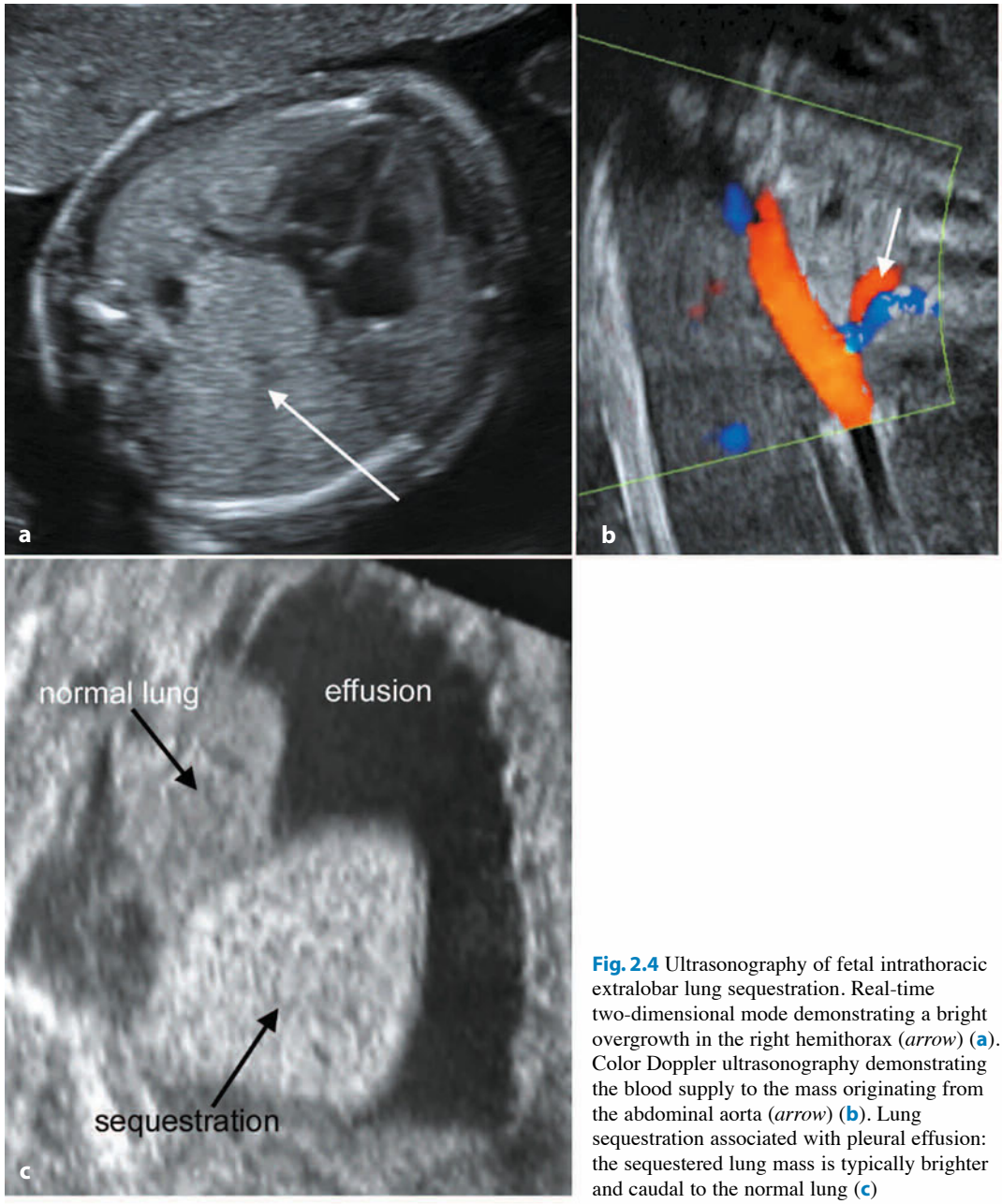

Fig. 2.4 Ultrasonography of fetal intrathoracic extralobar lung sequestration. Real-time two-dimensional mode demonstrating a bright overgrowth in the right hemithorax (*arrow*) (**a**). Color Doppler ultrasonography demonstrating the blood supply to the mass originating from the abdominal aorta (*arrow*) (**b**). Lung sequestration associated with pleural effusion: the sequestered lung mass is typically brighter and caudal to the normal lung (**c**)

the pulmonary circulation but rather from the descending aorta (usually through a vessel that crosses the diaphragm). If a pleural effusion is present, it may be possible to visualize separately the normal lung and the sequestration, which is usually caudad and brightly echogenic. Polyhydramnios and fertal hydrops may be present. The prenatal diagnosis of intralobar pulmonary sequestration has not been reported and would seem to be difficult. Extralobar LS should also be considered in the differential diagnosis of intra-abdominal solid masses (particularly over the echogenic area located cranial to the kidneys).

The natural history and outcome of LS are very similar to those of CCAMs. A large mass is usually seen at around mid-gestation, decreases in size in the third trimester, and infants are usually asymptomatic at birth. Intact survival is the rule with the exception of those cases that develop intrauterine hydrops (which tend to be slightly more frequent than with CCAMs). Amelioration of hydrops with thoraco–amniotic shunting is possible, and in several cases we have been able to continue the pregnancy for several weeks. In the absence of hydrops, vaginal delivery at term is possible. The sequestered mass needs to be removed surgically, and this is usually postponed until the fist months of post-natal life [6–7].

2.2.3 CSE

The prenatal sonographic appearance of CSE is similar to that of CCAMs: a lung mass that is brightly echogenic or cystic [10]. The pathophysiology is identical to that of CCAMs, with the fundamental difference that bronchial obstruction is incomplete, resulting in a valve mechanism with progressive overinflation of the sequestered mass after birth [10]. This may result in severe respiratory insufficiency, and is the main reason why fetuses with lung masses diagnosed *in utero* should be monitored after birth.

2.2.4 CHAOS

CHAOS is a rare congenital anomaly of the lungs secondary to complete obstruction at the level of the larynx or trachea. This results in massive accumulation of pulmonary secretions, leading to overgrowth of both lungs, most frequently associated with hydrops [12]. CHAOS is usually demonstrable earlier than CCAMs or LS (≈15 weeks' gestation). The sonographic appearance is dominated by severe bilateral enlargement of the lungs with diaphragmatic inversion. Typically, the trachea and main bronchi appear enlarged due to the accumulation of fluid (Fig. 2.5). The prognosis of CHAOS is severe and perinatal death is the rule (although exceptional cases have survived after intrapartum tracheostomy) [12].

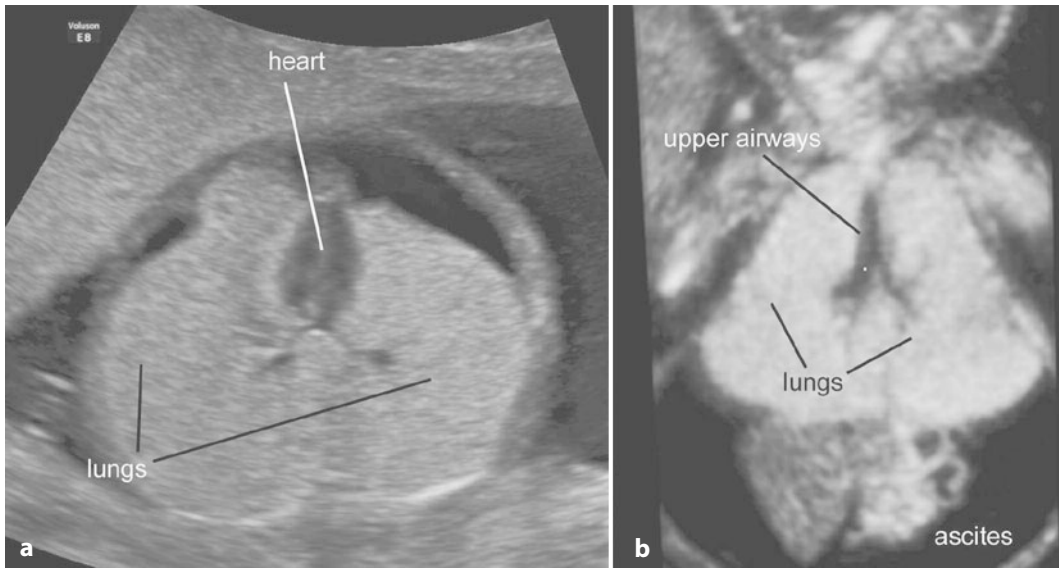

Fig. 2.5 Fetal congenital high airway obstruction syndrome (CHAOS) at 17 weeks' gestation. Severe bilateral enlargement of the lungs with inversion of the diaphragm, enlargement of the upper airways and ascites are seen (**a**, **b**)

2.3 Pleural Effusions

Fetal pleural effusions may be an isolated finding or may occur in association with generalized edema and ascites (Fig. 2.6) [15]. Irrespective of the underlying cause, presentation is usually in the neonatal period with severe (and often fatal) respiratory insufficiency. This is either a direct result of pulmonary compression caused by the effusions or due to pulmonary hypoplasia secondary to chronic intrathoracic compression. Isolated pleural effusions in the fetus may resolve spontaneously or can be treated effectively after birth. Nevertheless, in some cases severe and chronic compression of the fetal lungs can result in pulmonary hypoplasia and neonatal death. In others, mediastinal compression leads to the development of hydrops and polyhydramnios, which are associated with a high risk of premature delivery and perinatal death. Attempts at prenatal therapy by repeated thoracocentesis for drainage of pleural effusions have, in general, been unsuccessful in reversing the hydropic state because the fluid re-accumulates within 24–48 h of drainage. A better approach is chronic drainage by the insertion of thoraco–amniotic shunts. This is useful for the diagnosis and treatment. Firstly, the diagnosis of an underlying cardiac abnormality or other intrathoracic lesion may become apparent only after effective decompression and return of the mediastinum to its normal position. Secondly, it can reverse fetal hydrops, resolve polyhydramnios and thereby reduce the risk of preterm delivery, and may prevent pulmonary hypoplasia. Thirdly, it may be useful in the prenatal diagnosis of pulmonary hypoplasia because in such cases the lungs often fail to expand after shunting. Furthermore, it may help distinguish between hydrops due to primary accumulation of pleural effusions, in which case the ascites and skin edema may resolve after shunting, as well as other causes of hydrops such as infection in which drainage of the effusions does not prevent worsening of the hydrops. Survival after thoraco–amniotic shunting is ≈50% and is more likely with isolated pleural effusions than with generalized hydrops [16].

2.4 Diaphragmatic Hernia

Diaphragmatic hernia is found in ≈1 per 4,000 births. Development of the diaphragm is usually completed by the ninth week of gestation.

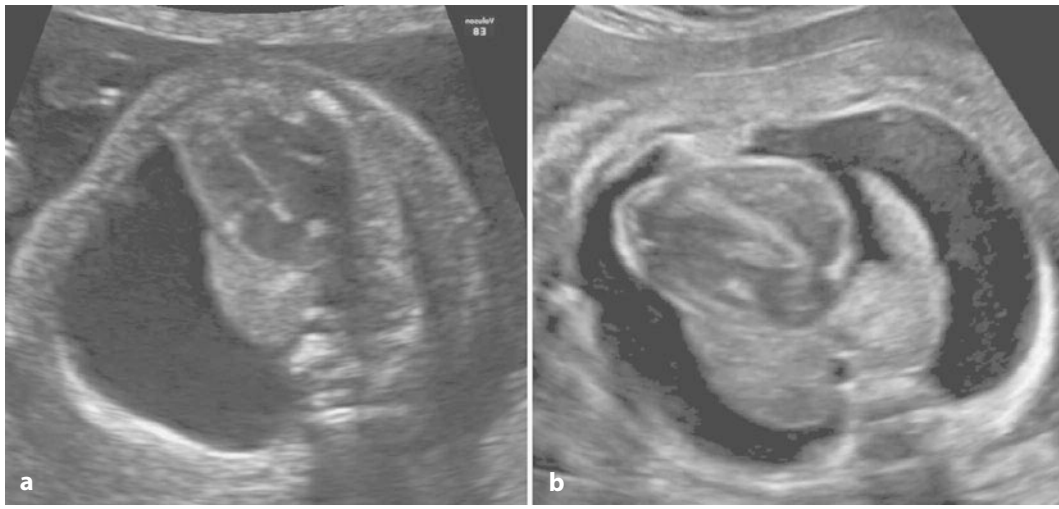

Fig. 2.6 Fetal pleural effusion. Unilateral right (**a**) and bilateral (**b**)

In the presence of a defective diaphragm, there is herniation of the abdominal viscera into the thorax at ≈10–12 weeks, when the intestines return to the abdominal cavity from the umbilical cord. However, intrathoracic herniation of viscera may be delayed until the second or third trimesters of pregnancy. Displacement of abdominal organs is probably exacerbated by the respiratory activity that begins around mid-gestation and increases progressively throughout pregnancy. Diaphragmatic hernia is usually a sporadic abnormality. However, in ≈50% of affected fetuses there are associated chromosomal abnormalities (mainly trisomy 18, trisomy 13, Pallister–Killian syndrome (mosaicism for tetrasomy 12p)), other defects (mainly craniospinal defects such as spina bifida, hydrocephaly and the otherwise rare iniencephaly, and cardiac abnormalities) and genetic syndromes (e.g., Fryns, de Lange, Marfan).

Prenatally, the diaphragm is imaged by ultrasonography as an echo-free thick line between the thorax and abdomen. However, the integrity of the diaphragm is usually inferred from the normal disposition of the thoracic and abdominal organs. Diaphra-gmatic hernia is usually diagnosed by the ultrasonographic demonstration of the stomach, intestines or liver in the thorax and the associated mediastinal shift to the opposite side (Fig. 2.7). Herniated abdominal contents are associated with a left-sided diaphragmatic hernia and are easy to demonstrate (at least in the third trimester of pregnancy) because the echo-free, fluid-filled stomach and small bowel contrast dramatically with the more echogenic fetal lung. A prenatal sonographic diagnosis is made in about only 50% of cases [17]. MRI clearly shows diaphragmatic hernia (Fig. 2.8). However, MRI is not used for diagnostic purposes because ultrasonography is usually straightforward. Identifying the lesion in routine examinations is difficult because the images may be subtle at times, but usually, once suspicion is aroused, a specific diagnosis is easy. MRI may be useful in assessment of the severity of the lesion because it allows better visualization of fetal lungs [18]. Antenatal prediction of pulmonary hypoplasia remains the greatest challenge of prenatal diagnosis. Poor prognostic signs include herniation of the liver into the fetal chest and a small lung-to-head ratio (area of the demonstrable lung divided by head circumference) [1, 2, 18–26].

In humans, the bronchial tree is fully developed by the sixteenth week of gestation, by which time the full adult number of airways is established. In diaphragmatic hernia, the reduced thoracic space available for the developing lung leads to a reduction in the number of airways, alveoli and arteries. Thus, although isolated diaphragmatic hernia is an anatomically simple defect which is easily correctable, mortality is high in cases with severe hernia. A high probability of survival has been reported in selected centers, but large population-based series suggest that the overall survival is ≈50–60% of cases, and is less likely in cases diagnosed *in utero* (probably because these are associated with a greater anatomical and (presumably functional) derangement [27].

Attempts at *in utero* repair of diaphragmatic hernia to allow lung development date back several decades. Hysterotomy and open fetal surgery have been abandoned due to the high prevalence of prematurity and maternal complications. Endoscopic occlusion of the fetal trachea has also been carried out. One preliminary experience using a metallic clip was not encouraging [28], but this procedure is in progress with technological refinements, and results with the use of an inflatable balloon are awaited [1]. The role of fetal surgery remains controversial [2, 29]. Even minimally invasive endoscopic treatment carries a significant risk of severe prematurity, and the major challenge remains patient selection. It is difficult to distinguish between lesions that: can be treated effectively after birth; can be ameliorated by prenatal surgery; are untreatable.

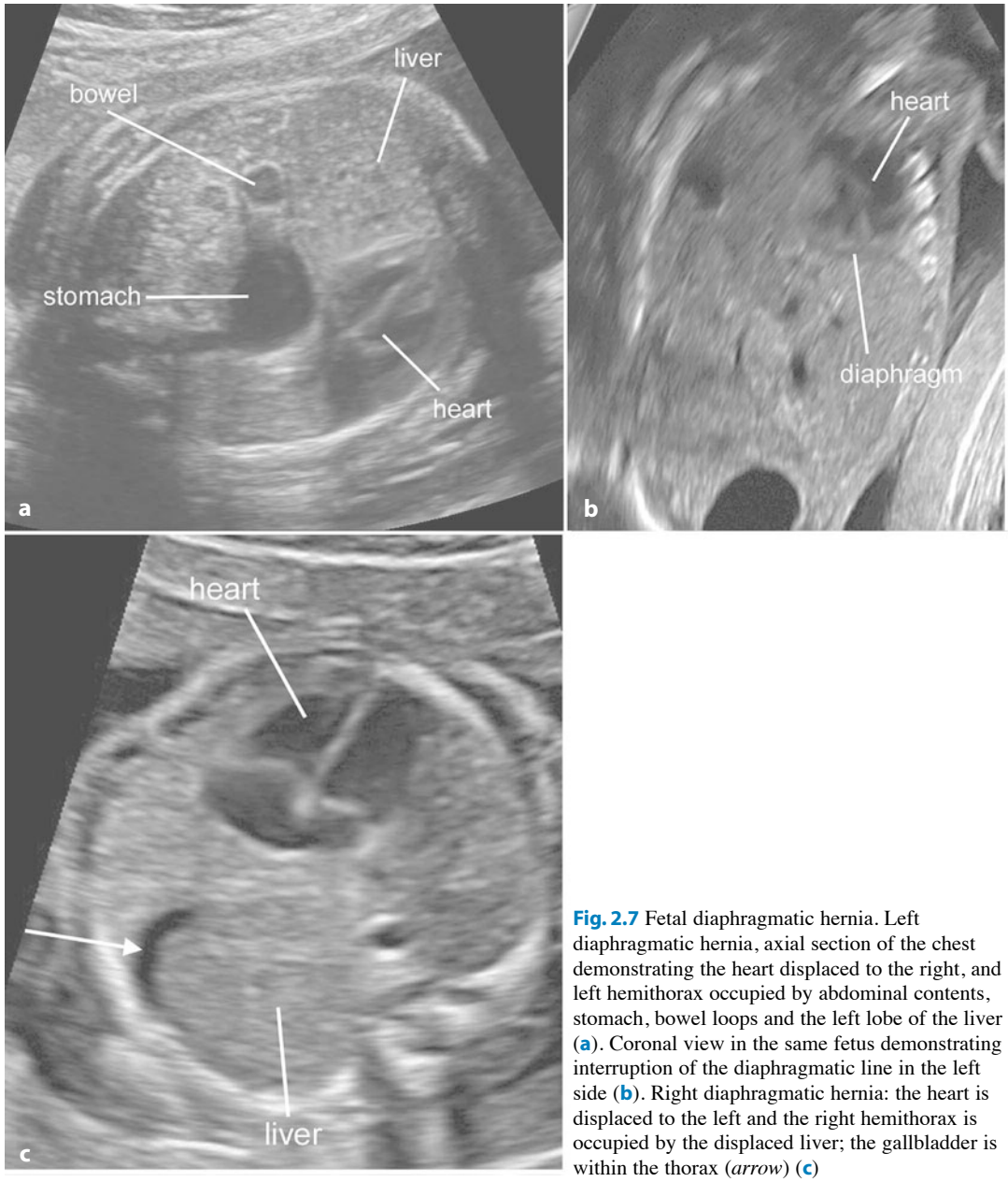

Fig. 2.7 Fetal diaphragmatic hernia. Left diaphragmatic hernia, axial section of the chest demonstrating the heart displaced to the right, and left hemithorax occupied by abdominal contents, stomach, bowel loops and the left lobe of the liver (**a**). Coronal view in the same fetus demonstrating interruption of the diaphragmatic line in the left side (**b**). Right diaphragmatic hernia: the heart is displaced to the left and the right hemithorax is occupied by the displaced liver; the gallbladder is within the thorax (*arrow*) (**c**)

2.5 Conclusions

Ultrasonography allows for the detection of many congenital anomalies of the thorax. Echogenic lungs and diaphragmatic hernia are the most common entities. The former are usually benign and, although they may have a dramatic sonographic presentation, in general they have a good prognosis. Diaphragmatic hernia continues to be associated with significant mortality and long-term morbidity. The value of antenatal treatment remains uncertain. The key points of the prenatal diagnosis of thoracic anomalies are shown in Table 2.1.

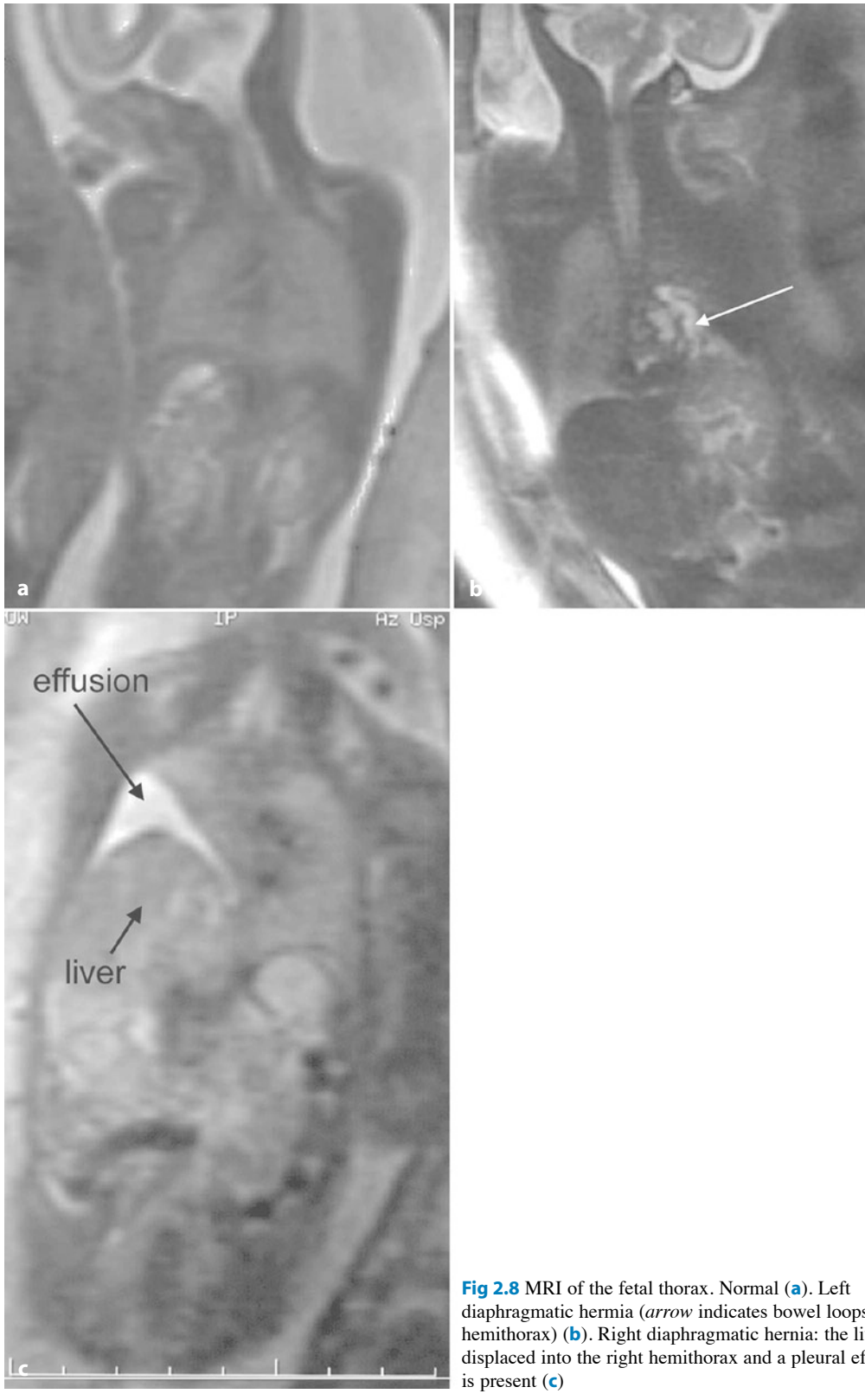

Fig 2.8 MRI of the fetal thorax. Normal (**a**). Left diaphragmatic hermia (*arrow* indicates bowel loops in left hemithorax) (**b**). Right diaphragmatic hernia: the liver is displaced into the right hemithorax and a pleural effusion is present (**c**)

Table 2.1 Key points of the prenatal diagnosis of thoracic anomalies

1. Echogenic lungs arise as a consequence of cystic adenomatoid malformation of the lungs, airway obstruction or lung sequestration. There is clinical as well as pathophysiological overlapping among these entities that share in common a good outcome when not complicated by hydrops.
2. Pleural effusion may be isolated or a part of fetal hydrops. Primitive pleural effusion may evolve towards hydrops probably because they compress the mediastinum and obstruct venous return to the heart. Prenatal treatment is possible by implantation of a thoraco–amniotic shunt. Survival is ≈50%.
3. Diaphragmatic hernia is a severe fetal anomaly that can be treated after birth but continues to be associated with significant mortality and morbidity as a consequence of lung hypoplasia. The diagnosis is possible and is based upon demonstration of abdominal organs into the fetal chest. Identification of cases with only bowel loops herniated in the second trimester and of right diaphragmatic hernias remains difficult. Some ultrasonographic findings (including the herniation of the liver into the chest and the ratio of the demonstrable lung to the head) have prognostic implications.
4. Prenatal treatment of diaphragmatic hernia has been attempted using different strategies. Open fetal surgery had been abandoned. More recently, attempts have been made by tracheal occlusion using endoscopic techniques.

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Imaging of the Thorax

3

Michelangelo Baldazzi, Filomena Carfagnini
and Giovanni Tani

3.1 Introduction

Study of the thorax in children is possible through various diagnostic methods. Each method has its own unique characteristics and an optimal time when it should be carried out to answer a specific clinical question. The first level of investigation is ultrasonography (US) and radiography; the second level is computed tomography (CT) and magnetic resonance imaging (MRI). A diagnostic pathway that provides the lowest radiation dose possible must be used. That is, a pathway that complies with the "as low as reasonably achievable" (ALARA) concept. The need to respect this principle is based on the organ-sensitivity of children and their longer life expectancy, which subjects them to an increased risk of developing a radiation dose-related disease.

3.2 Radiography

Plain radiography of the chest is the most widely used method in different age groups of children (especially in the study of acute illness). Radiography is relatively inexpensive, easy to carry out and is widely available; the information it provides can be processed rapidly; and radiography exposes the patient to a low dose of radiation.

The examination can be conducted in one or two projections in relation to the specific indication. A single radiograph of the chest in supine, anteroposterior or posteroanterior projections is usually sufficient for diagnostic purposes. The collimation of the X-ray beam should be as narrow as possible to avoid exposure of organs and systems that do not need to be imaged. The decision whether the lateral projection is used (especially in younger children) is made by the radiologist.

In children aged >3 years, it may be possible to carry out plain radiography of the chest in the upright position but, if not, the parents can be asked to assist the child to stand correctly (Fig. 3.1). To reduce radiation exposure, protective pads for more radiosensitive tissues (e.g., gonads, breasts) can be used. The chest radiograph allows: evaluation of lung expansion and heart size; study of the mediastinum; positioning of catheters, endotracheal tubes and chest drains (Fig. 3.2).

3.3 US

US was initially used for the quantification and evaluation of pleural effusions. However,

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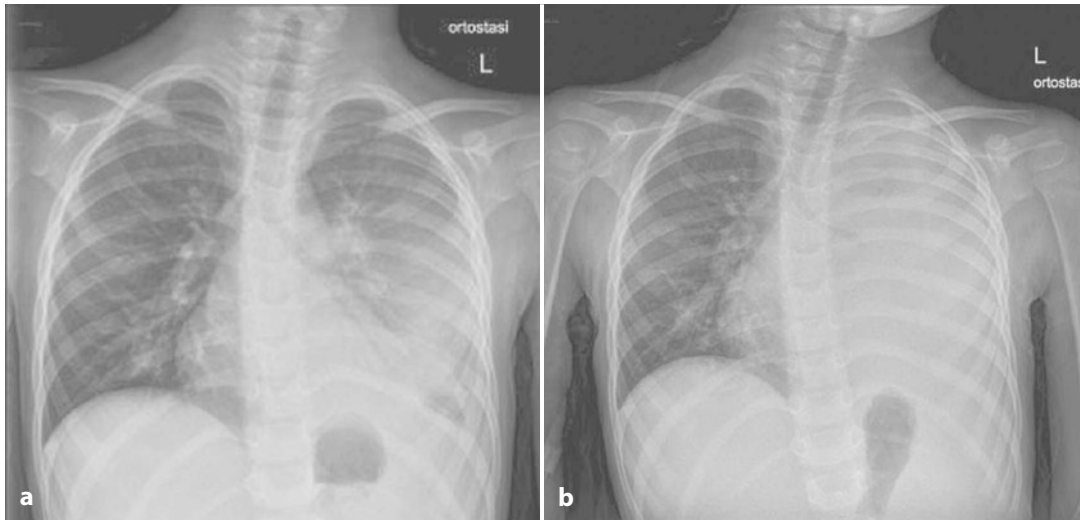

Fig. 3.1 Chest radiograph, AP projection (**a** and **b**). Large left bronchopneumonic focus complicated by pleural effusion

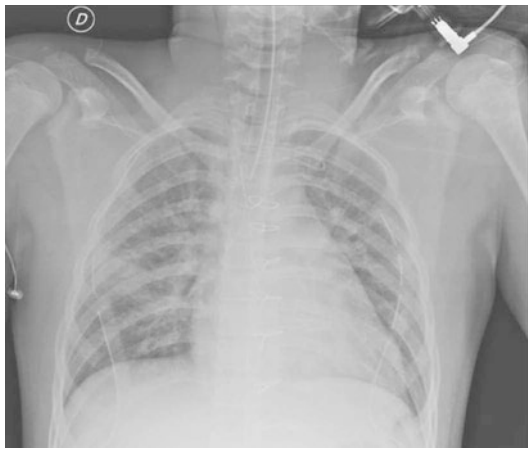

Fig 3.2 Chest radiograph with patient in the supine position showing placement of medical-evaluation devices (central venous catheter, drain)

over time, its use been has been extended to the study of the parenchyma and mediastinum [1, 2]. The procedure is highly operator-dependent, does not use ionizing radiation and, in most cases, does not require sedation. These characteristics are of fundamental importance if using US in children.

Penetration of the ultrasound beam is hampered by bone and air in healthy lungs. Study of parenchymal and mediastinal lesions can be conducted through special "acoustic windows". Furthermore, the low mineralization of bone permits approaches that cannot be used in adults.

The investigation must be carried out after careful evaluation of chest radiographs. This evaluation guides the choice of the most appropriate position for the patient (supine, prone, lateral). The indications for US are for the study of: pneumonia (especially if complicated by pleural effusions (Figs 3.3–3.5)); solid pulmonary lesions; congenital lung malformations; diaphragm profiles; the mediastinum. In addition, thoracentesis and biopsies can be done under US guidance [3]. Color and Doppler procedures (Fig. 3.6), although potentially problematic because of the lack of compliance from young patients, permit evaluation of the vascular structures without the need for intravenous administration of contrast agents. They are very useful as adjuncts to conventional investigations for the study of lung seizures, pulmonary masses and parenchymal masses [3, 4].

3.4 CT

The advent of CT in 1970 by Hounsfield radically changed radiology. In children, introduc-

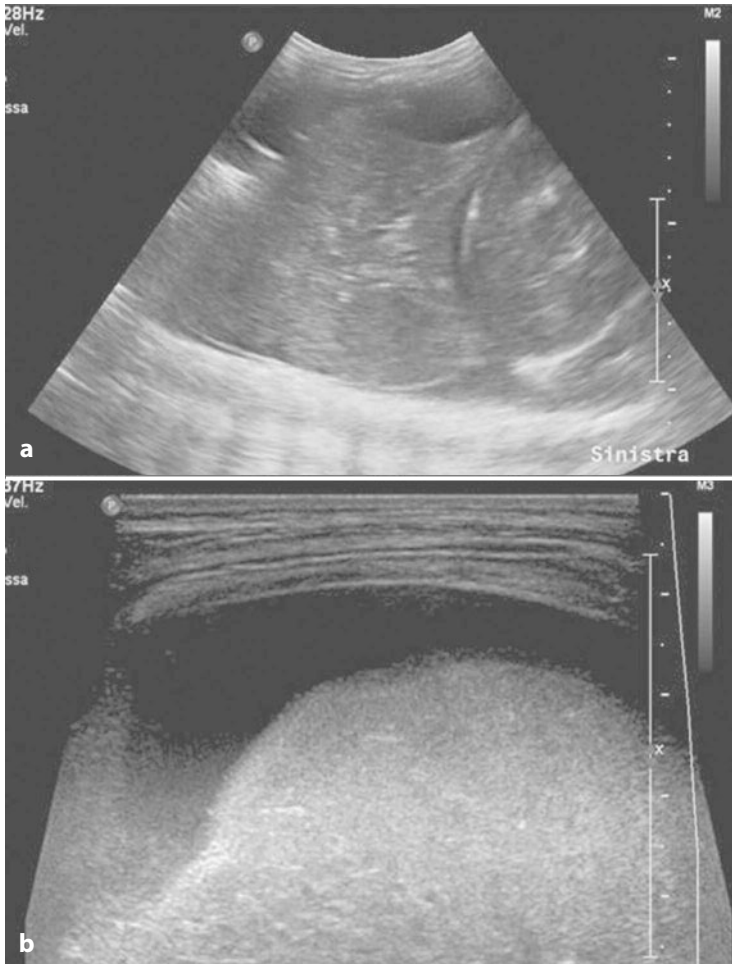

Fig. 3.3 Ultrasound of the lung (**a** and **b**) showing parenchymal hepatization with pleural effusion

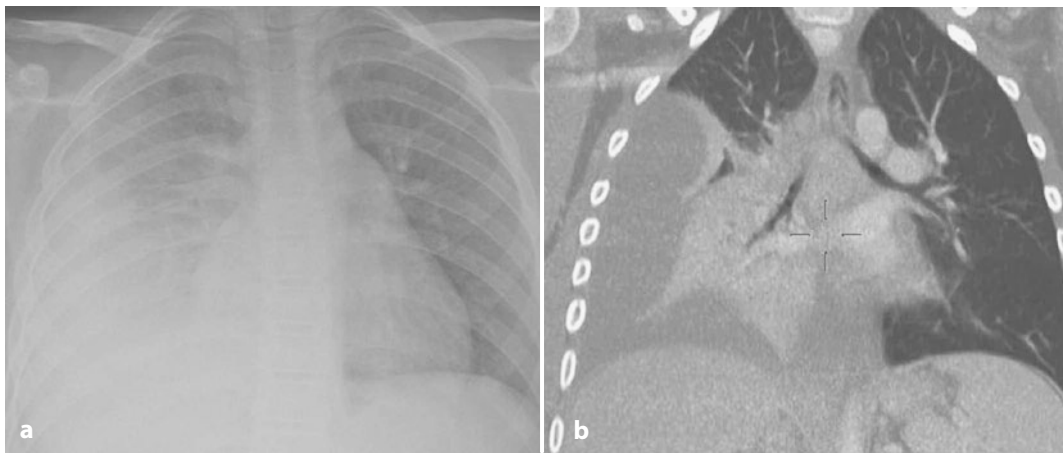

Fig. 3.4 Radiography (**a**) and (**b**) CT of the chest. The right pleural effusion is: organized; along the marginal rib; associated with parenchymal atelectasis

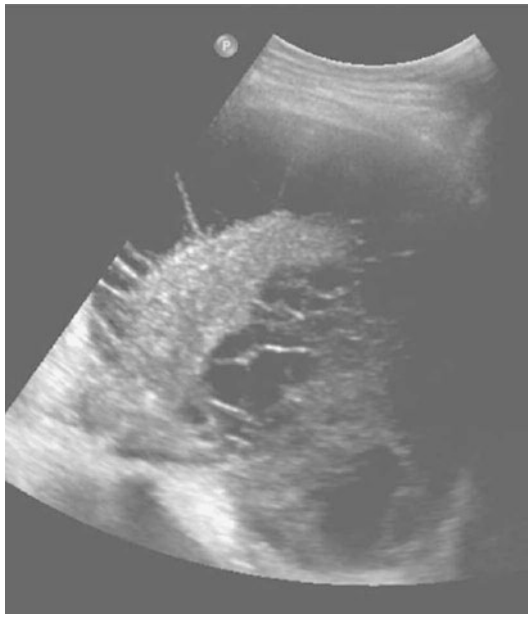

Fig. 3.5 Ultrasound of the lung of the same patient shown in Figure 3.4. Pleural effusion has evolved into empyema with cavities and septa, and is associated with major parenchymal atelectasis

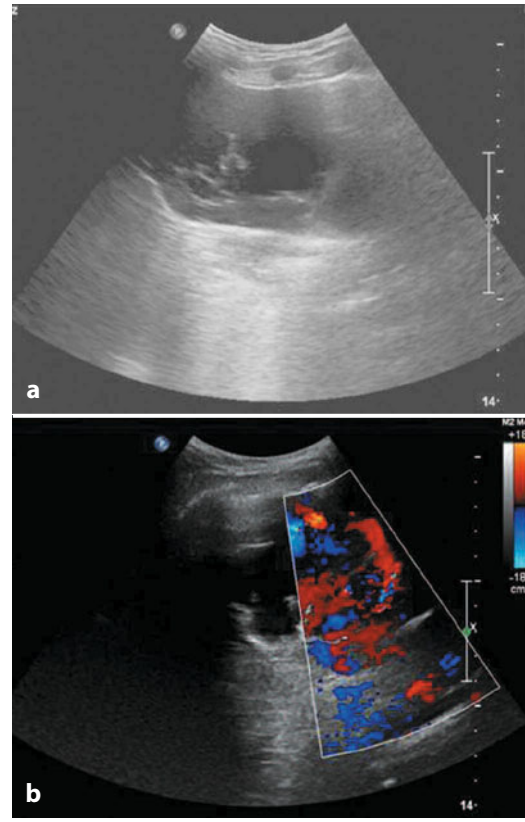

Fig. 3.6 Ultrasound (**a**) and echo-color Doppler (**b**) of the lung showing a mediastinal mass

tion of the spiral method (particularly the subsequent advent of MDCT) has greatly increased the sensitivity and specificity of CT. It has also significantly improved the diagnostic yield as well as extended the indications for use, especially in the study of the chest in pediatric patients.

With respect to spiral CT, MDCT also allows the acquisition of larger volumes in less time and the use of ever-thinner slices to allow multiplanar reconstructions from raw data [5]. These methods allow: study of the airways; evaluation of vascular structures; CT angiography to be undertaken; virtual endoscopy. The diagnostic possibilities are increased because of multiplanar reconstructions and post-processing of data. Reworking of acquired data is another important resource provided by this method. Several types of CT can be afforded, including multiplanar reconstructed (MPR; Figs 3.7–3.9); three-dimensional (3D) shaded surface display (SSD); volume reconstruction (VR); and volume rendering (VR; Fig. 3.10). These subsequent revisions add value to the axial images, allowing more accurate and reliable diagnostic evaluations in a high percentage of cases [6].

The paucity of visceral fat and difficulty in acquiring images marred by motion artifacts makes the acquisition of good-quality images problematic, thereby complicating recognition of normal structures and certain types of diseases. With respect to motion artifacts, subjects aged <3 years are usually sedated, whereas those aged >5 years can undergo CT if made to feel comfortable with verbal assurances and use of toys.

Single acquisition of the thorax should be carried out after the intravenous administration of contrast medium. This administration should be avoided in cases of interstitial disease (in which only high-resolution computed

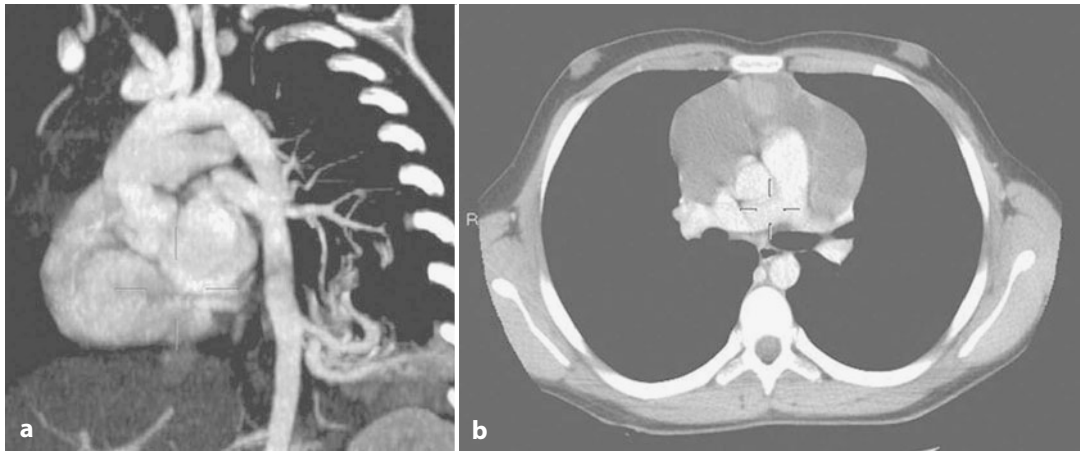

Fig. 3.7 CT: maximum intensity projection (MIP) multiplanar reconstruction (MPR) (sagittal reconstruction) showing pulmonary sequestration (**a**). MIP MPR axial reconstruction showing a thymic mass (**b**)

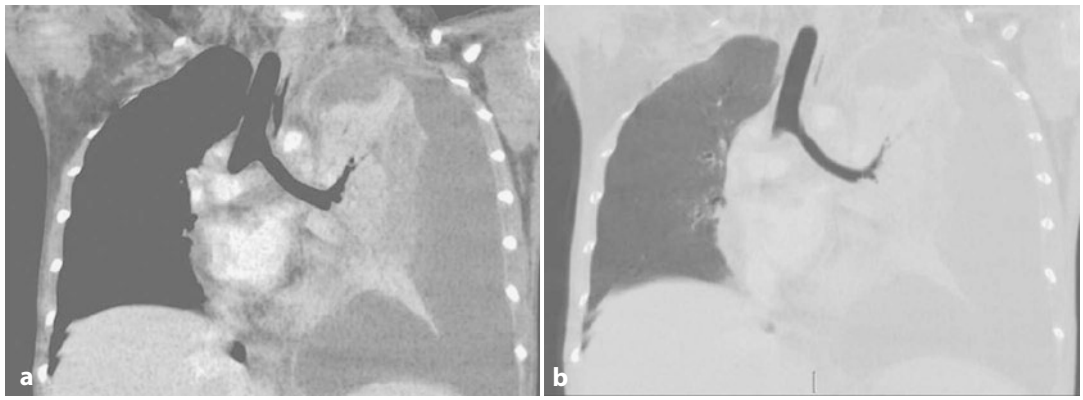

Fig. 3.8 Coronal MIP MPR (**a**) and minimum intensity projection (MinIP) (**b**) showing a focus complicated by a pleural effusion

tomography (HRCT)) should be done) or for studies of malformations of the chest wall (Fig. 3.11) [7]. A non-ionic, organo-iodinated contrast agent at about 2 mL/kg should be employed. Administration of these contrast agents can be slightly more complex than in adult patients due to the wide variability of circulation and caliber of the small vessels of pediatric patients. The injection should ensure even distribution of the contrast agent. Imaging is usually carried out approximately 20–30 s after injection (the first 20 s if the patient is aged <2 years). Image acquisition is in the inspiratory phase in cooperative patients, free-breathing in the non-cooperative. The main disadvantage of CT is the radiation dose to which patients are exposed, which is especially important in children. Hence, before subjecting a patient to CT, one must ascertain if the same information can be obtained without the use of ionizing radiation [8, 9].

One indication for the diagnostic use of contrast-enhanced CT in children is mediastinal/thoracic nodules and masses, particularly those localized in areas that cannot be seen using conventional methods (lung apex; near the diaphragm; adherent to the chest wall; at the level of the central airways). Obtaining reconstructed images with thin overlapping sections allows detection of small lesions and

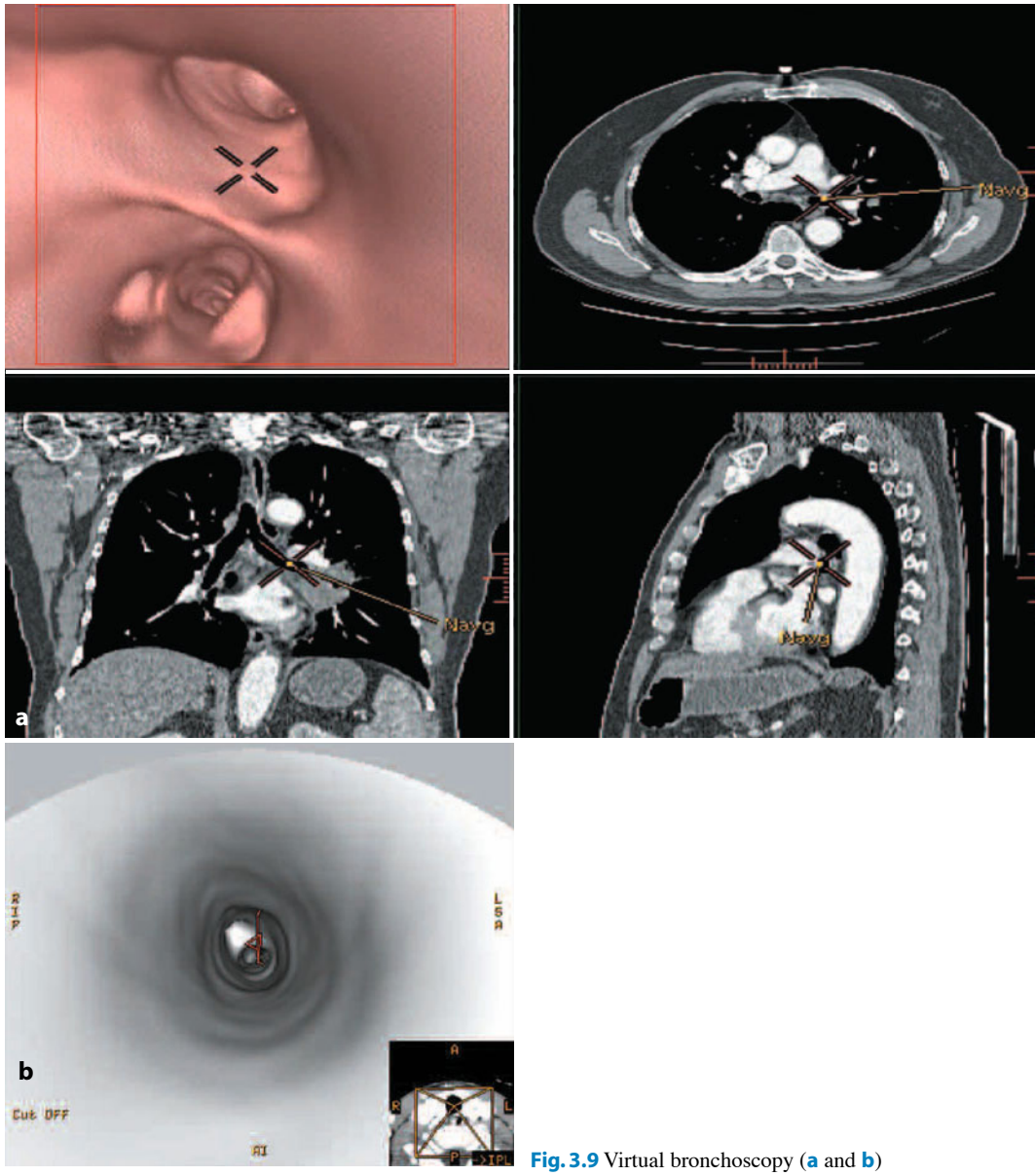

Fig. 3.9 Virtual bronchoscopy (**a** and **b**)

eliminates breathing artifacts. Another important indication is the study and follow-up of tumor lesions. CT permits assessment of the level of infiltration of tissues, vascular structures and airways, resulting in the possibility of better surgical planning and radiotherapy. Also, CT angiography allows the study of vascular malformations (congenital and acquired) (Fig. 3.12). The bolus-tracking technique allows correct synchronization of the time of acquisition of arterial and venous phases [5, 10, 11].

Important anatomical features of surgical interest can also be provided if CT is used to study diaphragmatic hernia (Fig. 3.13) and cystic parenchymal malformations. In studies of congenital diaphragmatic hernia (CDH), partial or complete discontinuity of the diaphragmatic profile can be ascertained, as can abnormal migration of abdominal structures in the chest (which can result in compression of the parenchyma and thus hinder development). The prognosis is strongly related to gestation-

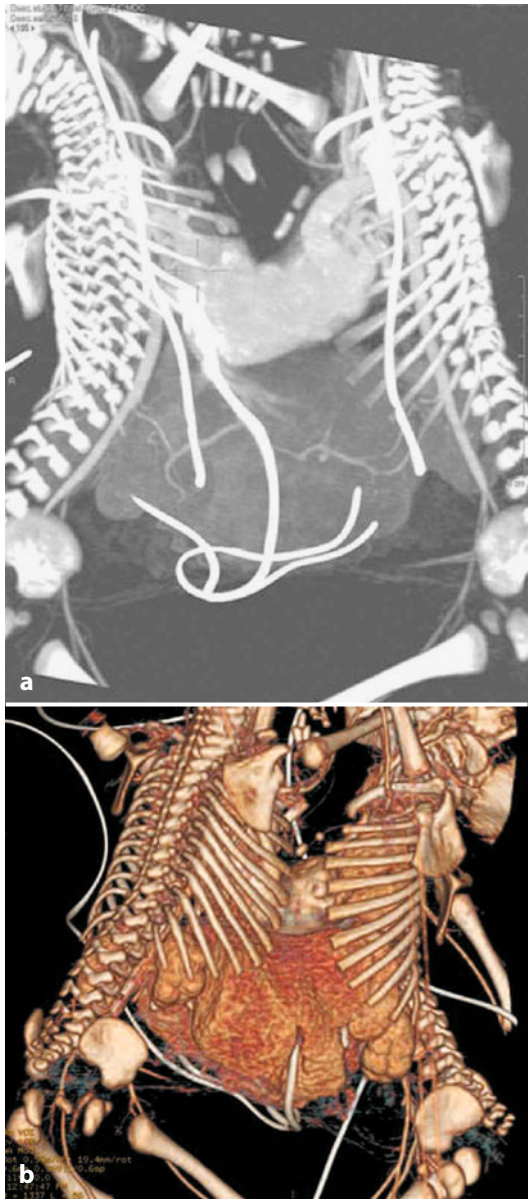

Fig. 3.10 MIP MPR (**a**) and three-dimensional volume rendering (VR) (**b**) showing thoracopagus conjoined twins

al age at onset, so quantification of pulmonary hypoplasia using CT is essential. In fact, anomalies which occur before the 25th week of life are associated with severe developmental abnormalities of the lung that carry a poor prognosis. The most common abnormality is the foramen of Bochdalek, which develops more frequently on the left side.

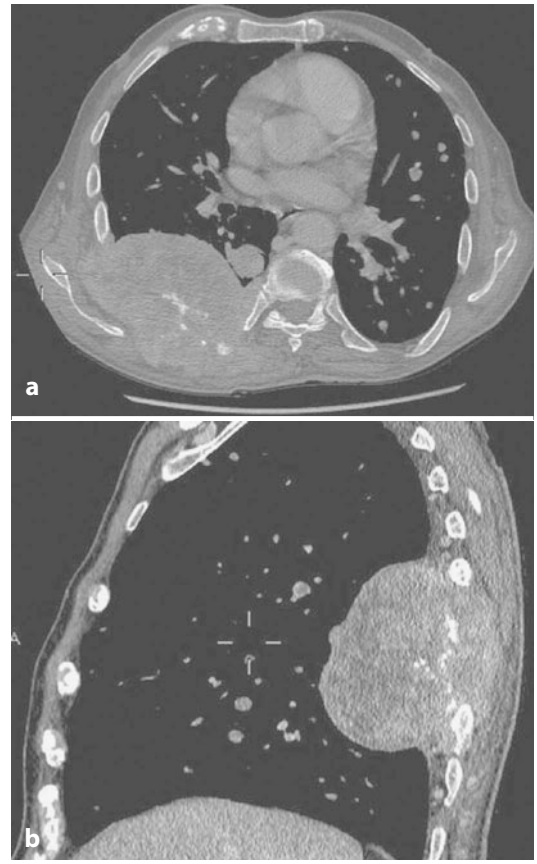

Fig. 3.11 Axial (**a**) and sagittal CT (**b**) showing an expansive formation in the chest wall with rib erosion

CT can be used to study cystic parenchymal malformations. This group of diseases includes: simple congenital thoracic cysts; cysts within the mediastinum and parenchyma (bronchogenic cysts, duplication cysts, pleuropericardical cysts); and adenomatoid cystic disease of complex congenital cystic-pulmonary sequestration (CAM); and pulmonary sequestration [12–15].

The management of simple mediastinal cysts is according to symptoms. All cysts within the lung parenchyma should be considered to be bronchogenic and require surgical treatment. The definitive diagnosis is established by study of the cyst wall; the diagnosis may be more difficult if there are signs of inflammation in the cyst wall. Bronchogenic cysts are, in general: solitary and spherical in shape; surrounded by a thin layer of bronchial epithelium; and com-

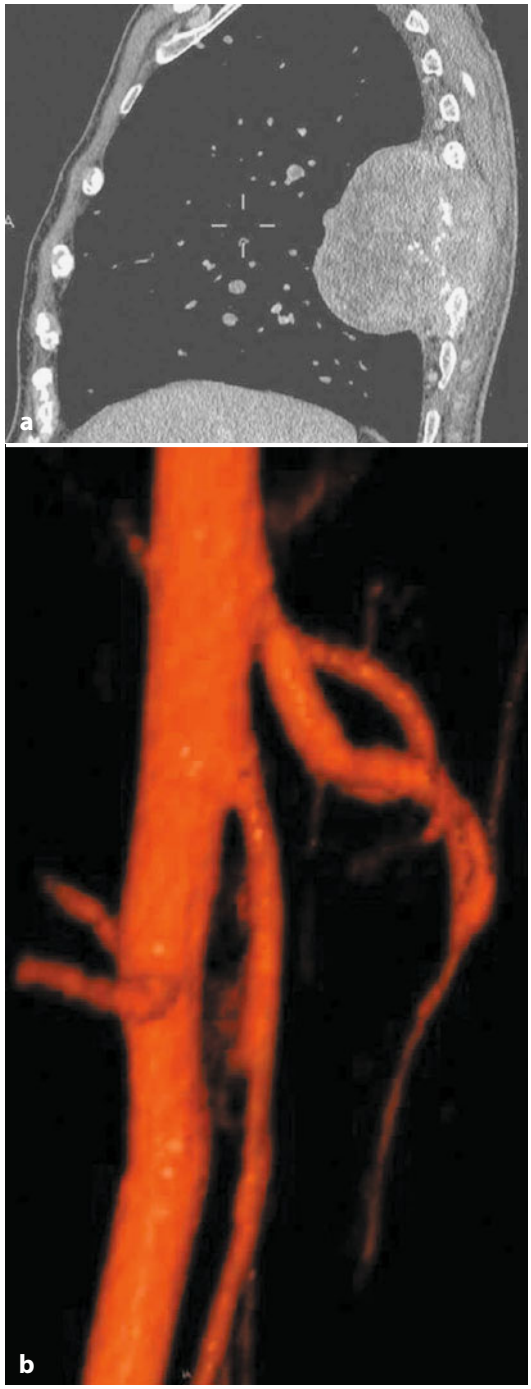

Fig. 3.12 MIP (sagittal reconstruction) (**a**) and VR reconstruction (**b**) showing the arteries in the abdominal aorta and their branches

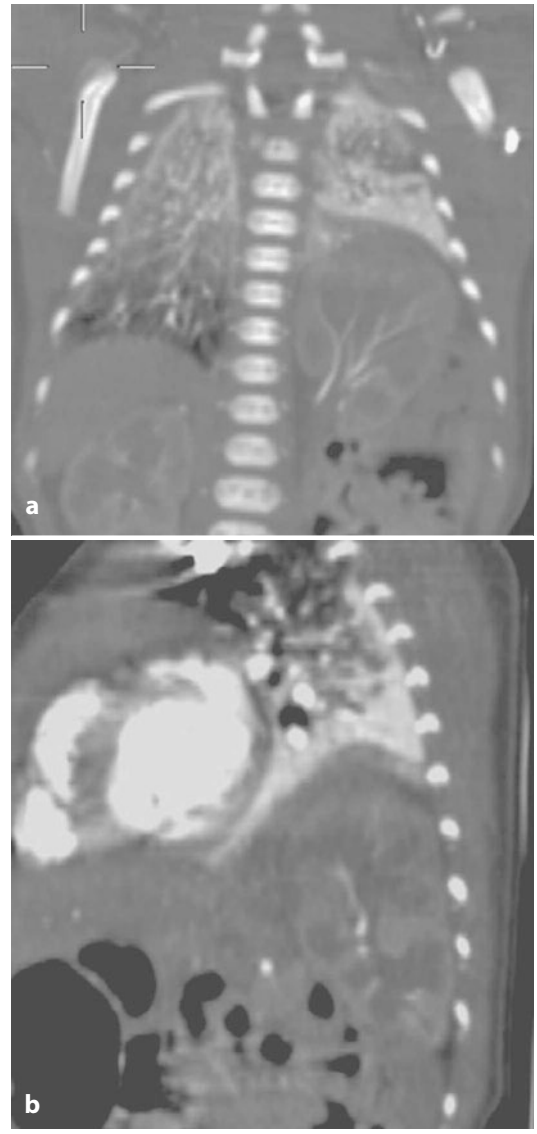

Fig. 3.13 Coronal (**a**) and sagittal MPR (**b**) showing a left diaphragmatic hernia

prise viscous, mucoid, hemorrhagic or aqueous content. They may contain calcium, internally or at the level of the wall, or are completely calcified and in communication with the airway. Sometimes bronchogenic cysts can be in association with other malformations such as pulmonary sequestration, lobar emphysema or bronchial atresia. The panels may also show moderate enhancement after administration of contrast agent [16]. Mediastinal cysts show

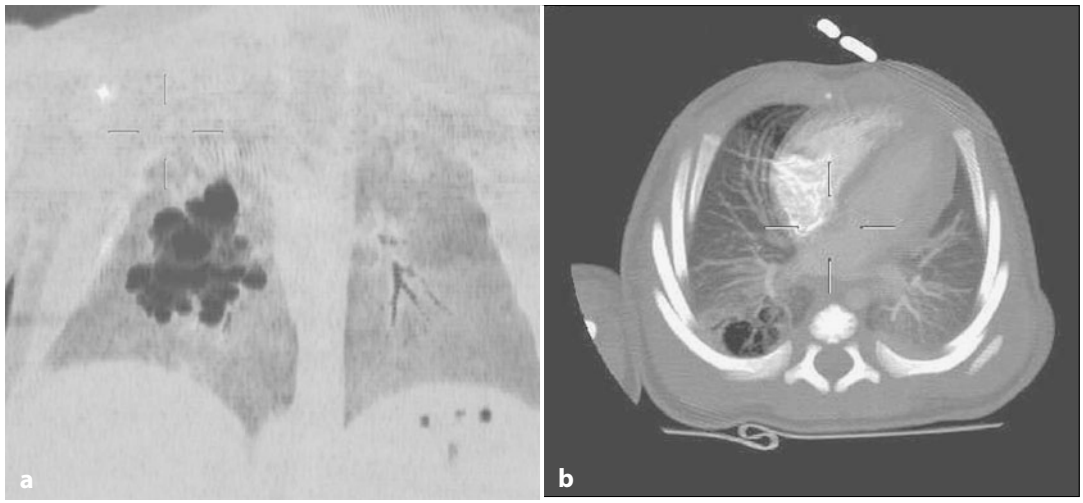

Fig. 3.14 MPR images: MinIP coronal (**a**) and axial MIP (**b**) showing right pulmonary CAM

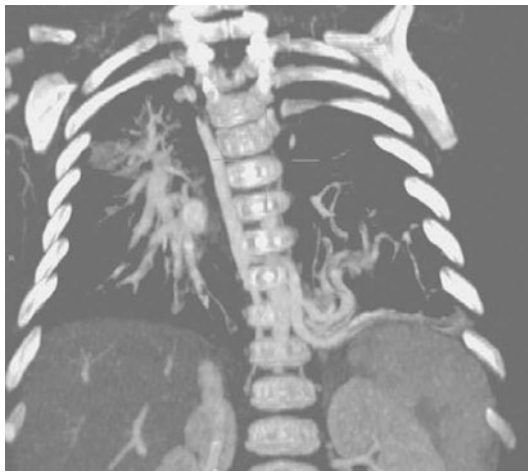

Fig. 3.15 MIP coronal MPR showing postero-basal left pulmonary sequestration

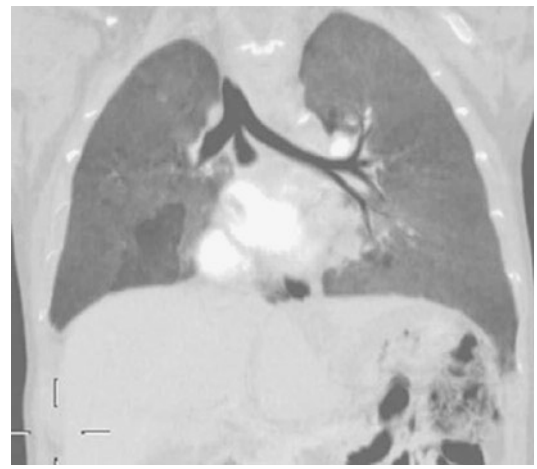

Fig. 3.16 MinIP coronal MPR showing right basal pulmonary sequestration

rather more obvious effects: they compress the esophagus, trachea and vascular structures of the airway.

CAM (Fig. 3.14) can be associated with macroscopic cysts. The anatomy and characteristics of these formations lend themselves to CT, which allows evaluation of communication of the cyst with the airways, and its blood supply from the pulmonary circulation. These malformations are often perfused by systemic vessels and distinguishing them from pulmonary sequestration is difficult. These malformations can be differentiated according to the size of the cysts (which may vary from a few millimeters to >10 cm). These malformations may be associated with other congenital abnormalities of the lung.

Pulmonary sequestration (Figs 3.15 and 3.16) comprises a mass of lung tissue that is not in communication with the airway, and which is perfused by a systemic-type vascular component. CT allows distinction between the

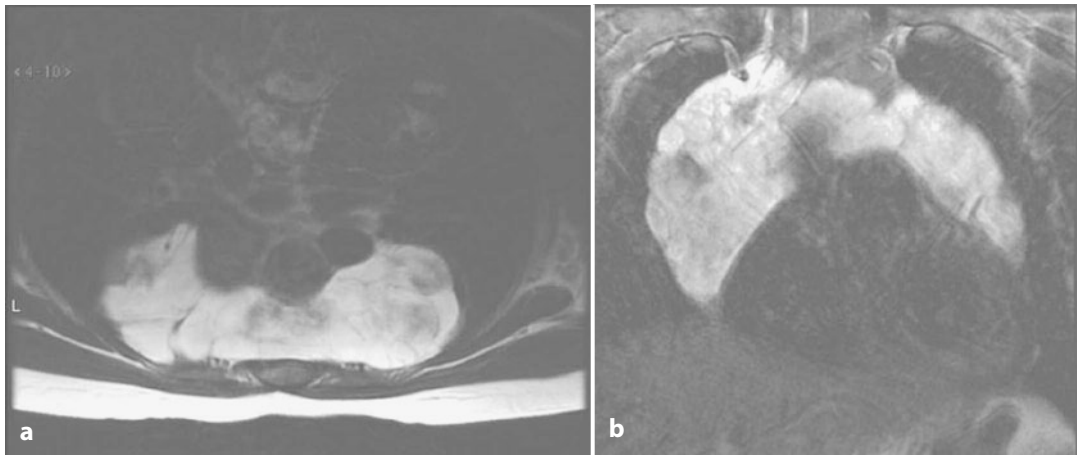

Fig. 3.17 Axial (**a**) and coronal T2-weighted (**b**) images showing a cystic neoplasm of the thymus gland

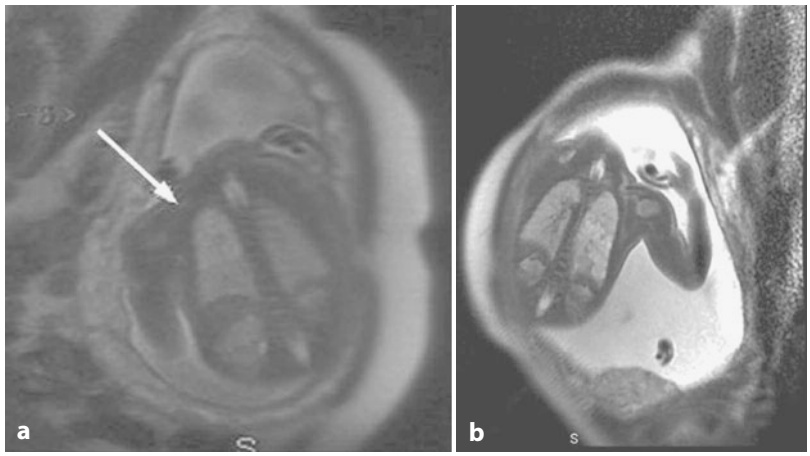

Fig. 3.18 Prenatal MRI (**a** and **b**) showing an adenomatoid cystic malformation

two types: intralobar (tissue is surrounded by normal lung tissue and located in the inner face of the visceral pleura) and extralobar (tissue is disconnected from the airways and has its own pleural lining). Venous drainage of the intralobar type is directed towards the pulmonary circulation, whereas extralobar sequestration is mediated by the system from the azygos portal.

3.5 MRI

For many years, MRI was considered to be an experimental method in the study of lung parenchyma. This judgment was based on the low-quality images it provided due to the many motion artifacts from breathing and heart beating as well as from the low signal/noise ratio. However, over the years, evolution of certain sequences (e.g., turbo spin echo (TSE) T2-weighted) and the use of triggers have extended the indications for the use of MRI in the lung. In the future, MRI may replace CT in follow-up examinations and the diagnosis of certain congenital lung malformations (e.g., pulmonary sequestration).

One of the main research areas in the study of the thorax in children is of mediastinal

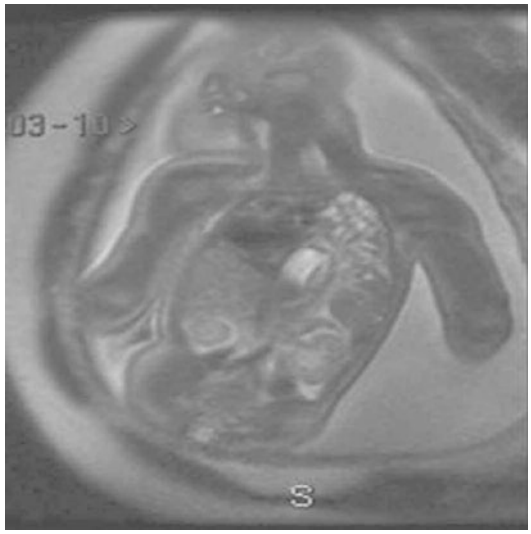

Fig. 3.19 Prenatal MRI showing a diaphragmatic hernia

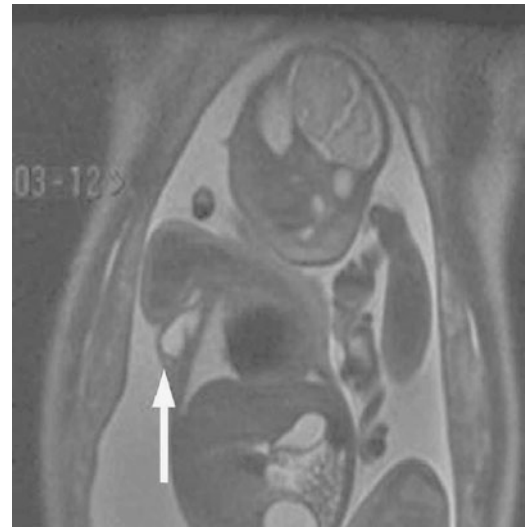

Fig. 3.20 Prenatal MRI showing a cystic lymphangioma

masses (particularly those of the posterior mediastinum). Imaging is with T1 and T2 TSE (Fig. 3.17) sequences and, in younger children (especially sedated subjects), single-shot sequences. MRI is also of utmost importance in prenatal diagnosis (Figs 3.18–3.20), particularly the study of congenital lung malformations (which are typically detected with US but which are then framed and evaluated with MRI).

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Anesthesia for Thoracic Surgery

4

Giulia Bottazzi, Andrea Gentili, Maria Elena Latrofa and Simonetta Baroncini

4.1 Introduction

Thoracic surgery in the pediatric patient may be carried out for a wide variety of congenital, neoplastic, traumatic and infectious diseases. An optimal approach to the planning of anesthesia for thoracic surgery requires not only a good knowledge of the technical features and an understanding of the anesthetic physiological alterations associated with the and surgical procedure, but also of the patient's underlying status. The approach needs to take into account the problems and risks related to airway management, potential preoperative respiratory compromise and respiratory consequences associated with a possible lung resection, as well as those connected with the changes due to the lateral decubitus position, the lung exclusion and, in thoracoscopy, CO_2 insufflation in the pleural cavity. In addition, the magnitude of the physiological modifications associated with thoracic surgery is influenced by the anesthetic agents administered, the underlying myocardial and respiratory function, and the patient's age (many critical diseases need quick surgical correction in the neonatal age group) [1].

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4.2 Anatomical and Physiological Characteristics of the Respiratory System in Neonates, Infants and Children

Major differences exist between the characteristics of the respiratory system of preterms, neonates, infants and very-young children and those of adults. With increasing age these differences tend to lessen and the basic characteristics of the respiratory system become more similar. This condition can be explained by defining the anatomical compartments and their developmental differences in pediatric patients that influence the execution of anesthesia and thoracic surgery.

Differences in the extrathoracic airways in pediatric *versus* adult patients include the following:

- the small size of the airway is one of the primary differences in infants and children younger than 8 years compared with older patients;
- neonates and infants are obliged nasal breathers until the age of 8–12 months because of the proximity of the epiglottis to the nasopharynx. Obstruction of the anterior or posterior nares (nasal congestion, stenosis, choanal atresia) can lead to clinically significant distress in this age group;
- the tongue of neonates, infants and young

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children is relatively large in proportion to the remainder of the oropharynx and thus obstructs the airways more easily;
- the larynx of neonates, infants and young children is higher in the neck (C3–C4) than in adults (C5–C6);
- the epiglottis is larger and more horizontal to the pharyngeal wall;
- the subglottic region is narrow. In children, the subglottic area is cone-shaped, with the narrowest area at the cricoid cartilage. A small amount of subglottic edema can lead to significant narrowing, high airway resistance and increased work of breathing. Older patients and adults have a cylindrical airway that is narrowest at the glottic opening;
- tonsillar and adenoidal lymphoid tissue in slightly older children is prominent and can contribute to respiratory infections and airway obstruction.

Moreover, the differences in the respiratory center, respiratory muscles, chest wall, intrathoracic airways and lung among children include the following:
- the respiratory center is immature in neonates and leads to irregular ventilations and an increased risk of apnea;
- the respiratory rate is higher in infants and young children than in adults;
- the diaphragm and intercostal muscles are not fully developed. The slow-twitch, fatigue-resistant muscle fibers in the neonate and infant are underdeveloped. Thus, any condition that increases the work of breathing may easily fatigue the respiratory muscles and result in respiratory failure;
- the ribs are oriented horizontally. During inspiration, a lower volume is displaced, and the capacity to increase tidal volume is limited (compared with that in older patients);
- the small surface area for the interaction between the diaphragm muscle and thorax limits the displacing volume in the vertical direction;
- infants and young children have relatively little cartilaginous support of the airways. As cartilaginous support increases, dynamic compression during high expiratory flow rates is prevented;
- smaller intrathoracic airways are more easily obstructed than larger ones. With age, the airways enlarge in diameter and length;
- infants and young children have fewer alveoli than adults. The number increases during childhood, from ≈20 million after birth to ≈300 million by 8 years of age. Therefore, infants and young children have a relatively small area for gas exchange;
- the alveolus is small. Alveolar size increases from 150–180 μm to 250–300 μm during childhood;
- collateral ventilation is not fully developed; therefore, atelectasis is more common in children than in adults. During childhood, anatomical channels form to provide collateral ventilation to alveoli. These pathways are between adjacent alveoli (pores of Kohn), bronchioles and alveoli (Lambert channel), and adjacent bronchioles. This important feature allows alveoli to participate in gas exchange even in an obstructed distal airway;
- alveolar ventilation is high (about twofold that of adults in relation to corporeal body mass);
- the respiratory system of the neonate is characterized by a relatively stiff lung and a very compliant chest wall;
- the soft compliant chest wall provides little opposition to the deflating tendency of the lungs. This leads to a lower functional residual capacity (FRC), a volume that approaches the alveolus critical closing volume; furthermore, both lung compliance and airway resistance are adversely related to lung size.

In addition, the cardiovascular system of children has characteristics that differ from those of adults. Blood pressure is lower and heart rate is higher in infants. The infant's systemic vascular resistance is lower, a factor that correlates well with high metabolism and O_2 consumption. Cardiac output is also higher

in infants, especially when calculated according to body weight. Heart rate has a more important role in determining cardiac output [2, 3].

4.3 Preoperative Evaluation

The preoperative history-taking and physical examination are directed at identifying acute problems and underlying medical conditions as well as previously undiagnosed diseases that may place the child at an increased risk during perioperative management.

Preoperative history-taking must include information about exercise intolerance, cyanosis, respiratory tract infections and symptoms of respiratory distress such as cough, agitation, wheezing, tachypnea, dyspnea, nasal flaring and chest-wall retractions. Generalized complaints may accompany such symptoms, including fatigue and weight loss.

The physical examination also focuses on the cardiorespiratory system, but begins with the pathology, overall assessment, and clinical status of the child.

Preoperative examination of the upper airway should also attempt to identify previously undiagnosed problems, such as an abnormal airway, and extrinsic tracheal compression or deviation, which may place the patient at increased risks during the induction of anesthesia [5].

Active bronchospasm has considerable significance because further preoperative evaluation and treatment may be necessary and intraoperative anesthetic techniques may be required to prevent the exacerbation of bronchoconstriction of the small airways.

Cardiocirculatory function should be evaluated with attention to all the determinants of myocardial performance. In particular, preload evaluation if a mediastinal mass compresses the superior or inferior vena cava and treatment of cor pulmonale and pulmonary hypertension in the case of chronic respiratory disease are essential.

Laboratory and instrumental evaluations are often important in the preparation of anesthesia for thoracic surgery. Particular attention should be given to the hematocrit (which may indicate polycytemia as a reflection of chronic hemoglobin desaturation) and the white blood cell count and indices of infection (which may indicate active pulmonary infection). In addition, arterial blood gas-analysis is recommended in patients with significant respiratory compromise: children who are hypoxic and/or hypercapnic while breathing room air are at an increased risk for intraoperative problems and postoperative respiratory failure.

Imaging (chest radiographs, CT, MRI are essential for the assessment of intrathoracic anatomy and additional information concerning alterations associated with findings that may influence anesthetic and surgical management (Table 4.1).

Echocardiography is done to check for cardiovascular anomalies, the performance of the right and left ventricles, and pulmonary pressure. Lung function tests are used widely in children aged ≥6–8 years of age. Simple spirometry is the easiest to obtain. The results of such tests are used as indicators of the complexity of perioperative management [6].

In patients with compromised respiratory function, preoperative evaluation may be used to:

- estimate the risk of intraoperative/postoperative respiratory compromise;
- ensure optimization of preoperative therapy (Table 4.2).

4.4 Pathophysiological Considerations

Respiratory changes may occur during thoracic surgery in the pediatric age group. The pathophsiological modifications are related to the lateral decubitus position, the opening of the chest wall, lung exclusion, one-lung ventilation and, in thoracoscopy, CO_2 insufflation into the pleural cavity.

Table 4.1 Preoperative preparation for thoracic surgery

Problem and disease	Treatment and drugs
Atelectasis	Chest physiotherapy Postural drainage Fluidificant drugs Suction of tracheobronchial secretions Bronchoscopy
Respiratory tract infections	Diagnostic microbiological culture Select antibiotic therapy on the basis of microbiological culture
Bronchospasm	ß$_2$-adrenergic agents Methyl-xanthines (aminophylline) Corticosteroids Cromolyn sodium
Pulmonary hypertension	Endothelin inhibitors Phosphodiesterase V inhibitors (Sildenafil) Nitric oxide
Cor pulmonale	Supplemental oxygen Diuretics Inotropic agents
Malnutrition	Achieve positive calorific balance Gain weight

Table 4.2 Correlation between imaging findings and potential anesthetic problems

Imaging finding	Potential anesthetic problem
Compression or deviation of the trachea	Airway obstruction/collapse Difficulty of intubation or ventilation
Pulmonary infiltrates	Decreased lung compliance Increased V/Q mismatch Increased pulmonary shunt Decreased systemic oxygenation
Pulmonary hyper-insufflation	Bronchospasm Increased lung resistance Increased dead space
Parenchymal air–fluid levels	Rupture of abscess Soiling of healthy lung
Pleural effusion	Compression of pulmonary parenchyma Decreased lung compliance
Cardiac enlargement	Potential cardiac failure Potential pericardial effusion

In awake children in the lateral decubitus position, gravity causes a vertical gradient for pulmonary blood, and perfusion of the dependent lung is much greater than blood flow to the non-dependent lung (West's zone model). Simultaneously, the pleural pressure is greater in the dependent lung, thereby improving its own ventilation in comparison with that in the non-dependent lung: this allows a more favorable position on the compliance curve. In addition, abdominal contents exert more distension on the muscular fibers of the dependent diaphragm compared with that of the non-dependent diaphragm, result-

ing, on the basis of the Starling curve, in more efficient muscle contraction during spontaneous ventilation. For these reasons, ventilation and perfusion are preferentially distributed in the dependent lung without significant alterations in the ventilation:perfusion ratio.

In anesthetized children in the lateral decubitus position with a closed chest, pulmonary blood flow increases with lung dependency and is greater in the dependent lung. The induction of anesthesia decreases the FRC in both lungs, but certainly to a greater extent in the lower lung due to the weight of mediastinal and abdominal contents. The loss of FRC results in a decrease in compliance. This condition shifts ventilation away from the dependent lung to the upper, non-dependent lung. If the child is given neuromuscular blocking agents and submitted to mechanical ventilation, the muscular advantage of the dependent diaphragm is also eliminated, which subsequently favors the redistribution of ventilation in the upper lung. In anesthetized children in the lateral decubitus position, during two-lung ventilation, there is relatively good ventilation and reduced perfusion in the non-dependent lung due to the gravitational distribution of the blood flow. Conversely, the dependent lung is relatively hypoventilated while overperfused.

In anesthetized children in the lateral decubitus position with an open chest, the distribution of pulmonary blood flow is not affected, but the distribution of ventilation is increased in the upper lung. Because the chest wall and pleura are open, the total compliance of the non-dependent lung is reduced to that of the pulmonary parenchyma alone. The lower lung remains compressed by the chest wall, mediastinum and abdominal content. Thus, the non-dependent lung is overventilated and underperfused, whereas the dependent lung is underventilated and overperfused.

In anesthetized children in the lateral decubitus position with an open chest during one-lung ventilation, an obligatory transpulmonary shunt is created through the upper non-ventilated lung. Hypoxia may occur, mainly in the younger age groups. Hypoxic pulmonary vasoconstriction, which diverts blood flow away from the underventilated lung, minimizes ventilation:perfusion mismatch.

In anesthetized children in the lateral decubitus position submitted to thoracoscopy with CO_2 insufflation into the thoracic cavity, the lung is not completely excluded, but is constricted by CO_2 insufflation under positive pressure. This in the upper lung has a limited effect on the ventilation-perfusion relationship and intrapulmonary shunt with less possibility of hypoxia compared with one-lung ventilation condition. Hypercapnia may occur during thoracoscopic surgery, partly due to CO_2 absorption across the pleura, and partly because, even if lung exclusion is avoided, thoracoscopy brings about mechanical constriction of the pulmonary parenchyma, reducing tidal volume, FRC and total lung capacity. CO_2 insufflation and the increase in intrapleural pressure may cause serious cardiocirculatory effects that are directly proportional to the level of intrapleural pressure applied. The hemodynamic alterations are related to the decrease in preload, stroke volume cardiac output, the cardiac index and systemic arterial blood pressures.

In infants and very young children, it has been shown that ventilation is distributed preferentially to the uppermost lung. The chest wall of an infant is less firm than that in older children, and resting pleural pressure is closer to atmospheric pressure. Thus, in the lateral decubitus position, closure of the peripheral airways occurs in the dependent lung, and ventilation is distributed toward the uppermost lung. A further explanation is that, in smaller children, there is less cephalic displacement of the dependent hemidiaphragm by abdominal organs than in larger subjects. Thus, according to the Starling law, contraction is less forceful in the dependent lung compared with the upper hemidiaphragm, limiting the efficiency of ventilation in the dependent lung. Finally, the infant's small size results in a reduced hydrostatic pressure gra-

dient between the non-dependent and dependent lungs. Consequently, the favorable increase in perfusion to the dependent lung is reduced in infants [7].

In anesthetized children in the lateral decubitus position submitted to thoracoscopy with one-lung ventilation, a significant lack of balance emerges in the ventilation–perfusion relationship. With lung exclusion, a marked decrease in arterial oxygenation results from an increased intrapulmonary shunt due to the unventilated and collapsed upper lung. Ventilation is penalized, but there are only a few hemodynamic changes related to one-lung ventilation, causing a slight reduction in the preload, but without any major effects on cardiac output and systemic arterial pressures [8–11].

4.5 Anesthesiological Approach

The literature suggests that achieving a level of anesthesia which allows safe execution of the surgical procedure and which does not have significant effects on cardiorespiratory function, subjected to the pathophysiological changes mentioned above, is important [1, 5, 8].

Anesthetic techniques, the wide availability of drugs, and the accuracy of the monitoring of vital signs and subsequent treatment in the Intensive Care Unit provide a high level of security in conducting anesthesia. The anesthesiological approach for this type of disease includes: monitoring; anesthetic management; one-lung intubation; intraoperative ventilation; and the choice of drugs and locoregional anesthesia.

4.5.1 Monitoring

Standard intraoperative monitoring is invasive and non-invasive. Cardiovascular function is monitored by measuring the heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP). If indicated, a radial arterial catheter and central venous catheter (CVC) are placed for the invasive monitoring of blood pressure and central venous pressure (CVP), respectively.

Respiratory function is monitored by the monitoring of peripheral arterial oxygen saturation (SpO_2), end-tidal CO_2 ($ETCO_2$) and measurement of respiratory frequency, tidal volume (inspiratory and expiratory), minute volume as well as peak inspiratory pressure and mean airway pressure by means of a mechanical ventilator.

A new approach is used to measure cerebral oxygenation (using near infrared spectroscopy) to reduce the potential risks of neuro degenerative events caused by conventional intraoperative ventilation that influence intracranial pressure, cerebral blood flow and cerebral perfusion pressure [12]. The influence of positive end expiratory pressure (PEEP) on cerebral blood flow has not been demonstrated, whereas cerebral perfusion is known to be mean arterial pressure (MAP)-dependent, and suggests that cerebrovascular autoregulation may be altered. The hypocapnia associated with hypotension may cause neuronal cell death in the hyppocampus in neonate rabbits. Metabolic changes induced by hypocapnia may contribute to the apoptosis of neuronal cells.

Body temperature (BT), urine output and the inspiratory and expiratory concentration of volatile anesthetics is also monitored. In all patients, neuromuscular blockade is monitored by stimulating the ulnar nerve using the train-of-four pattern of stimulation.

4.5.2 Anesthetic Management

Techniques of inducing anesthesia include inhalation using halogenated gases or one of the various intravenous anesthetic agents (e.g., propofol, thiopental). With respect to inhalation anesthesia, sevoflurane at an increasing concentration from 1% to 8% is adopted in patients younger than 5 years.

In many cases, tracheal intubation is preceded by administration of fentanyl (2 μg/kg) and

facilitated by administration of atracurium besylate (0.4–0.5 mg/kg), or cisatracurium besylate (0.2 mg/kg), or vecuronium (0.06–0.08 mg/kg/). Depending on the age and surgical necessity, tracheal intubation is carried out with oral or nasal tracheal tubes (uncuffed in patients younger than 7 years, cuffed in patients older than 7 years) for two-lung ventilation or with devices to establish one-lung ventilation (double-lumen endotracheal tube, univent tube, bronchial blocker).

General anesthesia is maintained intravenously with propofol (9–12 mg/kg/h), whereas for children younger than 5 years it is maintained with sevoflurane (expired concentration, 1.5–3%); anesthesia is supplemented with fentanyl (1–3 μg/kg/h) or remifentanyl (0.3–1 μg/kg/min) and muscle relaxation is maintained with atracurium besylate (0.2-0.4 mg/kg/h) or cisatracurium besylate (0.1–0.3 mg/kg/h) or vecuronium (0.08–0.1 mg/kg/h). High doses of fentanyl or remifentanyl promote adequate anesthesia without interfering with cardiocirculatory stability. Residual respiratory depression is not a problem for these patients because most will need immediate postoperative respiratory assistance.

Intraoperative crystalloid infusion is 20 mL/kg during the first hour in patients under 3 years of age and 15 mL/kg for older patients. In the hours that follow, the infusion dose is 8–10 mL/kg/h for all patients. Extravascular or interstitial sequestration of fluid ("third space" fluid loss) can occur during surgery. Estimated third-space fluid deficits are replaced with iso-osmotic fluids at rates that are depenent upon the type of surgery (≈4 mL/kg). The infusion rate used is 1–2% dextrose in a polyelectrolyte solution or in a quarter-strength normal saline solution (0.2% NaCl) and lactated Ringer's solution [13, 14].

Two important clinical conditions need to be discussed regarding anesthetic induction: mediastinal masses and large lung cysts in contact with the airways.

A series of case reports have shown that children with anterior mediastinal masses may demonstrate severe cardiopulmonary compromise upon the induction of anesthesia, including cardiac arrest and death [15, 16]. The tumor may surround the large airways, the heart, and the great vessels, resulting in three types of intrathoracic compromise: compression of the tracheobronchial tree; compression of the pulmonary artery; and superior vena cava syndrome. Tracheal compression >50% of the cross-sectional area of the trachea on CT has been suggested for identification of a high-risk population. In these patients, anesthesia is preferably induced, thereby maintaining spontaneous respiration and tracheal intubation by topical administration of lidocaine (3–4 mg/kg) associated with flexible tracheobronchoscopic evaluation. Rigid bronchoscopy may be lifesaving in the event of tracheal or bronchial collapse under anesthesia [15–18].

In addition to mediastinal masses, some pulmonary diseases in neonatal and pediatric age groups characterized by large lung cysts compressing pulmonary parenchyma and the mediastinum and in contact with airways are at increased risk of rupture related to positive pressure ventilation. The literature suggests the induction of anesthesia maintaining spontaneous respiration without application of a positive pressure *via* a face mask and avoiding the use of N_2O. Some case studies have documented the use of positive pressure ventilation and the use of N_2O during the induction of anesthesia without major problems or complications. Under these conditions, however, intubation should be atraumatic by avoiding coughing and laryngeal reflexes, with topical administration of lidocaine (19–21).

4.5.3 One-lung Intubation

In thoracic surgery, the indication for one-lung ventilation is common and there are many devices to realize the procedures, which usually involve endoscopy. However, this is not always possible in the pediatric age group because the tracheal and bronchial dimensions are small and the devices too large. Endoscopic guidance is required for the entire procedure.

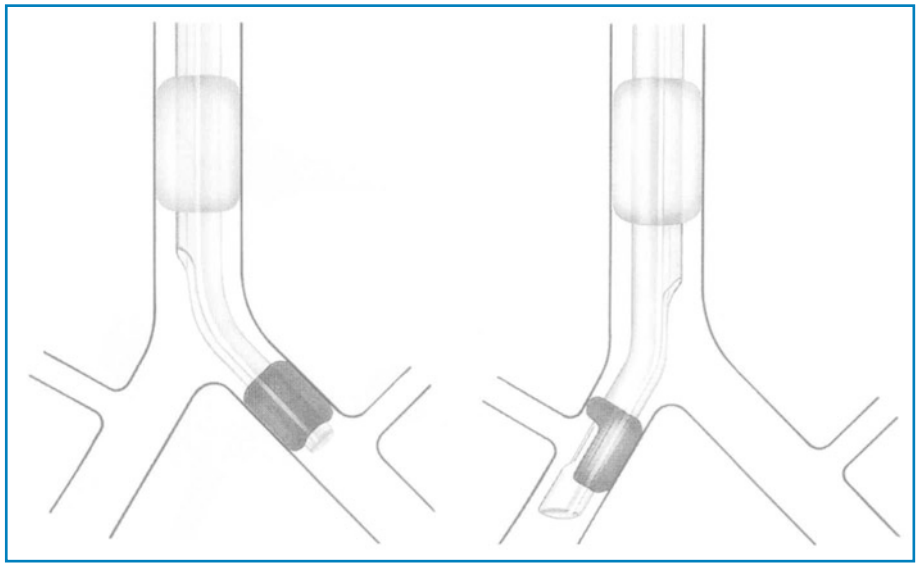

Fig. 4.1 Double-lumen tube (schematic)

Fig. 4.2 Univent tube

Single-lumen tubes are available from an internal diameter (ID) size of 2.5 mm for nasal or oral intubation, both uncuffed and low-pressure cuffed.

Double-lumen tubes: Paediatric sizes are available in 26 F, 28 F and 32 F, compatible for children aged between 6 and 8 years weighing >25 kg. These tubes have two independent lumina and two cuffs. The proximal lumen is tracheal, and the distal one is for selective intubation (Fig. 4.1). The fiberoptic endoscope verifies the correct position of the tube.

Univent tubes: The smaller size (ID, 3.5 mm/external diameter (ED), 7.5 mm) is useful for patients aged >6 years (Fig. 4.2) and is easy to manipulate. The blocker cuffed catheter is inserted into the wall of the single-lumen tube. The blocker catheter has a central channel for the aspiration of bronchial gases and secretions. A disadvantage of the univent tube is the large amount of cross-sectional area occupied by the blocker channel, especially in the smaller sized tubes.

Bronchial blockers with endotracheal tube (ET): Many years ago, a balloon-tipped catheter, such as a Fogarty or Swan–Ganz catheter (balloon sizes from 0.5 mL to 3 mL), was the only device for selective bronchus exclusion. Today, this catheter is used for neonates only under particular conditions. The Arndt blocker is available in different sizes and forms of balloons as a kit (Fig. 4.3). The

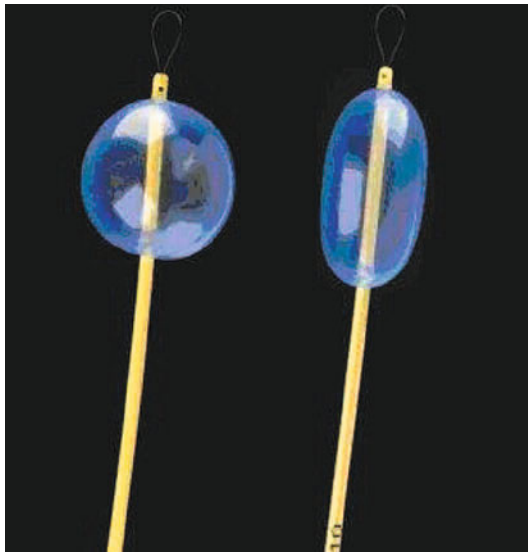

Fig. 4.3 Different balloons for the Arndt blocker

classic technique involves prior intubation with a tracheal single lumen tube, and then the blocker is placed under endoscopic guidance. A loop protruding from the distal end of the blocker channel, fixed on the endoscope tip (Fig. 4.4), is placed slowly and atraumatically into the desired bronchus. Alternatively, the bronchial blocker may be removed before the endotracheal tube. In any case, the flexible endoscope acts as a guide and, after verification of exclusion of the correct lung, is removed. The cuff may change its position during the surgical procedure and endoscopic control is necessary (22–24).

4.5.4 Intraoperative Ventilation

The aim of intraoperative ventilation techniques is to maintain normal levels of oxygenation and normocapnia. These techniques also aim to facilitate resection and avoid high pressure in the airways.

Bipulmonary mechanical ventilation for these patients reflects conventional intraoperative ventilation techniques. Initially, patients undergo mechanical ventilation using an oxygen/air mixture with an oxygen inspired fraction (FiO_2) between 0.35 and 0.50. The tidal volume (TV) is adjusted to 9–10 mL/kg and respiratory rate (RR) regulated based on the patient's age. The ratio of inspiratory time to expiratory time is usually 1:2. Positive end-expiratory pressure (PEEP) is set at 3–4 cmH_2O.

During lung exclusion or intrapleural insufflation, TV is reduced to 6–8 mL/kg, and

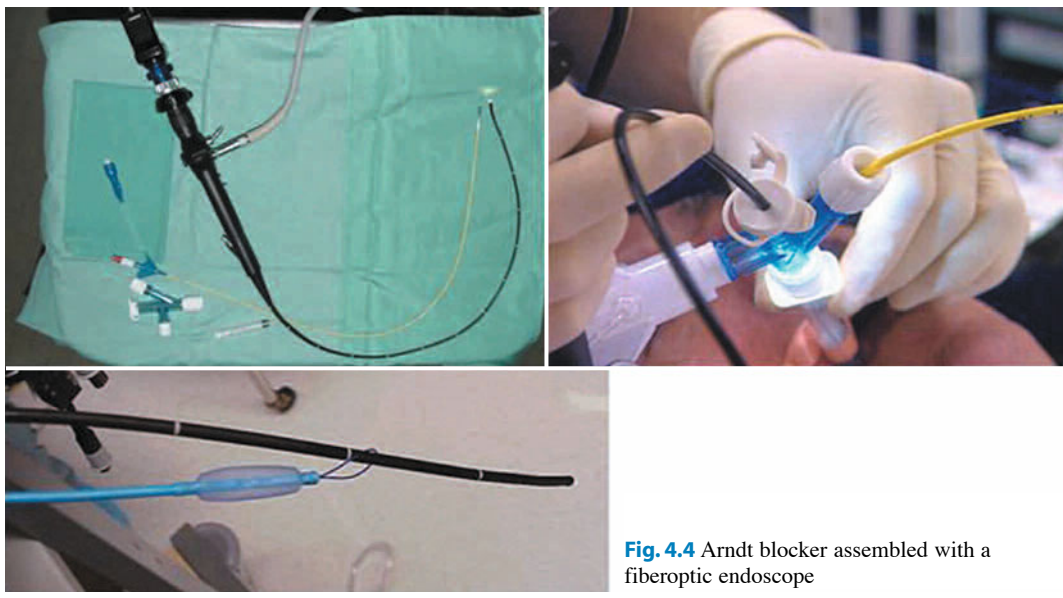

Fig. 4.4 Arndt blocker assembled with a fiberoptic endoscope

the RR increased by 20% compared with the RR recorded initially. The FiO_2 is increased to 0.7–0.9 and PEEP mantained. At the end of thoracic surgical procedure, the respiratory settings are returned to the previous conditions. Nitrous oxide is never used.

Hypoxia may commonly occur in the pediatric population, mainly during one-lung ventilation. The increase in FiO_2 is the principal maneuver allowing adequate oxygenation. Hypoxic pulmonary vasoconstriction is a secondary physiological mechanism that maintains oxygenation during one-lung anesthesia by restricting pulmonary blood flow to the non-ventilated lung. Management of one-lung ventilation should reduce to a minimum any condition that might directly vasodilate hypoxically constricted lung vessels, such as infection, infusion of vasodilator drugs, and certain anesthetics [1, 10]. Intravenous anesthesia does not influence pulmonary vasoconstriction, whereas isoflurane, desflurane and sevoflurane have been shown to have less impact on hypoxic pulmonary vasoconstriction than halothane. To limit their effects on oxygenation, inhalation agents should be used at the minimal alveolar concentration (MAC) or less [5, 13]. The level of intraoperative hypoxia can be reduced by delivering low-flow oxygen to the operated lung through a bronchial blocker with a distal port, or continuous positive airway pressure through a double-lumen tube [9, 11]. In case of refractory hypoxia, re-inflation of the non-ventilated lung should be considered.

Hypercapnia can occur partly because thoracic surgery brings about a mechanical constriction on the pulmonary parenchyma, reducing TV, FRC, total lung capacity and pulmonary compliance, and partly due to CO_2 absorption across the pleura during thoracoscopy [5, 10, 26]. Moreover, there is a general consensus on the method of allowing CO_2 to increase while reducing TV and minute ventilation to prevent alveolar overdistention or the propagation of lung injury [26–28]. Excessive airway pressures may increase pulmonary vascular resistance in the dependent lung and increase flow through the non-dependent lung. In all children undergoing thoracoscopy the lungs should be protected against high airway pressures during one-lung ventilation or two-lung ventilation with intrapleural insufflation by carefully balancing TV, RR, minute ventilation and $ETCO_2$ [5, 13, 14, 28].

In many studies, CO_2 showed the tendency to increase during the thoracic surgical procedure. The values observed, although sometimes higher than the norm, were nevertheless always within the ranges foreseen for moderate permissive hypercapnia [27, 29].

4.5.5 Thoracoscopic Implications

Video-assisted thoracic surgery (VATS) in children is being used with increasing frequency for various diagnostic and therapeutic procedures. Thoracoscopy in the pediatric patient reduces surgical trauma and minimizes postoperative morbidity. The advantages of thoracoscopy compared with open thoracotomy include decreased postoperative pain, shorter stay in hospital, more rapid return to normal activities, better cosmetic results and decreased incidence of chest-wall deformity [30, 31].

Thoracoscopic procedures in pediatric populations entail (just as in adults) surgical access after provoking lung collapse (at least partially). There are two methods of achieving this: (i) lung exclusion by one-lung ventilation (allowing the lung to collapse passively) and (ii) lung compression by CO_2 insufflation. The disease and age of the patient often influence the achievement of lung exclusion. Lung exclusion can be conducted with a double-lumen tracheal tube in children >6 years of age, whereas the same technique can be adopted in younger children with the help of bronchial blockers. By using the Arndt bronchial blocker we were able to achieve lung exclusion even in 1–2-year-old children [5, 13, 14, 22, 23]. Both methods are associated with severe respiratory and cardiocircula-

tory problems that have been studied extensively in adult patients, but to a lesser extent in children.

With lung exclusion a marked decrease in oxygenation results from an increased intrapulmonary shunt due to the non-ventilated and collapsed lung. While ventilation is penalized, there are only a few hemodynamic changes related to one-lung ventilation [5, 17, 32]. In a recent study, hypercapnia targeting CO_2 at 50–70 mmHg was associated with increased cardiac output, central venous O_2 tension and arterial O_2 tension in patients undergoing video-assisted thoracoscopic closure of patent ductus arteriosus using one-lung ventilation without deleterious cardiopulmonary effects [33].

With pleural insufflation the rise in pleural cavity pressure brings about notable hemodynamic effects that greatly decrease the preload, stroke volume, cardiac output and MAPs. Cardiovascular function is penalized in direct proportion to intrapleural insufflation, whereas respiratory parameters are only slightly compromised and hemogasanalytic changes are unremarkable. Pleural CO_2 insufflation brings about a fall in cardiocirculatory performance, which is generally well tolerated in the euvolemic patient with normal cardiac function. Limiting the insufflating pressure, a slow artificial pneumothorax, and optimization of cardiovascular function (by fluid administration or possible use of inotropic agents) can be useful to limit negative cardiocirculatory effects [5, 8, 13, 33–43].

4.5.6 Anesthetic Agents

Anesthetics can be inhaled or administered intravenously. Inhalational anesthesia is widely used, especially in children up to 4–5 years of age. Inhalational anesthesia is extremely adjustable for depth and reversibility, can be monitored fully and, in neonates, is often the procedure of choice. It also allows the induction of anesthesia while avoiding venous cannulation in a conscious child. The halogenated agent most used in children is sevoflurane. Intravenous anesthesia can also be used with good results, but the different pharmacokinetic characteristics present in the newborn, infant or child must be evaluated. Table 4.3 describes the drugs, anesthetics, analgesics and muscle relaxants most commonly used in children.

4.5.7 Locoregional Anesthesia

A combination of locoregional anesthesia with general anesthesia is particularly desirable in thoracic surgery. Various locoregional anesthetic techniques have been described, includ-

Table 4.3 Drugs used during thoracic anesthesia in pediatric age groups

Drug	Induction dose	Maintenance dose
Anesthetic agents		
Sevoflurane*	1–8% (2-3 MAC)	2–3% (1 MAC)
Thiopental	3–6 mg/kg	
Propofol	2.5–3 mg/kg	9–12 mg/kg/h
Opioids		
Fentanyl	1–2 μg/kg	1–3 μg/kg/h
Alfentanyl	7–15 μg/kg	0.5–1.5 μg/kg/min
Remifentanyl	0.5–1 μg/kg	0.3–1 μg/kg/min
Neuromuscular blocking agents		
Atracurium besylate	0.3–0.5 mg/kg	0.2–0.4 mg/kg/h
Cisatracurium besylate	0.15–0.25 mg/kg	0.1–0.3 mg/kg/h
Vecuronium	0.08–0.1 mg/kg	0.06–-0.08 mg/kg/h

*Sevoflurane is a halogenated gas. Its administration is related to the minimum alveolar concentration (MAC).

ing intercostal blocks, intrapleural infusions and epidural anesthesia. Of these, epidural anesthesia best facilitates intraoperative and postoperative analgesia. Epidural analgesia in pediatric age groups provides good pain relief after thoracotomy and its use may reduce stay in the ICU and hospital. Pain protection and the use of minimum efficacy doses of drugs are closely associated with the combined use of general and locoregional anesthesia in all pediatric age groups. Furthermore, the use of epidural analgesia may preserve pulmonary function and hasten postoperative mechanical ventilation in children with severe pulmonary diseases. An advantage of epidural catheters is that dose adjustments can be made postoperatively according to the level of comfort [44]. Nevertheless, in contrast to adults, locoregional anesthesia in children is characterized by remarkable hemodynamic stability, even if the level of the block reaches the thoracic dermatomes. In particular, limited cardiovascular modifications are observed with changes in patient positioning. This seems to be linked to two factors: the relatively small venous capacity in the lower extremities of children and the relative lack of resting sympathetic peripheral vascular tone. An indwelling epidural catheter can be inserted using caudal, lumbar or thoracic approaches.

The drugs used are local anesthetics and opioids for "top-up" boluses or continuous infusion. The binding of local anesthetics with plasma proteins (albumin and α-glicoprotein) is reduced in newborn and infants, and can result in accumulation of the drugs themselves, especially if a continuous infusion is planned, with potential toxic risks. The selected local anesthetics for pediatric techniques are left-handed enantiomers (levobupivacaine and ropivacaine) and this makes the technique safer. The association of local anesthetics with opioids allows the use of low doses of both. Morphine (which was once the most widely used opioid), owing to the increased incidence of respiratory depression, vomiting and itching, is now often replaced by fentanyl. When applying the epidural technique, the contraindications and possible complications should be considered [45–48].

4.6 Postoperative Intensive Care

Intensive postoperative treatment can be indicated in children after thoracic surgery. In addition to the preoperative features described above, postoperative treatment is based on intensive support and monitoring of vital signs, above all cardiorespiratory. The level of care consists of varied and tailored management. Table 4.4 outlines the main treatments that are undertaken in pediatric intensive care after thoracic surgery.

Table 4.4 Main treatments conducted in pediatric intensive care after thoracic surgery

Treatment	Methods and drugs
Mechanical ventilation	Conventional ventilation or HFOV until full recruitment of non-ventilated lung
Removing tracheobronchial secretions	Suction of bronchial secretions, fiberoptic bronchoscopy, chest physiotherapy
Early weaning from the ventilator	SIMV, PSV, CPAP, NIV
Sedation	Midazolam
Analgesia	Fentanyl, alfentanyl, remifentanyl, epidural analgesia
Cardiocirculatory support	Optimizing preload, cardioactive agents
Delivery of adequate nutrition	Parenteral and enteral nutrition
Prevention of infections	Microbiological monitoring, aseptic nursing maneuvers, antibiotics

HFOV, high-frequency oscillatory ventilation; *SIMV*, synchronized intermittent mandatory ventilation; *PSV*, pressure support ventilation; *CPAP*, continuous positive airway pressure; *NIV*, non-invasive ventilation.

A fundamental feature of intensive treatment is ventilatory assistance which, by recruiting the lung parenchyma penalized by intraoperative maneuvers, leads to the progressive autonomy of patients. Early respiratory weaning and extubation is safe and feasible in many patients, but this might not be possible in a significant minority. Several factors have been shown to contribute to delayed weaning from the ventilator. These include: preoperative factors (e.g., known chromosomal and neurological abnormalities); preoperative pulmonary malformations; airway problems; pulmonary disease; complexity of the surgical procedure; postoperative complications; and myocardial dysfunction.

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Operative Approaches to the Thorax

5

Steven S. Rothenberg

5.1 Introduction

The wide range of neonatal and pediatric chest pathology requires various approaches to manage these lesions surgically. Over the last 20 years there has been a huge shift in the approach to these lesions, with many now being addressed thoracoscopically. However, the use of this technique for more advanced procedures and for some tumors or masses is not widespread, and many of these lesions are approached using a standard open incision.

Depending on the type and location of the lesion, the approach and incision may vary widely. Lung lesions are usually approached *via* a lateral or posterolateral incision, as are several anterior and posterior mediastinal lesions. Some anterior mediastinal lesions are amenable to an anterior thoracotomy or Chamberlain procedure. Large anterior mediastinal masses may require a median sternotomy.

Mediastinoscopy can also give access to the anterior mediastinum, primarily for diagnostic procedures. However, this is a difficult skill to master safely, especially in the pediatric patient and, in most cases, thoracoscopy is a better and safer surgical approach. The pediatric surgeon should be familiar with all of these approaches and be able to choose and use the most appropriate incision for any particular lesion (Table 5.1).

Table 5.1 Traditional standard approaches to access the thoracic cavity

Lateral thoracotomy
Posterolateral thoracotomy
Anterior thoracotomy
Chamberlin procedure
Muscle-sparing procedures
Medianstinoscopy
Median sternotomy

5.2 Lateral or Posterolateral Thoracotomy

The most common and versatile incision is the posterolateral thoracotomy incision. It gives wide access to the entire chest cavity for pulmonary and extrapulmonary lesions. The advantages and disadvantages of this approach are listed in Table 5.2, but this incision is the choice for lung resections.

The patient is positioned in a lateral decubitus position and padded appropriately. In general, the surgeon stands at the back of the

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Table 5.2 Lateral or posterolateral thoracotomy

Advantages	Disavantages
Wide access to chest cavity	Difficult to access apex of chest
Easy access to anterior and posterior mediastinum and hilar structures	Division of large chest wall muscles
Can enter at variable interspaces	Painful
	Limited access between ribs

patient with the assistant at the front of the patient. This is reversed if the lesion is located in the posterior mediastinum.

The incision can start anywhere form the middle to anterior axillary line and then extends 1–2 cm below the tip of the scapula and then gradually curves upwards behind the scapula (Fig. 5.1). Dissection is then carried down through the subcutaneous tissue until the latissmus dorsi muscle is reached. The anterior border of the muscle crosses near the anterior third of the incision. In most cases, this muscle is then divided to provide access to the serratus anterior muscle and the appropriate interspace. The muscle should be divided as inferiorly as possible to preserve the innervation to the majority of the muscle. An alternative is to mobilize the anterior border of the latissimus dorsi muscle and retract it posteriorly to expose the serratus anterior muscle. The posterior border of the serratus anterior muscle is then easily visualized. The serratus anterior muscle can be divided, again inferiorly as possible, as necessary to expose the desired intercostal space. It may also be mobilized along its posterior border to allow for anterior retraction, again avoiding the division of the muscle (Fig. 5.2) This total muscle-sparing technique decreases the pain and recovery associated with formal thoracotomy, as well as the long-term morbidity of scoliosis, chest-wall deformity, and shoulder-girdle weakness, which are the comorbidities of this approach.

Once the rib cage is reached, the appropriate interspace is chosen. For most lung resections, this is the fourth or fifth interspace. If the lesion is in the apex of the chest or in the base, the interspace can be adjusted accordingly. Cautery is then used to score the periosteum longitudinally, in the middle, along the length of the lower rib. The periosteum is then stripped off the top half of the rib, thereby releasing the intercostal muscle from the rib. The pleura is then opened on the top of the rib and the incision extended along the top of the rib.

The interspace is then slowly widened and a chest retractor inserted. Attachments between the intercostal muscle and the lower rib are slowly released anteriorly and posteriorly as the space is gradually widened.

When the procedure is completed the ribs are re-approximated with 1–3 pericostal sutures which encircle the ribs and pull them back together. The fascia on the lower border of the intercostal muscle is then re-approximated to the periosteum of the rib using a running absorbable suture. The rest of the incision is closed in the appropriate layers.

As mentioned above, this incision is excellent for lung resections, decortications and pleurectomies, anterior and posterior mediastinal masses, and posterior procedures such as tracheoesophageal atresia repair or foregut duplications, and ligation of patent ductus arteriosus.

Some authors have advocated an axillary thoracotomy. In this case, the incision runs in the mid-axillary line longitudinally, but the mobilization and division of muscle is similar to the posterolateral incision. Some authors believe a longitudinal incision in the axilla is more cosmetically pleasing than the transverse one.

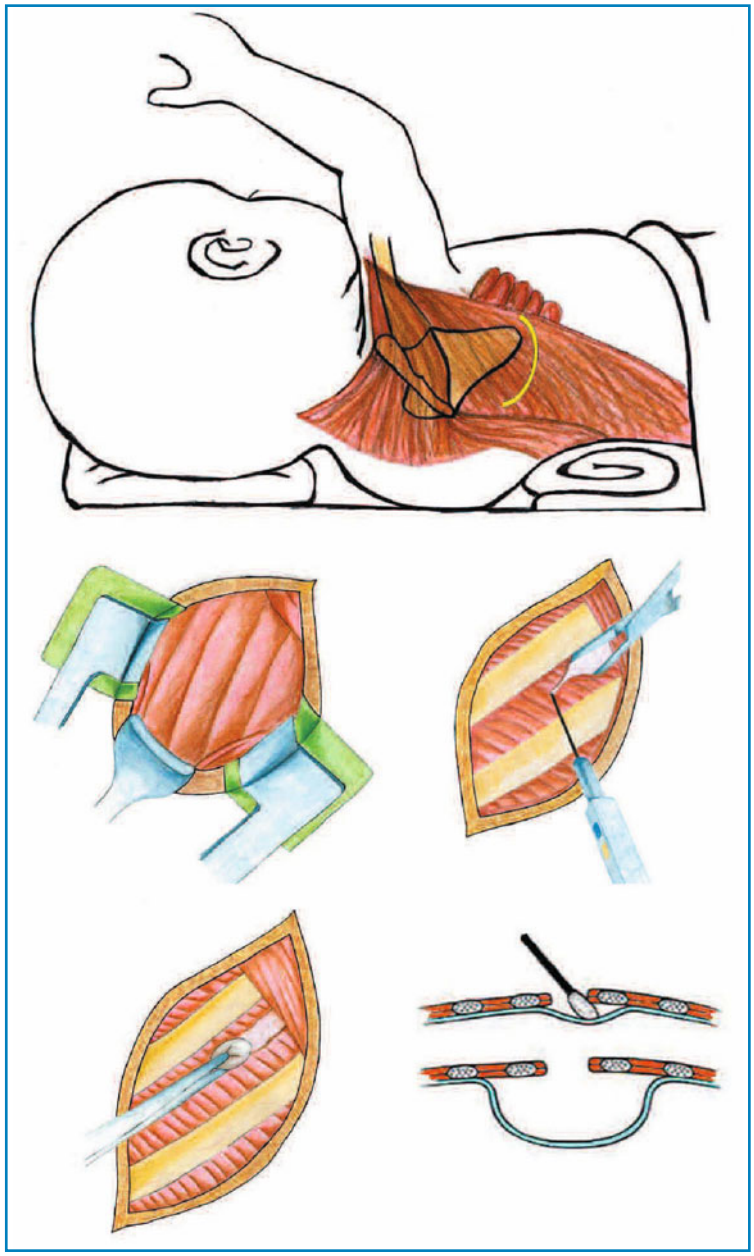

Fig. 5.1 Posterolateral thoracotomy

5.3 Anterior Thoracotomy (Chamberlain Procedure)

This incision is used primarily to biopsy anterior mediastinal masses. It is also used if an aortopexy is needed. The advantages and disadvantages are listed in Table 5.3. The patient is kept in the supine position. The chosen side may be elevated slightly with a roll under the back and shoulder if desired. The incision is made just lateral to the sternum, extending laterally to approximately the mid-clavicle. This is done over the third-to-fifth interspace (depending on the site of the mass (Fig. 5.3). The pectoralis muscle is divided. Then the intercostal muscle can be stripped off the lower rib as described above. If the lesion is in

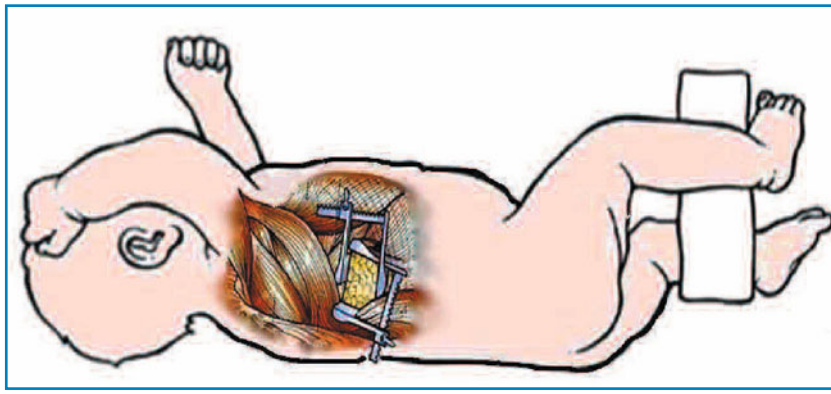

Fig. 5.2 Muscle-sparing thoracotomy

Table 5.3 Anterior thoracotomy (Chamberlain procedure)

Advantages	Disavantages
Limited incision	Limited exposure
Avoids complete division of muscle	Limited access
Access via interspace	
Decreased pain	
Access directly over pathology	

Table 5.4 Mediansternotomy

Advantages	Disavantages
Access to both chest cavities	Limited access to posterior mediastinum and lung surface
Less pain	Possibility of sternal non-union
Avoids bilateral procedures	lnjury to heart
? Quicker recovery	

the anterior mediastinum, an extraperitoneal approach can be used. If the lesion is in the pulmonary parenchyma or intra-pleural region, the pleura can be opened. The incision is closed in layers and in general a chest tube is not necessary after this approach.

5.4 Median Sternotomy

A median sternotomy is most often associated with open-heart procedures, but occasionally it is used in pediatric surgery for large anterior mediastinal tumors.

The advantages and disadvantages are listed in Table 5.4.

The patient is placed supine on the table. Occasionally a roll is placed in-between the shoulder blades to hyper-extend the chest. The incision extends in the midline from the sternal notch to the tip of the xiphoid process (Fig. 5.4). In general, cautery is used to separate the precoralis muscles in the midline and score the periosteum of the sternum. A combination of sharp and blunt dissection is then used to create a space at the top of the sternal notch, where the intraclavicular ligament is divided. A plane is then created behind the manubrium. This ma-

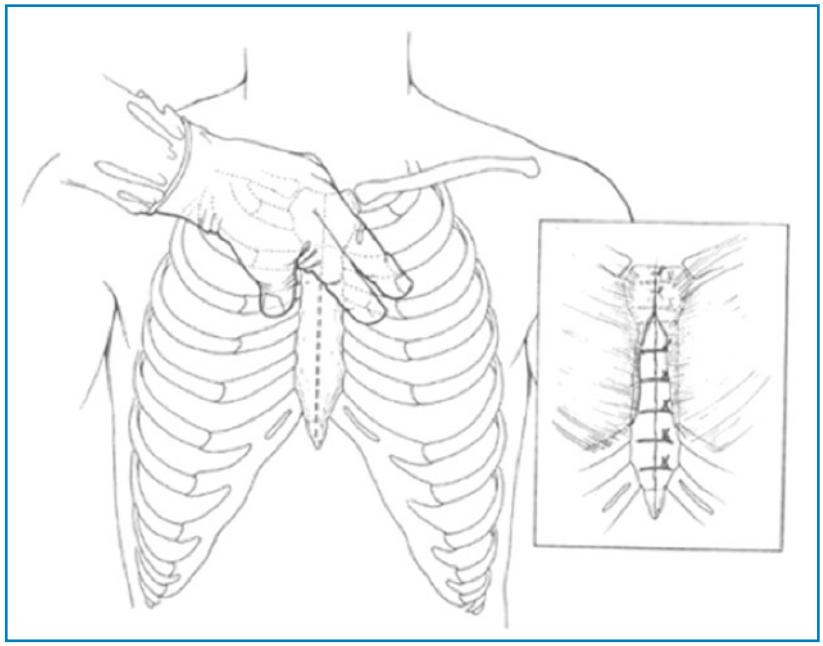

Fig. 5.3 Anterior thoracotomy

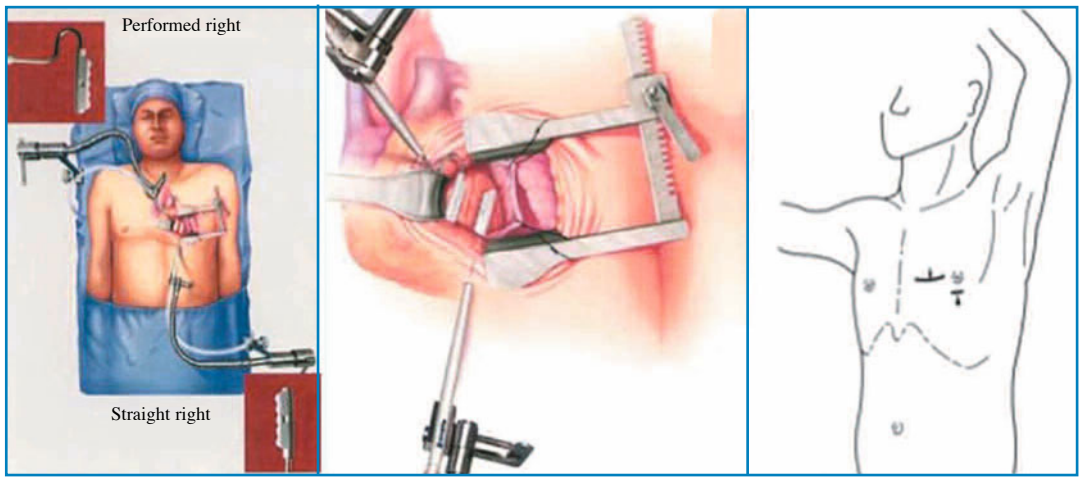

Fig. 5.4 Median sternotomy

neuver helps protect the innominate vein from injury during division of the sternum.

Inferiorly the tip of the xiphoid process is mobilized in a similar fashion and blunt dissection is used to create space behind the sternum. A saw or knife and then be used to split the sternum. There is usually some bleeding from the cut edges of the sternum but this is readily controlled with cautery. Once this is controlled, the sternal spreader is inserted and the edges retracted.

Once the procedure is completed, the edges are allowed to re-approximate. The sternum is then sutured together with sternal wire or a heavy-gauge suture. The rest of the incision is closed in layers.

Suggested Reading

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Thoracoscopy

6

Steven S. Rothenberg

6.1 Introduction

Thoracoscopy has been in use since the early 1900s but has undergone an exponential increase in popularity and growth since the early 1990s. The first experience in humans was reported by Jacobeus in 1910 and consisted of placing a cystoscope inserted through a rigid trocar into the pleural space to lyse adhesions and cause complete collapse of a lung as treatment for a patient with tuberculosis. He later reported the first significant experience with a series of >100 patients [1]. During the next 70 years, thoracoscopy gained some favor (primarily in Europe) for the biopsy of pleural-based tumors and limited thoracic explorations in adults. However, widespread acceptance was minimal [2, 3].

In the 1970s and 1980s, the first significant experience in children was reported by Rodgers et al. [4, 5]. Equipment modified for pediatric patients was used to carry out biopsies, evaluate various intrathoracic lesions, and undertake limited pleural debridement in cases of empyema [6]. During this same time period, there was increasing recognition of the morbidity associated with a standard thoracotomy (especially in small infants and children), including scoliosis, muscle-girdle weakness, and chest-wall deformity [7]: there was little acceptance or adoption of these techniques. This clear documentation of the effects of a thoracotomy on children led to attempts to minimize the morbidity by various muscle-sparing approaches, but all of these limited exposure and were still associated with large thoracotomy scars [8]. It was not until the early 1990s with the dramatic revolution in technology associated with laparoscopic surgery in adults that more advanced diagnostic and therapeutic procedures were undertaken in children [9-11]. The development of high-resolution microchips and digital cameras, smaller instrumentation, and better optics has enabled pediatric surgeons to carry out even the most complicated intrathoracic procedure thoracoscopically [12, 13]. Nowadays, every thoracic lesion from empyema to tracheoesophageal atresia has been approached and successfully managed using a thoracoscopic ap-proach, thereby dramatically reducing the pain, recovery, and long-term morbidity of these procedures.

6.2 Indications

There are a wide variety of indications for thoracoscopic procedures in children. The num-

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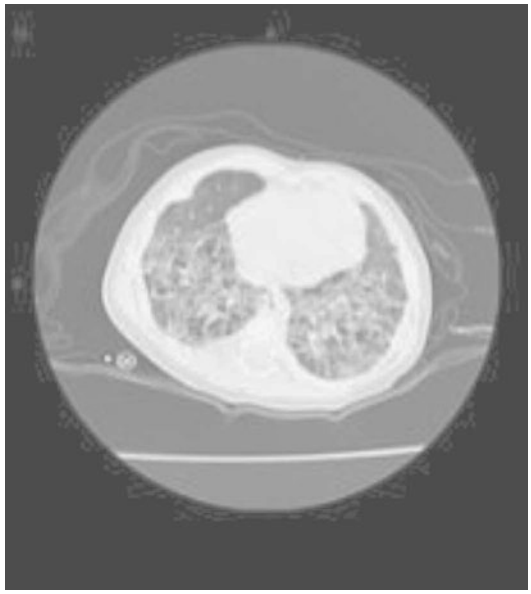

Fig. 6.1 CT scan of a patient with severe interstitial lung disease. The CT scan helps direct the biopsy

ber continues to expand with advances and refinements in technology and technique. Thoracoscopy is used extensively for lung biopsy and wedge resection in cases of interstitial lung disease (ILD) and metastatic lesions. More extensive pulmonary resections (including segmentectomy and lobectomy) are also being carried out routinely in many centers [14, 15]. Indications include resection for cavitary lesions, bullous disease, intra- and extralobar sequestrations, congenital lobar emphysema (CLE), cystic pulmonary adenomatoid malformations (CPAMs) and neoplasms. Thoracoscopy is also extremely useful in the evaluation and treatment of mediastinal masses. It provides excellent access and visualization for biopsy and resection of mediastinal structures such as lymph nodes, thymic and thyroid lesions, cystic hygromas, foregut duplications, ganglioneuromas, and neuroblastomas [16, 17]. Other advanced intrathoracic procedures such as decortication for empyema, closure of patent ductus arteriosus (PDA), repair of hiatal hernia defects, esophageal myotomy for achalasia, thoracic sympathectomy for hyperhydrosis, anterior spinal fusion for severe scoliosis, repair of congenital diaphragmatic hernia and, most recently, primary repair of esophageal atresia, have also been described in children [18]. The basic premise is that thoracoscopy provides better exposure because of the proximity and magnification that the optical system affords the surgeon. Couple this with the decreased morbidity associated with the minimal-access techniques, then thoracoscopy should be the preferred approach for nearly all pediatric thoracic procedures.

6.3 Preoperative Work-up

The preoperative work-up varies significantly depending on the procedure to be carried out [19]. Most intrathoracic lesions require routine radiographs as well as computed tomography (CT) or magnetic resonane imaging (MRI). A thin-cut, high-resolution CT is especially helpful in evaluating patients with ILD because it can be used to identify the most affected areas and help determine the site of biopsy. This is because the external appearance of the lung is usually not helpful (Fig. 6.1) [20]. CT-guided needle localization can also be used to direct biopsies for focal lesions which may be deep in the parenchyma and therefore not visible on the surface of the lung during thoracoscopy. This is usually done just prior to the thoracoscopy with the radiologist marking the pleura overlying the lesion with a small blood patch or dye [21, 22]. Intraoperative ultrasound may provide a more sensitive way for the surgeon to detect lesions deep to the surface of the lung and compensate for the lack of tactile sensation. Unfortunately, ultrasounf is still unreliable. MRI may be more useful in evaluating the vascular lesions or masses that can arise from or encroach on the spinal canal or in the form of vascular rings. These studies can be extremely important for determining patient positioning and initial placement of the port.

Another major consideration for the successful completion of most thoracoscopic procedures is whether or not the patient will tol-

erate single-lung ventilation, thus allowing for collapse of the ipsilateral lung to ensure adequate visualization and room for manipulation. Unfortunately, there is no specific preoperative test that will yield this answer. However, most patients (even those who are ventilator-dependent) can tolerate short periods of single-lung ventilation. This generally allows adequate time to carry out most diagnostic procedures such as lung biopsy. In cases in which single-lung ventilation cannot be tolerated, other techniques may be used (as discussed below).

6.4 Anesthetic Considerations

While single-lung ventilation is achieved relatively easily in adult patients using a double-lumen endotracheal tube, the process is more difficult in the infant or small child. The smallest available double-lumen tube is a 28 F, which, in general, cannot be used in subjects weighing <30 kg. Another option is a bronchial blocker. This device contains an occluding balloon attached to a stylet on the side of the endotracheal tube. After intubation, the stylet is advanced in the bronchus to be occluded, and the balloon is inflated. Unfortunately, size is again a limiting factor because the smallest blocker available is a 6.0 tube. For most cases in infants and small children, a selective mainstem intubation of the contralateral bronchus with a standard uncuffed endotracheal tube is effective. This can usually be done blindly without the aide of a bronchoscope simply by manipulating the head and neck. It is also important to use an endotracheal tube one-half size smaller then the anesthesiologist would pick for a standard intubation otherwise the tube may not pass into the mainstem bronchus (especially on the left side).

At times this technique will not lead to total lung collapse because there may be some overflow ventilation because the endotracheal tube is not totally occlusive. This problem is overcome by the routine use of a low-flow (1 L/min), low-pressure (4 mmHg) CO_2 insufflation during the procedure to help keep the lung compressed. If adequate visualization is still not achieved then the pressure and flow can be gradually increased until adequate lung collapse is obtained. Pressures of 10–12 mmHg can be tolerated for short periods of time without significant respiratory or hemodynamic consequences in most cases. This requires the use of a valved trocar rather than a non-valved port (Thoracoport™). This technique can also be used on patients who cannot tolerate single-lung ventilation. By using small tidal volumes, lower peak pressures, and a higher respiratory rate, sufficient lung collapse can be achieved to allow for adequate exploration and biopsy. In neonates with tracheoesophageal fistulae or other congenital malformations, CO_2 alone can be used to deflate the lung. Once the lung is collapsed, it will stay that way until the anesthesiologist makes a conscious effort to re-expand it. The surface tension of the collapsed alveoli in the newborn keeps the lung collapsed without excessive pressures being used.

This technique is also useful if bilateral procedures are being done, such as in the case of sympathectomy [23]. A slight tension pneumothorax gives adequate exposure to visualize the sympathetic chain without the need for changing which lung is isolated. Whatever method is used, it is imperative that the anesthesiologist and surgeon have a clear plan and good communication to prevent problems with hypoxia and excessive hypercapnia, and to ensure the best chance of having a successful procedure [24].

6.5 Patient Positioning

Positioning depends on the site of the lesion and type of procedure. Most open thoracotomies are done with the patient in the lateral decubitus position. Thoracoscopic procedures should be carried out with the patient in a position that allows for the greatest access to the areas of interest and which uses gravity to aid the uninvolved lung (or other tissue) out of the field of view.

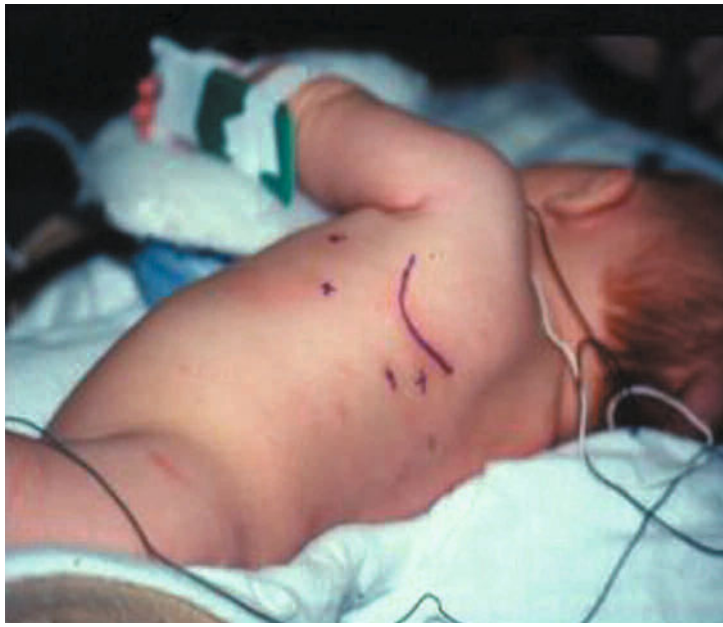

Fig. 6.2 The patient is positioned in a lateral decubitus position for a thoracoscopic lung resection

For routine lung biopsies or lung resections, the patient is placed in a standard lateral decubitus position (Fig. 6.2). This position provides for excellent visualization and access to all surfaces of the lung. It is also the most beneficial setup for decortications, pleurodesis, and other procedures in which the surgeon may need access to the entire pleural or lung surface. For anterior mediastinal masses, the patient should be placed supine with the affected side elevated at 20–30° (Fig. 6.3). This allows for excellent visualization of the entire anterior mediastinum while allowing gravity to retract the lung posteriorly without the need for extra retractors. The surgical ports may then be placed between the anterior and mid-axillary lines to give clear access to the anterior mediastinum. This position should be used for thymectomy, aortopexy, or biopsy/resection of anterior tumors or lymph nodes. For posterior mediastinal masses, foregut duplications, esophageal atresia, and work on the esophageal hiatus, the patient should be placed in a modified prone position with the affected side elevated slightly (Fig. 6.4). This maneuver allows for excellent exposure without the need for extra retractors. The patient can then be placed in the Trendelenburg or reverse Trendelenburg position as needed to help keep the lung out of the field of view.

Once the patient is positioned and draped appropriately, the monitors can be placed in position. For most thoracoscopic procedures it is advantageous to have two monitors, one on either side of the table. The monitors should be placed between the shoulders and hips of the patient depending on the site of the lesion. The goal as always with endoscopic procedures is to keep the surgeon in line with the camera, in line with the disease, and finally with the monitor. This allows the surgeon to work in the most efficient and ergonomic way. In some cases such as decortication, the field of interest may change constantly. In this case, the monitors should be placed at shoulder level and moved as necessary.

Most procedures can be undertaken with the surgeon and one assistant. The surgeon should stand on the side of the table opposite the area to be addressed so that he/she can work in line with the camera as the procedure is completed.

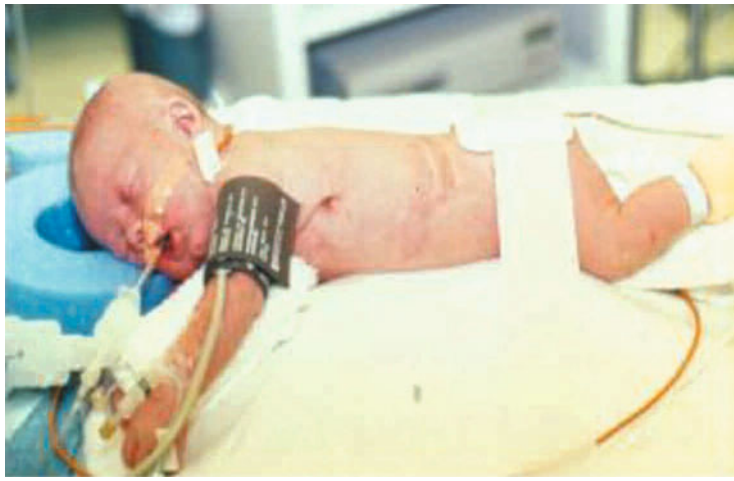

Fig. 6.3 The patient is placed in a modified prone position for a thoracoscopic procedure in the posterior mediastinum, such as a TOF repair

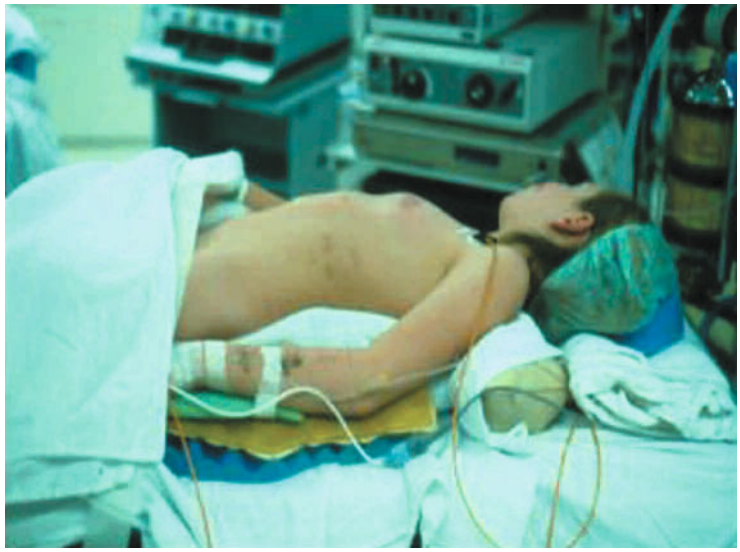

Fig. 6.4 The patient is in a modified supine position for a procedure in the anterior mediastinum

In most cases, it is preferable to have the assistant on the same side of the table as the surgeon so that he/she is not working against the camera because he/she is responsible for operating the camera and providing retraction as necessary (Fig. 6.5). This concept is even more important if the field of dissection is primarily on one side. Cases such as a mediastinal masses, esophageal atresia, or more complicated lung resections require greater surgical skill. It is imperative that the surgeon and assistant are working in line with the field of view to prevent clumsy or awkward movements. In cases such as decortication, in which the field of view and dissection are constantly changing and most movements are relatively gross, having the surgeon and assistant on opposite sides of the table is appropriate and may actually expedite the procedure.

6.6 Trocar Placement

Positioning of the trocars varies widely with the procedure and the site of the lesion. Thoughtful positioning of the trocars is more

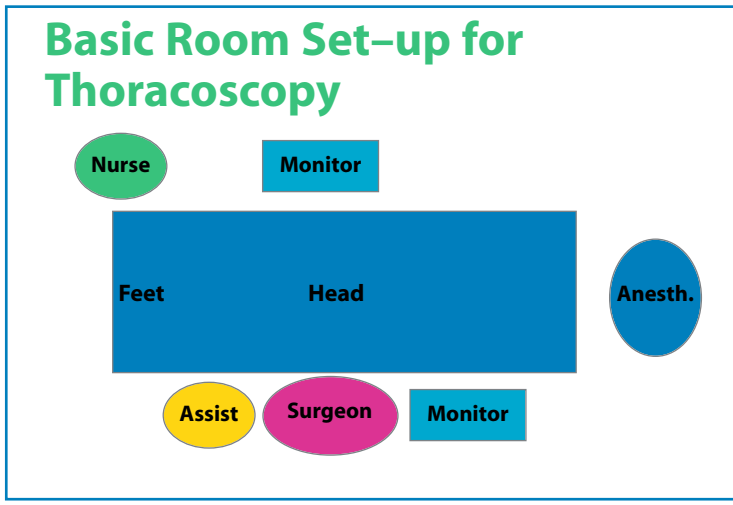

Fig. 6.5 Diagram of the basic room set up for thoracoscopic procedures

important than with laparoscopic surgery because the chest wall is rigid, and therefore the mobility of the instruments will be restricted as compared with surgery in the abdomen. The most common procedures, such as lung biopsy for ILD or decortication for empyema, may require wide access to many areas in the thoracic cavity. Therefore the ports are placed in such a fashion as to facilitate this. However, this may result in some degree of paradox during parts of the procedure. Other procedures are directed toward a very restricted area and therefore the trocars are placed to allow for the best visualization and access to a specific spot. In general, the camera port should be placed slightly above and between the working ports to allow the surgeon to look down on the field of view (much as in open surgery). This will also minimize instrument dueling, which can be a significant problem in smaller infants.

For example, with lung biopsies the trocars should usually be placed between the fourth and eighth intercostal space. The camera port is usually in the mid-axillary line at the fifth or sixth interspace. If an endoscopic stapler is being used, it requires a 12-mm port and therefore should be placed in the lowest interspace possible (especially in smaller children) because these are the widest and better able to accommodate the larger port. If the lesion is anterior, it should be positioned closer to the posterior axillary line and *vice versa*. This is to allow the greatest amount of space between the insertion in the chest wall and the lesion because the working head of the stapler requires ≥45–50 mm of space. The third or "grasping" port is placed closer to the lesion and provides traction on the lesion during biopsy. This arrangement allows the surgeon, camera, and primary working port to be in line with the area to be biopsied. The mid-axillary port should be placed first to allow for modification of the other two ports once an initial survey of the chest cavity has been completed. A triangular arrangement of the trocars has also been recommended because it allows for rotation of the telescope and instruments between the three ports, giving excellent access to all areas. However, the surgeon can find himself/herself working against the camera, a situation which can make the simplest procedure very difficult. Also, especially in children, the number of large ports should be limited. Therefore, careful planning should go into port placement to limit the number and size of ports needed. In general, trocar placement can be planned tentatively based on preoperative imaging studies and then modified once the initial trocar is placed.

6.7 Instrumentation

The equipment used for thoracoscopy is basically the same as that used for laparoscopy. In general, 5- and 3-mm instrumentation is of adequate size, so 5-mm and smaller trocars can be used. In most cases, valved trocars are used for the reasons discussed above.

The basic equipment should include 5-mm 0° and 30° lenses (most procedures are best done with a 30° lens). If procedures are being carried out in smaller children and infants, it is also helpful to have smaller lenses such as a short (length, 16–18 cm), 3- or 4-mm-diameter 30° scopes and specially designed shorter instruments (18–20 cm). These tools enable the surgeon to carry out much finer movements and dissection, allowing advanced procedures to be done in infants weighing as little as 1 kg. A good-quality digital camera and light source are also extremely important to allow for adequate visualization (especially when using smaller scopes, which transmit less light). The basic instrumentation should include curved dissecting scissors, curved dissectors, atraumatic clamps (i.e., 3- and 5-mm atraumatic bowel clamps), fan retractors, a suction/irrigator, and needle-holders. Disposable instrumentation which should be available includes hemostatic clips, endoloops (pre-tied ligatures) and an endoscopic linear stapler. The linear stapler is an endoscopic version of the GIA™ used in open bowel surgery. It lays down 6–8 rows of staples and divides the tissue between them, providing an air- and watertight seal.

This is an excellent tool for carrying out wedge resections of the lung, but unfortunately its size requires placement of a 12-mm trocar, precluding its use in patients weighing <10 kg because of the limited size of their thoracic cavity. Several energy sources are available that provide hemostasis and divide tissue. These include monopolar and bipolar cautery, ultrasonic coagulating shears, and LigaSure™ (Covidien), all of which can be helpful in difficult dissections. It is also helpful to have one of the various tissue glues available for sealing lung and pleural surfaces.

6.8 Postoperative Care

Postoperative care is straightforward in most patients. After biopsy or limited resection, most patients can be admitted directly to the surgical ward with limited monitoring (i.e., a pulse oximeter for 6–12 h). These patients are, in general, 24-h observation candidates and several are ready for discharge the same evening. If a chest tube is left *in situ*, it can usually be removed on the first postoperative day. Pain management is not a significant problem. Local anesthetic is injected at each trocar site prior to insertion of the trocar and then 1–2 doses of narcotic (i.v.) given in the immediate postoperative period. By that evening or the following morning, most patients are comfortable on codeine (p.o) or acetametaphine (p.o.) It is very important, especially in patients with compromised lung function, to start early with aggressive pulmonary toilet. The significant decrease in postoperative pain associated with a thoracoscopic approach results in much less splinting and allows for more effective deep breathing. This has resulted in a decrease in the number of episodes of postoperative pneumonia and other pulmonary complications.

6.9 Conclusions

Recent advances in technology and techniques in endoscopic surgery have dramatically altered the approach to intrathoracic lesions in the pediatric patient. Most procedures can now be done using a thoracoscopic approach with marked decrease in the associated morbidity. This has allowed for an aggressive approach in obtaining tissue for diagnostic purposes in cases of ILD or questionable focal lesions in immunocompromised patients without the fear of significant pulmonary complications previously associated with conventional thoracotomy. In general, a lung biopsy can now be done with little more morbidity than a transbronchial biopsy, yet the tissue obtained is far superior. The same is true for mediastinal

masses or foregut abnormalities. Patients undergoing limited biopsy can have the procedure the same day, and lesions such as esophageal duplications can be excised thoracoscopically with the patient ready for discharge the next day. Even patent closure of ductus arteriosus is now carried out safely thoracoscopically with hospitalization of <24 h. A thoracoscopic approach may not always result in a significant decrease in hospital stay, but it may result in a significant decrease in the overall morbidity for the patient. For example, in subjects with severe scoliosis patients, thoracoscopic anterior spinal fusion results in earlier extubation, a reduced stay in the Intensive Care Unit and, in general, earlier mobilization. Thoracoscopic surgery has clearly shown significant benefits over conventional open thoracotomy in many cases. With continued improvement and miniaturization of equipment, the procedures we can carry out and the advantages to the patient should continue to grow.

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Part II

Esophagus

Diagnostic Techniques in the Esophagus

7

Barbara Bizzarri, Alessia Ghiselli, Alessandro Fugazza and Gian Luigi de' Angelis

7.1 Introduction

Even in the pediatric age group many diseases can affect the esophageal tract. The only procedure that permits direct visualization of the esophageal mucosa is upper endoscopy. Upper gastrointestinal (GI) endoscopy is employed widely not only for diagnostic but also for therapeutic purposes. This technique allows biopsy collection, which permits confirmation of conditions such as inflammation or infection [1]. Moreover, it permits therapeutic interventions such as dilations, sclerotherapy, endoscopic band ligation, and extraction of foreign bodies.

In these last 20 years, a new technique, endoscopic ultrasound (EUS) has been introduced to evaluate not only the wall of the upper or lower GI tract but also structures or organs in the immediate proximity of it. This is possible because EUS combines two modalities: endoscopic visualization and high-frequency ultrasound. The GI wall appears as a series of definable layers that corresponds to histological findings. EUS has a diagnostic and surgical role in the evaluation of GI diseases. In fact, it is possible to guide fine needles precisely through the gut wall into the surrounding structures [2].

7.2 Preparation and Technique of Endoscopy

With regard to fasting before upper GI endoscopy, the American Society of Anesthe-siologists advises not consuming: clear liquid for 2 h, breast milk and from formula for 4 h, as well as non-human milk and solids for 6 h before elective sedation. In emergencies, the risks of sedation without appropriate fasting must be evaluated after consideration of the necessity of the procedure and the expected benefit *versus* the risks [3].

The American Heart Association recommends antibiotic prophylaxis for bacterial endocarditis for patients with complex cyanotic congenital heart disease undergoing high-risk procedures (e.g., upper GI endoscopy with sclerotherapy and dilation of strictures) but it is not recommended for routine endoscopy with or without biopsy [4].

Before upper GI endoscopy, it is mandatory to obtain informed consent from parents or legal guardians if the patient is under 18 years old. Medical history, medication history, allergy assessment, age and weight must also be recorded. Physical examination (including a

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focused airway examination) should be done to reduce the complications of deep sedation in children because hyper-reactive airways are observed during and for several weeks after upper respiratory infections [5]. Moreover, if surgery is being considered, the hematocrit must be evaluated, coagulation assays carried out and blood grouping must be done in case transfusion is required in the case of hemorrhagic complications.

Preparation for upper GI endoscopy may differ from that seen in adults. A topical anesthetic spray in the pharynx of a young infant is avoided and bite blocks are usually not required in edentulous infants. Intubation of the esophagus has to be done under direct visualization [6, 7].

There is no standard practice for anesthesia in children undergoing GI endoscopy. Sedation for upper GI endoscopy can vary from conscious sedation with benzodiazepines (e.g., midazolam) to deep sedation with propofol to general anesthesia with orotracheal intubation. General anesthesia should be considered necessary for highly complicated procedures such as removal of foreign bodies and for patients at high risk for cardiovascular complications [8]. During endoscopy, baseline vital signs (heart rate, oxygenation) should be monitored and routine oxygen administration provided because of higher oxygen consumption in children, with consequent oxygen desaturation [9].

7.3 Indications for Upper GI Endoscopy

The indications for upper GI endoscopy in the pediatric population are based on guidelines set by the North American Society for Pediatric Gastroenterology and Nutrition in 1996. With respect to esophageal disorders, Squires et al. stated that diagnostic upper GI endoscopy is indicated: in active, persistent or recurrent bleeding in the GI tract (especially to differentiate between non-variceal and variceal bleeding); in dysphagia; in odynophagia; if there is a persistent refusal to eat; in persistent chest pain; if known or suspected ingestion of a caustic material has occurred; if there is persistent vomiting of unknown cause.

Conversely, upper GI endoscopy is not indicated for uncomplicated gastroesophageal reflux, uncomplicated functional abdominal pain, or radiographic findings of uncomplicated gastroesophageal reflux. Upper GI endoscopy is contraindicated for a perforated viscus. Sequential or periodic upper GI endoscopy may be indicated for surveillance for Barrett's esophagus (BE) as well as for the follow-up of: certain types of ulcers; mucosal abnormalities if they are likely to alter management; the adequacy of prior sclerotherapy or other variceal treatment.

Endoscopy can also have a surgical role. It can be indicated: for sclerotherapy or banding of esophageal varices; during or after a bleeding episode; for dilation; for treatment of persistent bleeding that is unresponsive to medical therapy; for removal of foreign bodies in the esophagus. or emergently for button batteries. Endoscopy is not indicated for sclerotherapy or banding of esophageal varices before the first documented variceal bleed [10].

7.4 Clinical Features of Esophageal Disease

7.4.1 Foreign Bodies in the Esophagus

Infants put almost everything into their mouths, and toddlers eat just about anything. Most foreign-body ingestions occur in children between the ages of 6 months and 3 years [11]. Fortunately, most foreign bodies pass spontaneously. Only 10–20% of subjects will require endoscopic removal, and <1% require surgical intervention [12]. Although mortality from foreign-body ingestion is extremely low, deaths have been reported [12, 13].

Most children with esophageal foreign bodies tell their parents of the ingestion, or the ingestion is witnessed by the parents or report-

ed to them. In these settings, they are often asymptomatic [14, 15]. If symptoms occur, they are often related to the location of the foreign body. Older children may localize the sensation of something "stuck" to the neck or lower chest, suggesting irritation in the upper or lower esophagus, respectively. Patients of any age may present with refusal of feeding or dysphagia, drooling, or respiratory symptoms (including wheezing, stridor, or choking). Esophageal foreign bodies tend to lodge in areas of physiological narrowing, such as the upper esophageal sphincter (cricopharyngeus muscle), the level of the aortic arch, and the lower esophageal sphincter [14]. Objects that appear in the middle portion of the esophagus are more likely to represent esophageal disease, such as a stricture. Similarly, children presenting with impaction of a food bolus commonly have underlying esophageal disease (e.g., a stricture) that is directly responsible for the impaction [16]. Previous surgery or congenital malformations (e.g., tracheoesophageal fistula) pose an increased risk as sites for obstruction. Longstanding esophageal foreign bodies may cause weight loss or recurrent aspiration pneumonia. They also can damage the mucosa and lead to strictures, or erode the esophageal wall, creating a fistula with the trachea or other nearby structures. Sharp objects may perforate the esophagus, resulting in neck swelling, crepitus, or pneumomediastinum.

Careful history-taking and physical examination are the keystones for diagnosing an esophageal foreign body and for the prevention of its complications [17]. Imaging is used to confirm the findings and to localize the site of the foreign body. Urgent intervention is indicated if any of the following warning signs are present:

- the ingested object is sharp, long (>5 cm), consists of multiple magnets, and is in the esophagus or stomach;
- a disk battery is in the esophagus (and in some cases in the stomach);
- there are signs of airway compromise;
- there is evidence of near-complete esophageal obstruction (e.g., patient cannot swallow secretions) [18].

For blunt foreign bodies without the characteristics shown above that are lodged in the esophagus in an asymptomatic patient, observation for 12–24 h is reasonable because spontaneous passage often occurs [19, 20].

Objects lodged for >24 h or for an unknown duration should be removed promptly. After this period, complications are more likely to occur. Flexible endoscopy is preferred in most circumstances because the foreign body can be directly visualized and manipulated, and the surrounding GI tract can be examined for potential complications [21–23].

This procedure is undertaken under conscious sedation or general anesthesia depending upon the patient's age, ability to cooperate, as well as the type and number of objects to be removed. The endoscopist should have a complete array of equipment to grasp the foreign object: rat-tooth forceps, alligator forceps, polyp snare, retrieval net, and helical baskets. It is helpful to practice grasping a duplicate of the foreign body using the retrieval tools before beginning the procedure. A foreign body protector hood is the preferred method of protecting the esophagus if the object is sharp or pointed [24].

Coins are by far the most common foreign body ingested by children [25]. A small percentage of ingested coins become lodged in the esophagus, and these can cause serious complications (including aspiration) if they are not removed [26]. If a coin is visualized in the esophagus and the patient is asymptomatic, the child can be observed for ≤24 h after ingestion of the coin. In such patients, 20–30% of coins will pass into the stomach spontaneously during the observation period (two-thirds of these during the first 8 h). The esophageal coin should be removed promptly if the patient is symptomatic or if the time of ingestion is not known (Fig. 7.1). If the child is asymptomatic and the coin does not pass spontaneously by 24 h after ingestion, it should be removed.

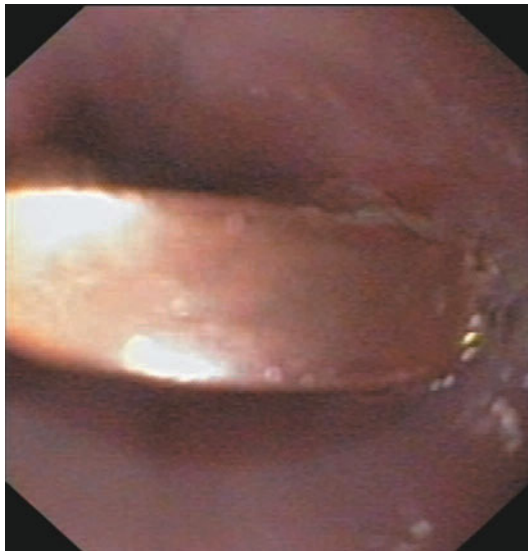

Fig. 7.1 Coin in the proximal esophagus

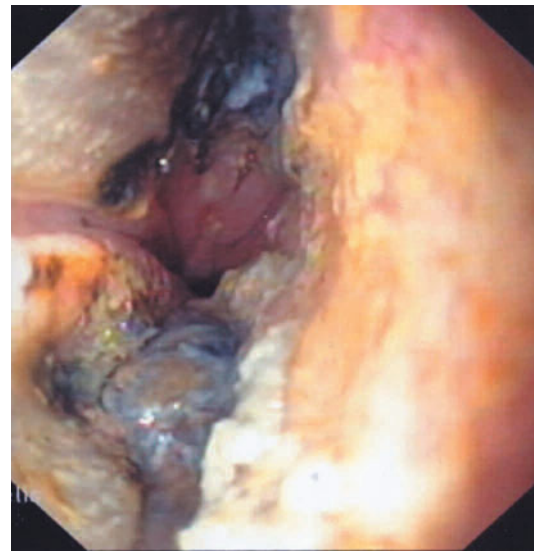

Fig. 7.2 Esophageal necrosis after button battery ingestion

Disk or "button" batteries: The number of ingestions of disk or button batteries is increasing substantially [27] and this is a medical emergency. In addition to direct-pressure necrosis, contact of the flat esophageal wall with both poles of the battery results in the conduction of electricity, resulting in liquefaction necrosis and perforation of the esophagus (Fig. 7.2). Retained batteries also can cause problems through leakage of caustic material (batteries contain a heavy metal such as mercury, silver and lithium, as well as a strong hydroxide of sodium or potassium) [28].

Sharp-pointed objects: The most common sharp-pointed objects ingested by children are straight pins, needles (Fig. 7.3) and straightened paper clips. Sharp-pointed objects lodged in the esophagus represent a medical emergency because of a high risk of perforation (15–35%). If the object is in the esophagus, it should be removed immediately. Endoscopic retrieval of sharp objects is accomplished with use of retrieval forceps or polypectomy snares [29]. The risk of mucosal injury during retrieval of a sharp object can be minimized by orienting the object with the sharp-end trailing during extraction and using a foreign body protector hood on the end of the endoscope or (in older children) an overtube [17].

Impacted meat or other types of food bolus are relatively rare in children. They usually present as dysphagia that begins acutely while eating. In children presenting with food impaction, there is a higher incidence of underlying esophageal pathology (strictures, achalasia, esophageal motility disorders) as compared with children with other esophageal foreign bodies [30]. Reflux esophagitis and eosinophilic esophagitis (EE) also predispose to food impaction [30, 31]. The optimal approach to removal of a food bolus depends on the location and consistency. Some authors find that polypectomy snares or retrieval nets fitted to the end of the endoscope are valuable for removal of a food bolus. The food bolus can be removed *en bloc* or in a piecemeal fashion. Once reduced in size, the bolus may be gently pushed into the stomach using the tip of the endoscope. Because food impaction is often caused by an underlying mucosal abnormality such as esophagitis or strictures, esophageal mucosal biopsies are recommended at the time of endoscopic dis-impaction [32].

Ingestion of magnets has become a serious health hazard in children [33–35]. Two or

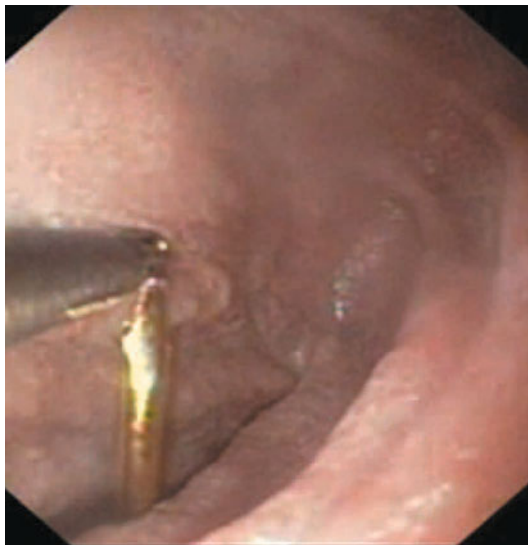

Fig. 7.3 Nail in duodenum

more strong magnets may attract across layers of bowel, leading to pressure necrosis, fistulas, volvulus, perforation, infection, or obstruction; this may result in serious consequences (including intestinal resection). Suspected magnet ingestion requires urgent evaluation. Radiographs of the neck and abdomen should be conducted (including a lateral view). Management depends on the timing, location, type and number of magnets, but magnets in the esophagus or stomach should be promptly removed *via* endoscopy.

Objects with high lead content: Acute lead toxicity may occur in children ingesting objects with high lead content, including lead weights used for fishing ("sinkers"), curtain weights, air-rifle pellets, and some toys or medallions. Objects suspected to have high lead content should be removed from the esophagus or stomach as quickly as possible. Use of proton pump inhibitors (PPIs) may decrease the dissolution of lead [36].

7.4.2 Caustic Ingestion

In infants and children, caustic ingestion is usually accidental, whereas in adolescents and adults it is usually deliberate. In ≈90% of cases the ingestion occurs at home and the exposure is to a single substance [37]. The literature suggests that household bleach accounts for 30–40% of caustic ingestions, laundry detergents for 20%, and acids and alkalis from cleaning products (e.g., oven, toilet, tile, drain) account for ≥50% [38, 39]. Caustic ingestion can cause severe damage to the esophageal mucosa, and the extent and the severity of the damage can depend upon the: type of caustic agent; amount and concentration of ingested caustic material; duration of contact between the mucosa and caustic agent [40, 41].

Alkalis cause liquefaction necrosis with deep penetration into the wall, and this can lead to perforations. Acid ingestion can cause coagulation necrosis, which limits the extent of penetration because the coagulum on the mucosal surface can limit the penetration of the caustic substance into the wall [42]. There is no correlation between the presence or absence of symptoms and the severity of injury to the GI tract, but an increased number of symptoms correlate with a greater likelihood of significant injury [43].

Also, the presence or absence of oral lesions does not correlate with esophageal injury. The most common symptoms are dysphagia, drooling, feeding refusal, retrosternal pain, abdominal pain and vomiting [37]. Symptoms involving the airway are less common (although dyspnea is associated with a high risk of significant GI injury) [43].

If patients have a strong history of ingestion, have oral burns, or are symptomatic, the most reliable method to establish the presence and extent of lesions is upper GI endoscopy (which must be carried out within 24 h). In asymptomatic patients, some authors suggest that upper GI endoscopy should be done anyway, but other authors suggest observation and liquid intake [37]. Upper GI endoscopy is useful to grade esophageal injury (Fig 7.4) and therefore to decide the most appropriate therapy. There are four grades of esophageal injury according to endoscopy: 1 (edema and

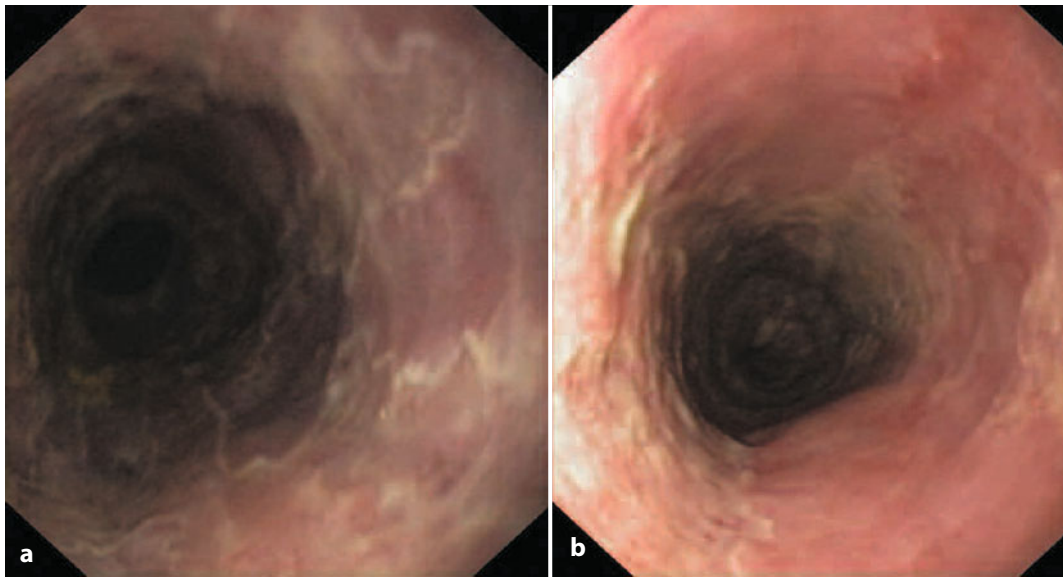

Fig. 7.4 a,b Esophagitis after caustic ingestion

erythema); 2 (linear ulceration and necrotic tissue with whitish plaques); 3 (circumferential injury which may be transmural with mucosal sloughing); and 4 (perforation).

Grade-1 lesions are present in 60–80% of patients who have an esophageal injury [44]. Grade-2 and -3 injuries can determine long-term consequences such as strictures which may occur in ≤2–38% of patients with caustic ingestion and in ≤3–57% of patients with documented esophageal burns. About 80% of patients with strictures will present with obstructive symptoms within 2 months from the ingestion [45].

The endoscopic treatment of patients with strictures comprises esophageal dilation or esophageal stenting. Patients with grade-4 lesions have a poor prognosis due to systemic complications [43]. Other complications secondary to caustic ingestion are dysphagia, esophageal motility abnormalities, esophageal perforations (which can also be due to esophageal dilations). Esophageal perforations can cause pneumothorax, pneumomediastinum, the need for esophageal or gastric surgery, or cause death [46]. Also esophageal carcinoma (adenocarcinoma, squamous cell carcinoma) is a late (but serious) complication of severe caustic injury, with a prevalence of 2–30%, and the time interval between ingestion and tumor detection is 16–42 years [37].

In patients with caustic ingestion, ipecac or oral dilutions (e.g., milk, water, neutralizing agents) are contraindicated because vomiting may lead to additional esophageal injury if gastric contents come into contact with the esophageal mucosa. Nasogastric tubes should be placed under direct vision in patients with extensive circumferential burns. They can provide a route for nutritional support during the healing phase, and they can be placed as stents to keep the esophagus open if stricture development is anticipated. Treatment with corticosteroids is controversial and is usually confined to patients with airway symptoms. This treatment does not seem to protect the airway against the development of esophageal strictures. If corticosteroids are needed, concomitant administration of broad-spectrum antibiotics is required [47].

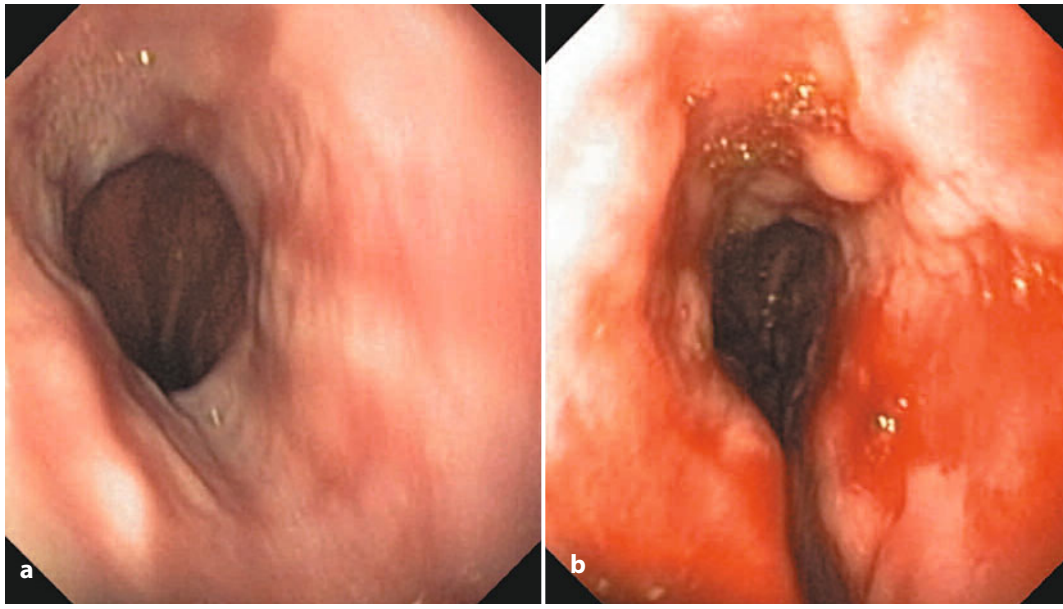

Fig. 7.5 a,b Esophagitis in GERD

7.4.3 Gastroesophageal Reflux (GER)

The passage of gastric contents into the esophagus (GER) is a normal physiological process that occurs in healthy infants, children, and adults. Most episodes are brief and do not cause symptoms, esophageal injury, or other complications. In contrast, gastroesophageal reflux disease (GERD) occurs if the reflux episodes are associated with symptoms or complications. The range of symptoms and complications of GERD in children vary with age.

GER is extremely common in healthy infants, in whom gastric fluids reflux into the esophagus ≥30 times daily [48]. Frequent episodes of regurgitation during infancy may be associated with an increased likelihood of having GERD symptoms in later childhood [49]. Infants can develop symptoms such as failure to thrive, hematemesis, and anemia, suggesting the possibility of GERD. A manifestation of GERD consisting of arching of the back, torsion of the neck, and lifting up of the chin (Sandifer syndrome) can be confused with torticollis.

Preschool age children with GERD may present with intermittent regurgitation. Less commonly, they may have respiratory complications such as persistent wheezing. Decreased food intake without other complaints may be a symptom of esophagitis in young children. All of these symptoms are non-specific and not sufficient to make a definitive diagnosis of GERD.

The pattern of symptoms and complications in older children and adolescents resembles that seen in adults. The cardinal symptoms are chronic heartburn and/or regurgitation [50]. Complications of GERD, including esophagitis (Fig 7.5), strictures, Barrett's esophagus, and hoarseness due to reflux laryngitis, may also be seen. Specific testing should be guided by the type of symptoms and their severity.

Monitoring of esophageal pH permits assessment of the frequency and duration of esophageal acid exposure and its relationship to symptoms even if is rarely useful in establishing the diagnosis of GER in infants because it does not detect anatomical abnor-

malities or directly measure the severity of esophagitis [51, 52]. Esophageal pH monitoring or multichannel intraluminal impedance monitoring (MII) can be useful in atypical symptoms of reflux, in reflux symptoms not responsive to medical or surgical therapy, or in infants with apnea or apparent life-threatening events [53].

The test is undertaken by the transnasal passage of a microelectrode containing a pH sensor into the lower esophagus. The pH electrode is positioned according to a formula that takes into account the length of the child. A device worn by the patient records the exposure to esophageal acids during monitoring. The procedure is considered to be very safe, but keeping the probe in place may be difficult in toddlers and uncooperative children. The results of a pH probe study are influenced by the type of recording device, its exact position within the esophagus, diet, position of the patient, and activity during the study. Interpretation of results after longer periods of monitoring (24 h) is more reliable than after shorter periods (e.g., 12 h), although longer periods of monitoring may not always be feasible [54]. In many centers, esophageal pH monitoring is combined with MII to allow measurement of weakly acidic and alkaline reflux episodes. In a trial comparing the two techniques, combined MII–pH monitoring detected associated symptoms twice as often as pH monitoring alone [55].

Endoscopic evaluation of the upper GI tract is indicated for patients: in whom esophagitis or gastritis is suspected; with recurrent regurgitation after 2 years of age; with dysphagia, odynophagia, or a history of food impaction. Endoscopy permits visualization of the esophageal epithelium as well as histological evaluation to determine the presence and severity of esophagitis and complications such as strictures or BE, and to exclude other disorders such as EE, allergic esophagitis, or infectious esophagitis. An esophagus that appears normal at endoscopy does not exclude the presence of GERD. Sensitivity can be increased with mucosal biopsies, which may reveal intraepithelial eosinophils or other histological findings consistent with GERD [56]. Biopsies of the esophagus, stomach or duodenum may reveal inflammation characteristic of dietary protein intolerance or other systemic disorders. Cellular injury stimulates cell proliferation, the morphological equivalent of which is thickening of the basal cell layer and elongation of the papillae of the epithelium. Findings of basal zone hyperplasia are uncommon in young children, and other histological features, such as the presence of neutrophils and eosinophils, and dilated vascular channels in the papillae of the lamina propria, are more typically seen in the pediatric population [57]. Endoscopy can be carried out in infants, toddlers, and older children. Procedure-related complications of diagnostic endoscopy and biopsy appear to be rare [58]. Complications may occur due to over- or under-sedation [59]. The most common complications are sore throat or hoarseness, which occur in 35% of patients.

For uncomplicated reflux, intervention is not required for most infants. Over-feeding and exposure to tobacco smoke should be avoided. A trial of a milk-free diet and thickening of feeds may be considered if the reflux causes significant adverse effects on quality of life [60]. Infants younger than 12 months of age should be placed in the supine position for sleep, even if they have reflux. The prone position tends to reduce reflux [61] but is also associated with a higher risk of sudden infant death syndrome (SIDS). This risk outweighs the potential beneficial effect of sleeping in the prone position on reflux [62].

The type of lifestyle changes that may be beneficial depend upon the patient's age and symptom characteristics. Weight loss or elevation of the head of the bed improves laboratory measures of reflux but there is no clinical evidence that they consistently improve reflux symptoms [63].

Acid-suppression and prokinetic medications have a limited role in the treatment of infants with regurgitation. They are not valuable in the treating children <1 year of age with un-

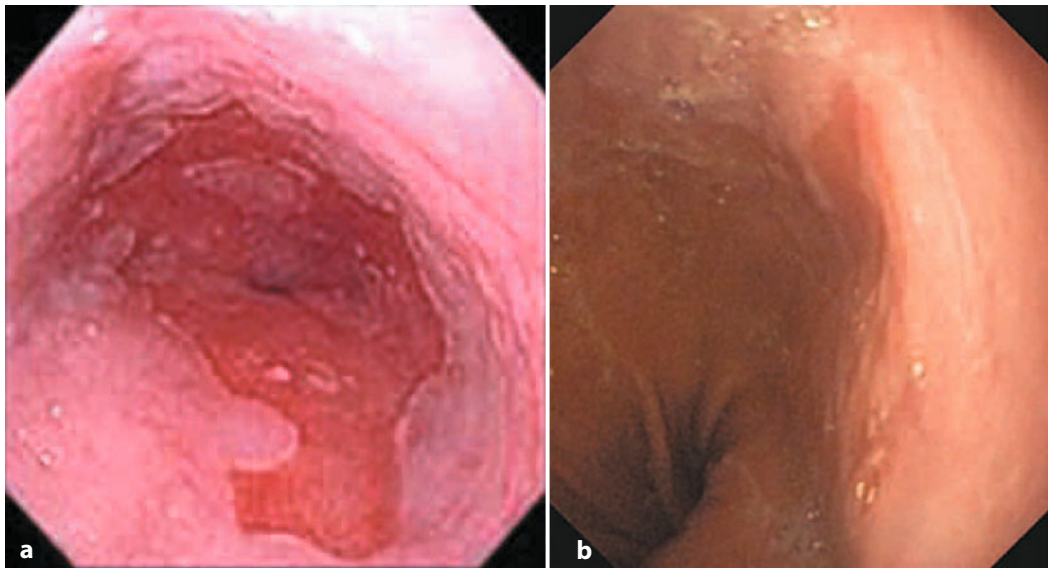

Fig. 7.6 a,b Barrett's esophagus

complicated GER ("happy spitters"). Many infants with symptoms suggestive of GERD will improve over time with conservative measures alone [64]. Infants with esophageal atresia, chronic neuromuscular diseases, chronic respiratory disease or diaphragmatic hiatal defects are more likely to develop erosive esophageal disease over time, and may benefit from early PPI treatment if indicated [65].

If acid suppression is chosen as a treatment or for a limited trial, a PPI that blocks acid secretion by irreversibly binding to and inhibiting the hydrogen–potassium ATPase pump is generally preferred [66]. Infants and younger children metabolize PPIs more rapidly than older children and require higher per-kilogram dosing than older individuals [67].

Histamine type-2 receptor antagonists (H2RAs) have moderate effects on GER as measured by symptom relief and mucosal healing. However, they are less effective than PPIs. Prokinetic agents enhance esophageal peristalsis and accelerate gastric emptying, providing a *rationale* for their use in GERD. They should be considered only in carefully selected patients, including those who have failed anti-secretory therapy (PPIs or H2RAs). They have a minimal role in the treatment of GER in this age group [60].

GER must be diagnosed correctly because it probably plays a major part in the development of BE through repeated mucosal damage. Reflux symptoms for >5 years increase the risk of Barrett esophagus (BE) by threefold, and by sixfold if symptoms occur for >10 years in adults [68]. BE is associated with a 30-fold increase in the risk on esophageal adenocarcinoma in adults, so an adequate and early diagnosis as well as surveillance even in children is important [69].

BE can be diagnosed only by using upper GI endoscopy to obtain biopsies of the esophagus. The diagnosis is based on the endoscopic findings of columnar epithelium lining the distal esophagus (Fig. 7.6) and confirmed by intestinal metaplasia in esophageal biopsy specimens [70]. Multiple closely spaced biopsies are required to minimize sampling error, and to detect possible dysplasia. The literature suggests that four-quadrant biopsies every 1 cm for circumferential metaplastic segments is best [71].

There are no firm guidelines for surveillance in children. However, in adults it is rec-

ommended to repeat endoscopy with biopsy within 1 year. However, if dysplasia has been diagnosed it is suggested to repeat endoscopy with biopsy after 6–12 months in the case of low-grade dysplasia, followed by yearly endoscopy if there is no progression [72].

7.4.4 EE

The esophagus, which is normally devoid of eosinophils, is an immunologically active organ that can recruit eosinophils in response to various stimuli [73]. EE is defined as "a chronic, immune/antigen-mediated, esophageal disease characterized by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation" [74]. The incidence of EE appears to be increasing. This may be partly due to an increased recognition of the disorder [75]. Among children, the disease is more common in boys (71% in the series described above) [76].

The pathogenesis of EE is incompletely understood but includes environmental and genetic factors. Eosinophils establish themselves as permanent residents of the GI tract early during embryonic development (even though they are not normally found in the esophagus). Eosinophil recruitment is observed in various inflammatory or infectious conditions, such as inflammatory bowel disease, GER, and after exposure to food allergens [77–79]. The manifestations of EE vary with age [80–82]. The most common presenting symptoms and the median ages at which they occur are:

- feeding dysfunction (2.0 years);
- vomiting (8.1 years);
- abdominal pain (12.0 years);
- dysphagia (13.4 years);
- food impaction (16.8 years).

There is a strong association between EE and allergic conditions such as food allergies, environmental allergies, asthma, and atopic dermatitis. It has been estimated that 42–93% of children with EE have another allergic disease [83–87]. An association with celiac disease (and response to a gluten-free diet) has been described [88]. In addition, an association with Schatzki ring has also been described [89] but the strength of this association is not clear.

The diagnosis of EE should be based upon symptoms, endoscopic appearance, and histological findings. In patients suspected of having EE, the first diagnostic test is typically an upper GI endoscopy with esophageal biopsies after 1–2 months of treatment with a PPI, though radiographic and laboratory findings may support the diagnosis. Other disorders that can cause esophageal eosinophilia, such as GERD, should be ruled out. Various morphological features in the esophagus have been described in patients with EE [90, 91]. Endoscopic findings (Fig. 7.7) include:

- stacked circular rings ("feline" esophagus);
- strictures (particularly proximal strictures);
- attenuation of the subepithelial vascular pattern;
- linear furrowing that may extend the entire length of the esophagus;
- whitish papules (representing eosinophil microabscesses);
- small-caliber esophagus.

Complications associated with endoscopy in patients with EE include esophageal perforation and mucosal tears [92, 93]. Esophageal biopsies from patients with EE show an increased number of eosinophils. Most patients have ≥15 eosinophils per high power field (HPF; peak value) in at least one biopsy specimen after taking a PPI. Esophageal eosinophilia in the absence of clinical features is not sufficient to make a diagnosis of EE. During endoscopy, biopsies should be obtained from the distal esophagus as well as the mid or proximal esophagus [94]. Two-to-four biopsies must be obtained from the distal esophagus, as well as another 2–4 from the mid or proximal esophagus.

Barium studies are not sensitive for diagnosing EE, but can help characterize anatomical abnormalities and provide information on the length and diameter of strictures [95, 96].

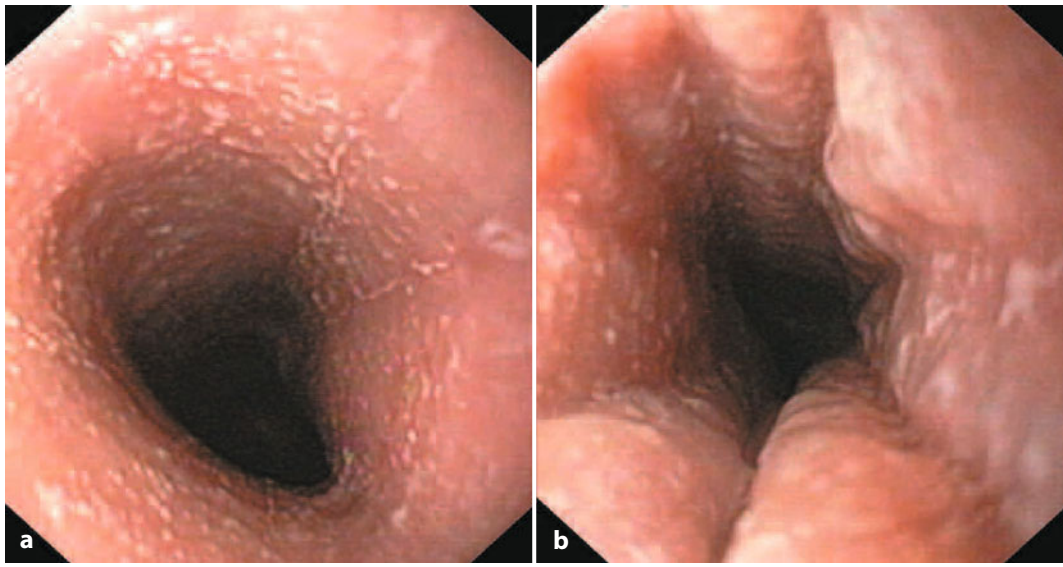

Fig. 7.7 a,b Manifestations of eosinophilic esophagitis

There are no diagnostic serum markers for EE. However, 50–60% of patients with EE will have elevated levels of IgE in serum (>114,000 units/L). Peripheral eosinophilia is seen in 40–50% of patients but is generally mild [97]. It decreases with topical glucocorticoid therapy [76].

The differential diagnoses include conditions that can cause morphological or histological findings that resemble EE. These include GERD, recurrent vomiting due to other causes, parasitic and fungal infections, congenital rings, Crohn's disease, periarteritis, allergic vasculitis, drug injury, connective tissue diseases, bullous pemphigoid, pemphigoid vegetans, graft-versus-host disease, achalasia, drug hypersensitivity, celiac disease, vasculitis, carcinoma, and several causes of peripheral eosinophilia in which the esophagus (along with other organ systems) may become involved. The most common consideration in the differential diagnosis of EE is GERD. As noted above, large numbers of eosinophils (>100/HPF) may be seen in association with GERD. Because of the association of GERD with esophageal eosinophilia, biopsies for EE should be obtained after 1–2 months of treatment with a PPI or after an esophageal pH study has excluded reflux [98].

The management of EE includes dietary, pharmacological, and endoscopic interventions [99]. Commonly used treatments include:

- elimination and elemental diets to decrease allergen exposure;
- acid suppression to treat GERD, which may mimic or contribute to EE;
- topical glucocorticoids to decrease esophageal inflammation;
- esophageal dilation to treat strictures.

Dietary therapy is effective for EE in children [85]. It is based upon the observation that patients with EE have a high prevalence of food allergies, and that those allergies may contribute to the development of EE. The appeal of the dietary approach is that it can offer effective non-pharmacological treatment.

Once symptoms are controlled, foods can be reintroduced sequentially. Any foods that result in the worsening of symptoms should be avoided indefinitely [81, 85]. GERD may mimic EE, coexist with it, or contribute to it. Conversely, EE may contribute to GERD [100]. The diagnosis of EE should generally

include demonstration of persistent esophageal eosinophilia at histology after treatment with a PPI (or with a normal pH study).

Most patients with EE respond to topical (*via* a metered-dose inhaler) glucocorticoids, especially with swallowed fluticasone without a spacer [76, 101]. Treatment is generally well-tolerated and patients who are destined to respond tend to do so quickly (within 1 week and often within 1–2 days). Patients frequently relapse if treatment is stopped, and a prevalence of relapse of 14–91% has been reported [102, 103]. Budesonide has been evaluated in case series and randomized trials, and appears to be effective for treating EE [75, 87].

7.4.5 Esophageal Varices

Esophageal varices link the portal and systemic venous circulation. They form as a consequence of portal hypertension, preferentially in the submucosa of the lower esophagus. Hemorrhage from varices is the result of increased pressure within the varix, with a change in the diameter of the varix and an increase in wall tension. Variceal bleeding is associated with a portal vein:hepatic vein gradient >12 mmHg. If the wall tension exceeds the variceal-wall strength, rupture of the varix occurs and therefore hemorrhage results [104]. The literature suggests that >50% of cirrhotic children have varices [104, 105] and that bleeding from varices occurs in 28% of A patients, 30% of B patients, and in 50% of C patients according to the Child–Pugh classification of varices [106].

Endoscopy is the "gold standard" for the diagnosis of esophageal varices because there are no satisfactory non-endoscopic indicators of varices [107]. Therefore, upper GI endoscopy should be done once portal hypertension is suspected or has been diagnosed [108].

Surveillance in adults suggests that in patients without varices upon initial screening endoscopy that endoscopy should be repeated after 3 years, whereas patients with small varices should undergo endoscopy in 1–2 years [109]. Depending on the endoscopic appearance of the varices, a classification according to their shape and size has been proposed [110]:

- F0: no esophageal varices detected;
- F1: small, straight esophageal varices;
- F2: slightly enlarged tortuous esophageal varices occupying less than one-third of the esophageal lumen;
- F3: large, coil-shaped esophageal varices occupying more than one-third of the esophageal lumen.

The management of esophageal varices can be divided into:

- preprimary prophylaxis;
- prophylaxis (primary) of the first episode of bleeding;
- emergency therapy;
- prophylaxis (secondary) of sub¬sequent bleeding episodes.

With regard to management, many data have been extrapolated from adult studies. There are no indications to treat patients to prevent the formation of varices, therefore pre-primary prophylaxis remains an interesting concept that is not applicable in clinical practice.

Prophylaxis of the first episode of bleeding should be carried out with the administration of non-selective beta-blockers (e.g., propranolol) in patients with small varices, whereas endoscopic sclerotherapy and band ligation can be useful in children with medium/large or growing esophageal varices. Of the two endoscopic procedures, band ligation in the pediatric population appears to be superior [104, 107].

The initial management of emergency therapy is stabilization of the patient. Then, intravenous antibiotic therapy (e.g., ceftriaxone) should be part of the treatment of these patients due to the high risk of potentially fatal infectious complications [108]. Endoscopy should be carried within 12–24 h in a stable patient to detect the site of bleeding and to initiate treatment (if indicated).

Endoscopic treatment is very effective in controlling bleeding and consists of sclerother-

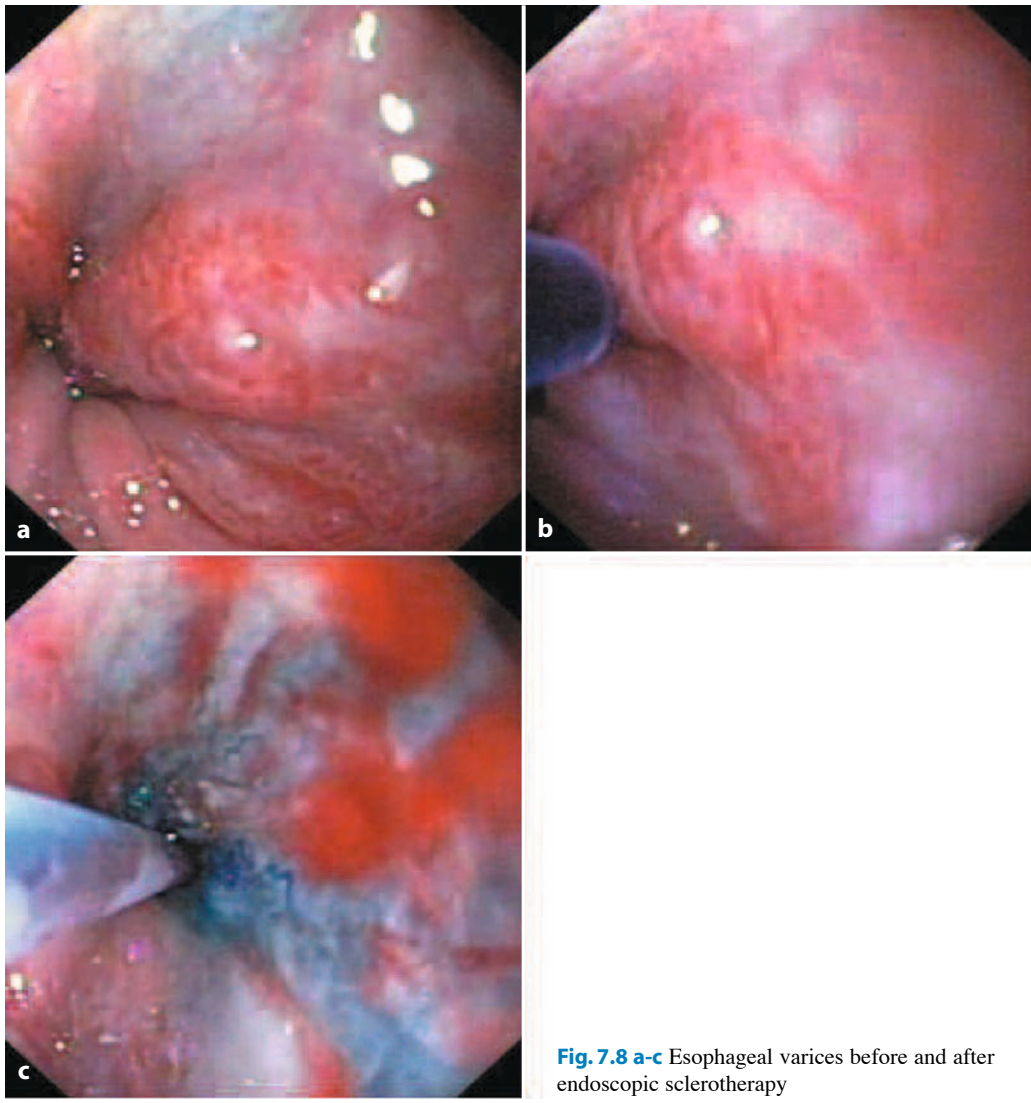

Fig. 7.8 a-c Esophageal varices before and after endoscopic sclerotherapy

apy and variceal ligation. Sclerotherapy requires the injection of agents such as sclerosants or chemically irritating compounds such as ethanolamine/tetradecyl sulfate through the intra- or para-variceal route until bleeding has stopped [104]. Even though sclerotherapy has been used widely in the treatment of esophageal varices in children, recently it has been used less widely because side effects such as perforation, bleeding, ulceration, and stricture formation at the injection site have been reported [108].

Nowadays, endoscopic band ligation (EBL) is recommended for endoscopic therapy. In this technique, a scope loaded with an elastic rubber band is passed through an overtube directly into the varix. After suctioning the bleeding varix into the tip of the endoscope, the rubber band is slipped over the tissue, causing necrosis, ulceration and eventual sloughing of the varix. EBL cannot be conducted in all children because of the size of the esophagus compared with the scope size and the associated ligature attachment, therefore sclerotherapy remains a good alternative (Fig. 7.8).

Secondary prophylaxis should start from day 6 of the bleeding episode. In patients with

cirrhosis, a combination of beta blockers and band ligation is probably the best treatment, but more randomized controlled trials are needed to confirm this finding.

If endoscopic and pharmacological treatment for the prevention of rebleeding is unsuccessful, the transjugular intrahepatic portosystemic shunt (TIPS) should be considered. It should also be considered as a "bridge" to liver transplantation that provides good long-term outcomes in class B/C cirrhosis according to the Child–Pugh classification [107].

7.4.6 Dilation

Esophageal strictures in children may be caused by congenital anomalies, ingestion of caustic agents or foreign bodies, complications of reflux esophagitis, EE, and after esophageal surgery. Such strictures represent a serious challenge for endoscopists.

Various dilators can be used, including "through-the-scope'' balloon dilatation; Savary–Gilliard bougies are the most commonly used in children [111]. The degree of dilation within a session should be based on the severity of the stricture. Initially, the scope is introduced to locate the stricture and (if possible) to pass it to determine its extent and the state of the mucosa. If Savary–Gilliard bougies are used, a guidewire is placed under endoscopic or fluoroscopic control through the stricture, respectively, if the scope can or cannot pass the stricture. The guidewire is then pushed into the stomach. The dilators are then slipped one after the other on the guidewire, thereby achieving longitudinal forces on the stricture [112]. If through-the-scope balloon dilators are used, they are introduced through the accessory canal of an endoscope until they reach the strictures. They are then inflated under fluoroscopic control to reach the desired diameter (Fig. 7.9). Endoscopic control is necessary for Savary–Gilliard or balloon dilators to determine the diameter of the dilated stricture and to ascertain the integrity of the esophagus and possible bleeding sources [111]. The principal complications of esophageal dilation are perforation, bleeding, and aspiration. The risk of perforation is the most dangerous, and is higher in caustic strictures (≤15%) [113].

7.4.7 EUS

There are three basic echo endoscope designs: radial array, curvilinear array, and high-frequency catheter-based mini-probes. The radial system permits circumferential views with angles from 270° to 360° and with frequencies from 5.0 MHz to 10 MHz. The curvilinear scope provides a 180° view that is parallel to the shaft of the echo endoscope, thereby allowing real-time visualization of fine-needle aspiration. Mini-probes pass through the accessory channels of conventional endoscopes and have high resolution but poor penetration. Therefore, they are used to define submucosal lesions or used in luminal strictures which do not permit the passage of conventional echo endoscopes [2].

EUS provides images of the wall of the GI tract that consists of five alternating hyperechoic and hypoechoic layers:

- the innermost layer (lumen) is hyperechoic, and is attributed to the initial echo interface between the ultrasound waves, the mucosa of the GI tract, and surrounding fluid;
- the second layer is a hypoechoic and corresponds to the mucosa and deep mucosa;
- the third layer is a hyperechoic and corresponds to the submucosa;
- the fourth layer represents the muscularis propria and it is hypoechoic;
- the fifth layer, which is seen as a hyperechoic band, is the esophageal serosa.

In the pediatric population, the need for these procedures is far less frequent in children than in adults; this is because of the higher incidence of malignant diseases in adults [9]. However, EUS may have an important diagnostic and therapeutic role in children, particularly in esophageal diseases.

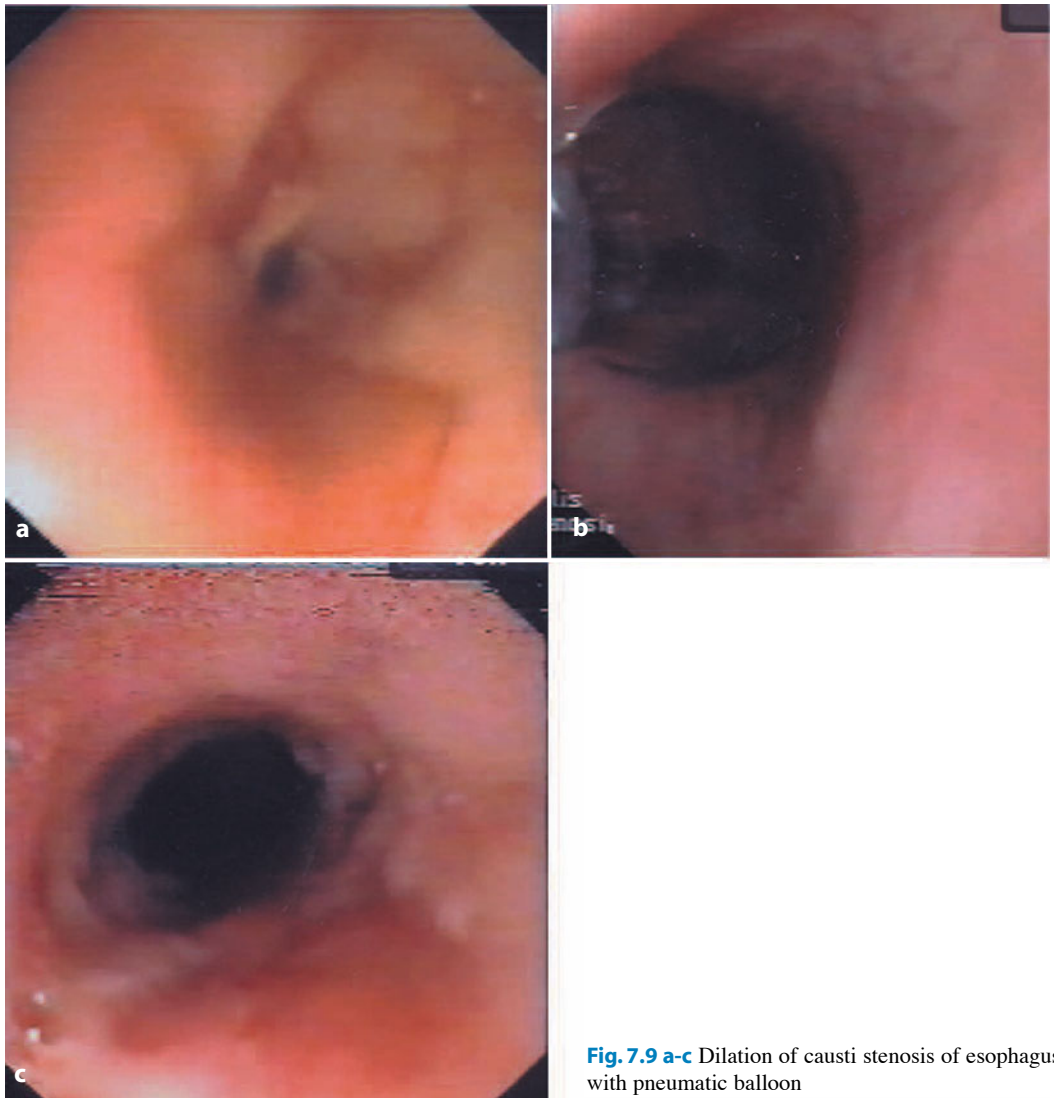

Fig. 7.9 a-c Dilation of causti stenosis of esophagus with pneumatic balloon

EUS can be useful in the differential diagnosis of EE. In fact, in these patients, EUS shows a thickened mucosa in the proximal and distal part of the esophagus compared with controls and in patients with GERD [114, 115]. EUS has been demonstrated to be superior to standard upper GI endoscopy for the identification of esophageal varices. Esophageal varices appear as hypoechoic or anechoic lumens in the esophageal wall, usually in the submucosal layers [108]. Moreover, EUS can more accurately determine the variceal size and the thickness of the variceal wall by measuring the radius of the external and internal wall of the varices [116]. Adult studies have shown that EUS can be used to guide injection sclerotherapy and then to verify the obliteration of varices after endoscopic treatment [117].

EUS can also be used for finding the cause and subsequent treatment strategy for esophageal stenosis in children. This is because EUS can show hyperechoic lesions, suggesting cartilage at the esophageal narrowing or hypertrophy of the muscular layer or hyperechoic rings outside the esophageal wall, indicating that a tracheobronchial remnant is present [118,

119]. In conclusion, EUS is feasible and safe and has a significant impact on the management of pediatric esophageal diseases [120].

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Esophageal Atresia and Tracheoesophageal Fistula

8

Steven W. Bruch, Arnold G. Coran and Shaun M. Kunisaki

8.1 Introduction

The treatment of esophageal atresia and tracheoesophageal fistula, although still a challenge, represents one of the true successes of newborn surgery. Thomas Gibson first described the classic form of esophageal atresia with tracheoesophageal fistula in 1697 [1]. In 1888, Charles Steele attempted the first surgical repair of a pure esophageal atresia. He carried out a gastrotomy and attempted to pass a steel probe through the suspected esophageal membrane. At autopsy, the probe exited the lower esophageal pouch but the two ends of the esophagus were noted to end blindly with a gap between them of 1.5 inches with no connection that could be identified [2]. Attempted repair of esophageal atresia with a tracheoesophageal fistula employing fistula division and primary anastomosis was first reported by Robert Shaw in Dallas in 1938 [3] but first attempted by Thomas Lanman in Boston in 1936, who later reported it along with 4 other attempts and 27 additional cases of esophageal atresia in 1940 [4]. All of these attempts were unsuccessful, but not all because of technical issues. After 5 failed attempts, the first in 1939, Cameron Haight undertook the first successful primary repair of esophageal atresia in 1941 using a left extrapleural approach, fistula ligation, and a single-layer anastomosis [5]. Over the years, improvements in surgical technique and neonatal care have improved outcomes in the treatment of esophageal atresia and tracheoesophageal fistula. In 1994, Spitz et al. created a system to stratify outcome based on birth weight (>1,500 g or <1,500 g) and the presence of a major cardiac anomaly [6]. In 2006, Spitz compared results in the present era to the 1994 results and noted that survival of babies with birth weight >1500 g and no cardiac anomalies was similar: 97% in 1994 *versus* 98.5% in 2006. Survival for babies that weighed <1,500 g at birth, or had a cardiac anomaly, improved from 59% to 82% during that interval. The babies with the worst outcomes, those that weighed <1,500 g at birth and had a cardiac anomaly, improved from 22% in the early era to 50% [7]. In 2009, Okamoto et al. reviewed the Japanese experience, and proposed a modification to the Spitz classification depicted in Table 8.1 [8].

8.2 Embryology

The trachea and esophagus develop from the primitive foregut during the fourth week of human embryonic development. The ventral

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Table 8.1 Survival of infants with esophageal Atresia with or without tracheoesophageal fistula based on birth weight and cardiac anomalies

Class	Birth weight (g)	Major cardiac anomaly	Survival (%)
Low risk	>2,000	No	100
Moderate risk	<2,000	No	82
Relatively high risk	>2,000	Yes	72
High risk	<2,000	Yes	27

portion of the foregut gives rise to the trachea and lungs, whereas the esophagus develops from the dorsal aspect [9]. Several authors have attempted to explain this separation, but the exact mechanism remains unknown [10]. The development of esophageal atresia and tracheoesophageal fistula appears to be a complex multifactorial process involving genetic and environmental factors to some degree. Up to 10% of patients with esophageal atresia have a defined genetic syndrome that can be diagnosed, leaving the remaining 90% with an unknown etiology for their malformation [11]. The environmental factors that have been suggested include: exposure to methimazole [12], diethylstilbestrol [13] or exogenous sex hormones [14]; infectious diseases [15]; combination of use of alcohol and tobacco by the mother [16]; maternal employment in agriculture or horticulture [17]; first-trimester maternal diabetes mellitus [18]; advanced maternal age [19]. The genetic syndromes associated with esophageal atresia and tracheoesophageal fistula include trisomies as well as single gene disorders. The trisomies include Down syndrome (21), Edwards syndrome (18), and Patau syndrome (13) [20].

The single gene disorders include CHARGE syndrome (CHD7 gene) [21], DiGeorge syndrome (TBX1 gene) [22], Feingold syndrome (MYCN gene) [23], Opitz syndrome (MID1 gene) [24], AEG syndrome (SOX2 gene) [25], and Fanconi anemia (FANCA, FANCC, and FANCG genes) [26]. Despite many recent advances, there remains a substantial gap in our understanding of the environmental, genetic, and other factors leading to abnormal development of the foregut.

8.3 Epidemiology

Esophageal atresia and tracheoesophageal fistula occurs in 1 out of every 3,500 live births [20]. The incidence varies depending on geographic location: 1 in 2,440 in Finland [27], 1 in 3,300 in England [28], and 1 in 4,500 in Australia [29] and the USA [30]. The risk that a second child will be born with esophageal atresia and tracheoesophageal fistula in the same family is approximately 1%. If one twin is born with esophageal atresia and tracheoesophageal fistula, there is only a 2.5% chance that the second twin will also have the anomaly [31]. This suggests that hereditary factors play a minimal part in the etiology of esophageal atresia. Parental characteristics that increase the risk of having a child with esophageal atresia and tracheoesophageal fistula include low maternal parity, older maternal age [32], older paternal age [33], and being a Caucasian mother compared with being a mother from other ethnic groups [32]. Obesity and low socioeconomic status of the mother are not risk factors [34].

8.4 Associated Anomalies

Although the surgical repair of esophageal atresia and tracheoesophageal fistula requires technical expertise, the outcome depends on the degree of prematurity and the presence of associated anomalies (especially cardiac and chromosomal abnormalities). Children born with esophageal atresia have a higher incidence of prematurity than the general population, most likely due to the polyhydramnios

caused by fetal esophageal obstruction [35]. Esophageal atresia and tracheoesophageal fistula present in two forms, either in isolation (50%) or as a syndromic form (50%) associated with other abnormalities [36]. Half of those in the syndromic group have random associated anomalies whereas the other half could be classified into a recognizable malformation syndrome or pattern. These syndromes or patterns include chromosomal abnormalities (trisomies 13, 18, and 21) occurring in 8% of esophageal atresia births, and several syndromes and associations, the most frequent being the VACTERL association. The VACTERL association occurs in 10–19% of cases. It consists of a non-random association of defects without specific features including **ve**rtebral, **a**norectal, **c**ardiac, **t**racheal, **e**sophageal, **r**enal, and **l**imb abnormalities. The presence of ≥3 of these abnormalities constitutes the VACTERL association [37]. The remaining syndromes and associations include the CHARGE, SCHISIS, Potter's, Feingold, Roger's, Opitz G, and Goldenhar's syndromes, and Fanconi anemia [36]. Combining data from 12 observational studies that involved 5,242 children with esophageal atresia and tracheoesophageal fistula, the following distribution of associated anomalies were found: cardiac 20.3%, digestive 16.0%, musculoskeletal 15.1%, urogenital 13.6%, central nervous system (CNS) 5.3%, and pulmonary 4.3% [37–48]. Following the initial repair or gastrostomy tube placement, an infant may develop persistent emesis. Infants with esophageal atresia and tracheoesophageal fistula have a higher incidence of pyloric stenosis than expected in the normal population [49].

8.5 Anatomy

An understanding of the anatomy involved with each case of esophageal atresia and tracheoesophageal fistula is important when devising a treatment strategy. There have been several classification systems, but a description of each type is the easiest and most practical way to depict the five combinations of esophageal atresia and tracheoesophageal fistula (Fig. 8.1). The most common configuration is esophageal atresia with a distal tracheoesophageal fistula. This configuration occurs in 86% of cases [50]. The proximal esophagus ends blindly in the upper mediastinum. The distal esophagus is connected to the tracheobronchial tree usually just above or at the carina. The second most common type is the isolated esophageal atresia without a tracheoesophageal fistula. This configuration occurs in 8% of cases [50]. The proximal esophagus ends blindly in the upper mediastinum, and the distal esophagus is also blind-ending and protrudes varying distances above the diaphragm. The distance between the two ends is often too far to bring together initially. The third most common configuration, occurring in 4% of cases [50], is a tracheoesophageal fistula without esophageal atresia. The esophagus extends in continuity to the stomach, but there is a fistula between the esophagus and trachea. The fistula is usually located in the upper mediastinum, running from a proximal orifice in the trachea to a more distal orifice in the esophagus. This is also known as an "H" type or "N" type tracheoesophageal fistula. The remaining two forms each occur in about 1% of cases [50].

These are esophageal atresia with a proximal and distal tracheoesophageal fistula, and esophageal atresia with a proximal tracheoesophageal fistula. These two forms correspond to the initial two forms described with the addition of a proximal fistula between the upper esophageal pouch and the trachea. A proximal fistula is often difficult to diagnose preoperatively even when bronchoscopy is carried out. Because of the difficulty identifying a proximal fistula, some "recurrent" fistulas in the past may have in fact been missed proximal fistulas [51]. Again the esophageal ateasia with proximal tracheoesophageal fistula, similar to its counterpart without a proximal fistula, will have a long gap between the two ends of the esophagus, making it difficult to repair initially after birth.

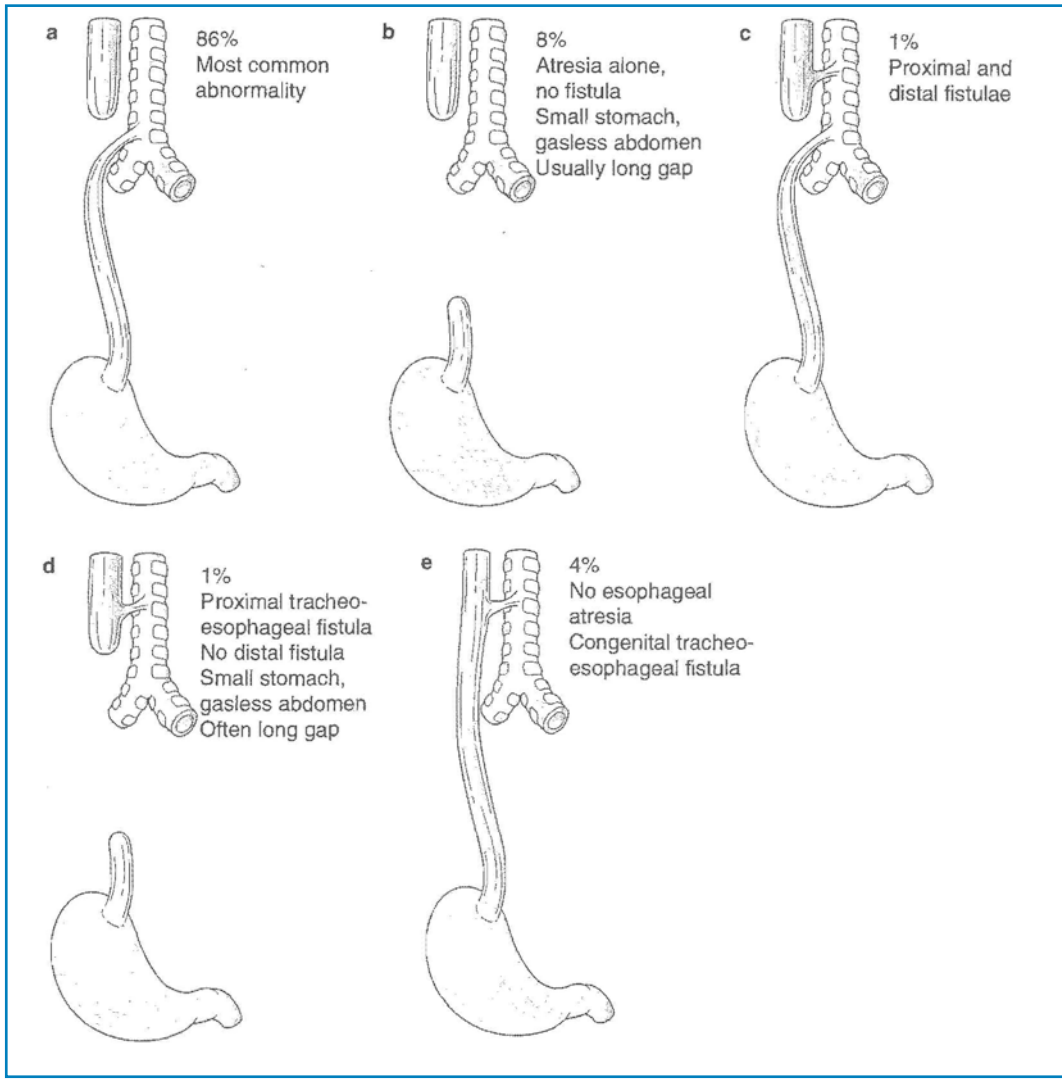

Fig. 8.1 Types of esophageal atresia and tracheoesophageal fistula

8.6 Presentation and Diagnosis

Prenatal ultrasonography attempts to predict the presence of esophageal atresia using the combination of polyhydramnios, an absent or small stomach bubble, and an "upper pouch" sign. These are non-specific findings that correctly predict esophageal atresia 56% of the time [52]. Using special image acquisition, magnetic resonance imaging (MRI) accurately demonstrates the upper pouch in fetuses with esophageal atresia [53]. Infants born with esophageal atresia and tracheoesophageal fistula have difficulty handling their oral secretions and will choke, cough, and possibly become cyanotic with their first feeding. After a feeding attempt, they will spit-up undigested formula or breast milk. This leads to an attempt to place a tube in the stomach, which does not travel as far as expected and meets resistance. A radiograph of the chest and abdomen shows the tube coiled in the esophageal pouch in the upper mediastinum, confirming esophageal atresia. The abdominal gas pattern determines if there is a distal tra-

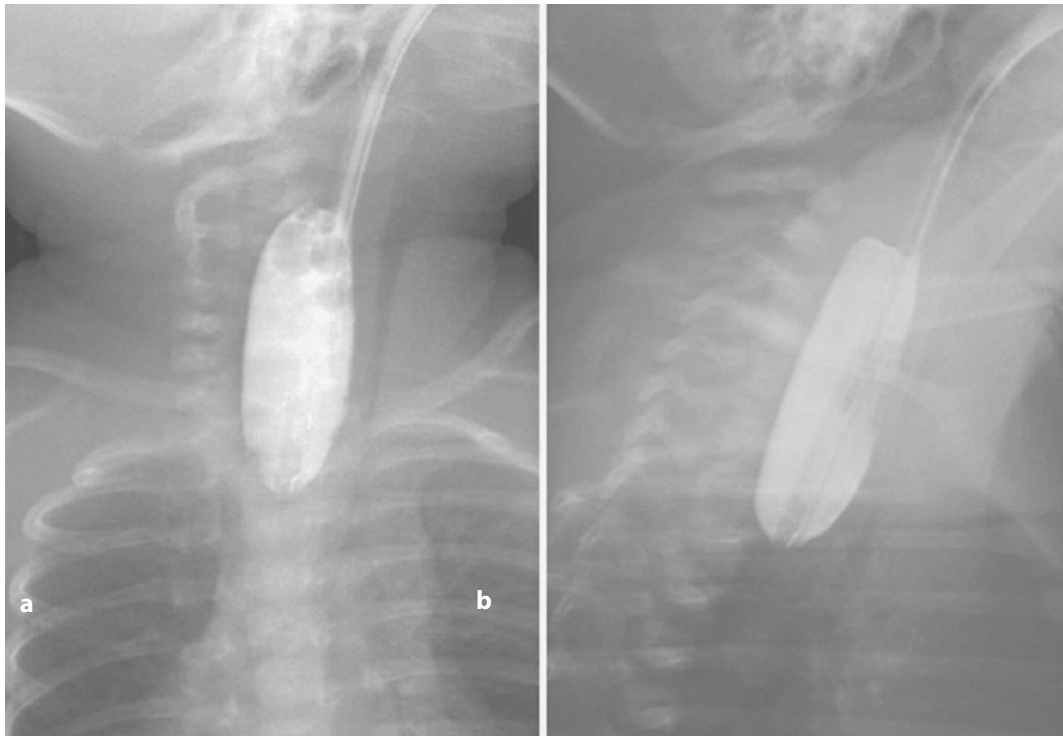

Fig. 8.2 Pouchogram obtained on a neonate without a proximal fistula. Anteroposterior view (**a**). Lateral view (**b**)

cheoesophageal fistula (gas throughout the intestines) or a pure esophageal atresia with no connection to the tracheobronchial tree (gasless abdomen). The diagnosis is made and the remainder of the preoperative evaluation attempts to define a proximal fistula between the esophageal pouch and the trachea, and to characterize associated anomalies. Chromosomal abnormalities are found with a karyotype. Four simple evaluations identify the anomalies of the VACTERL association. First, the physical examination evaluates anorectal and limb abnormalities. Second, the radiograph obtained to evaluate the placement of the esophageal tube is used to look for vertebral and limb abnormalities. Third, ultrasound of the abdomen will evaluate renal abnormalities. The pelvis should also be imaged to evaluate for a tethered spinal cord or pre-sacral mass. Finally, echocardiography evaluates cardiac anomalies and the position of the arch of the aorta (which is important in surgical planning). If a right-sided aortic arch is identified, magnetic resonance (MR) angiography is used to look for a vascular ring. A complete vascular ring is found 37% of the time in this situation [54].

Three options exist to find proximal fistulas that are not mutually exclusive. A contrast evaluation of the proximal pouch (Fig. 8.2) carried out by an experienced radiologist using a small amount of non-ionic contrast under fluoroscopic guidance often shows a proximal fistula if present. Rigid bronchoscopy just prior to surgical repair looking for an opening in the proximal membranous trachea will identify a proximal fistula. Bronchoscopy is also useful to identify the location of a distal fistula if one is present, and a laryngeotracheoesophageal cleft should be looked for as the bronchoscope is removed. The final strategy is to look for a fistula during the proximal pouch dissection. It is usually encountered near the distal aspect of the pouch, but can be located up in the neck [55]. A clue that a proximal fistula is present is that the proximal pouch will not be as dilated or thick-walled as expected because the fistula relieves

the distending pressure in the proximal pouch pre-natally and post-natally.

A tracheosophageal fistula without esophageal atresia (H-type fistula) may not present in the initial neonatal period and can be more difficult to diagnose. A tube will go into the stomach if passed, but persistent coughing and choking with oral feeds should prompt a search for an isolated fistula. A prone pull-back esophagram or bronchoscopy with esophagoscopy using methylene blue as a dye is used to find an isolated fistula. Placement of a catheter across the fistula during bronchoscopy aids the dissection greatly.

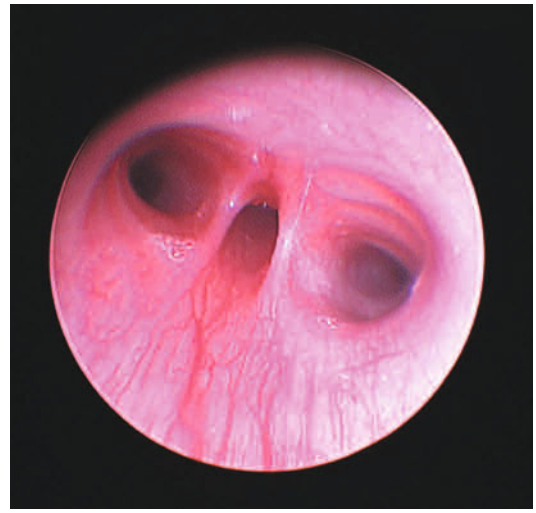

Fig. 8.3 Rigid bronchoscopic view of the carina with a distal tracheoesophageal fistula in the center

8.7 Treatment

After making the diagnosis, appropriate plans for repair should be made. In healthy newborns, the repair can be done in the first 24 h of life to minimize the risk of aspiration and the resulting pneumonitis. Prior to the procedure, the infant should be positioned supine with the head of the bed elevated 30–45°. A tube should be in the proximal pouch to constantly suction saliva and prevent aspiration. Intravenous access is established for fluid instillation along with broad-spectrum intravenous antibiotics and vitamin K. The goal of surgical therapy is to divide and close the fistula between the trachea and esophagus, and return continuity to the esophagus. In most situations, a primary repair is feasible. However, special situations require different tactics (see below).

In the usual situation, a stable infant (from the hemodynamic and pulmonary standpoint) is brought to the operating room and placed under general anesthesia. Rigid bronchoscopy (Fig. 8.3) begins the procedure to locate the distal fistula, usually at or near the carina, and to look for a proximal fistula in the more proximal trachea. Although a right posterolateral thoracotomy is the standard approach for repair of esophageal atresia, preoperative echocardiography may document a right-sided aortic arch in 2% of cases, and a left posterolateral thoracotomy should be used in these cases [56]. The difficulty repairing the esophagus through the right chest with a right-sided arch is the tension required to stretch the repair over the aortic arch, leading to a high prevalence of anastomotic leaks (about 40%) [57]. A right-sided aortic arch may be discovered intraoperatively because preoperative echocardiograpy identifies as low as 20%, and up to only 62% of the right-sided arches correctly [54, 57]. In that situation, the repair is attempted through the right chest, and if it cannot be completed, the tracheoesophageal fistula is divided, the right chest closed, and a left thoracotomy used to complete esophageal repair.

For the infant with the typical left-sided aortic arch, a right-sided posterolateral thoracotomy using a muscle-splitting, retropleural approach gives access to the mediastinal structures. The azygos vein is divided, revealing the tracheoesophageal connection. The distal esophagus is divided at the level of the trachea and the defect in the trachea closed (Fig. 8.4). Dissection of the distal esophagus is minimized to protect its segmental blood supply. The thyrocervical trunk provides a rich blood supply to the proximal esophagus, allowing extensive dissection. The anesthesiologist pushes on the tube in the proximal pouch to help identify it in the upper mediastinum. Dis-

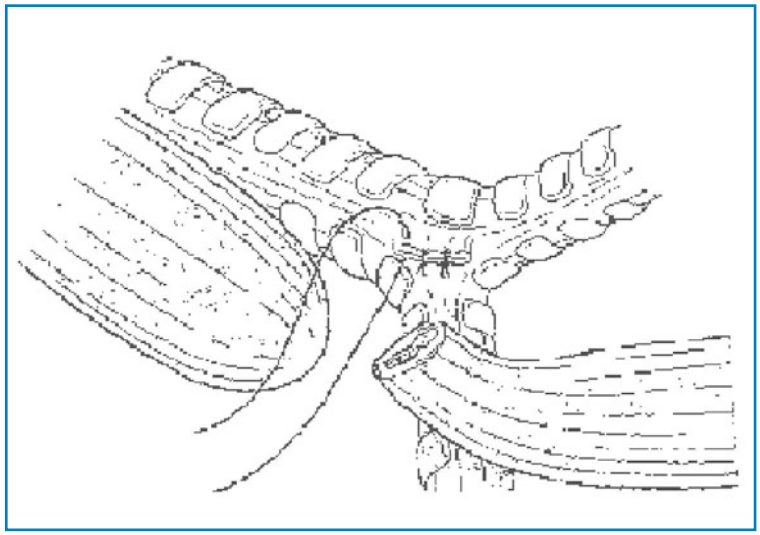

Fig. 8.4 Closure of the trachea after division of a distal tracheoesohageal fistula

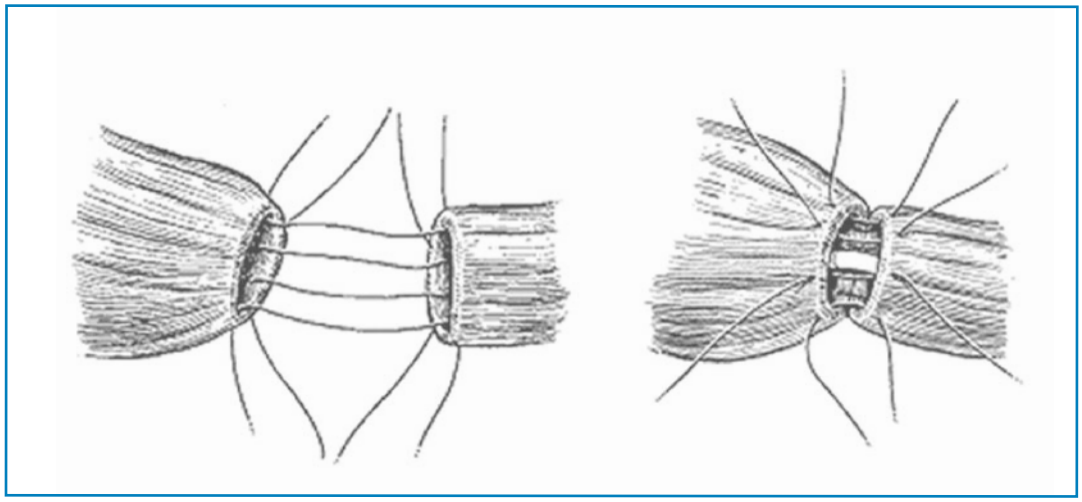

Fig. 8.5 Esophageal anastomosis with a nasogastric tube used as a stent

section of the proximal pouch proceeds on the thickened esophageal wall to avoid tracheal injury, and continues as high as possible to gain length for a tension-free anastomosis, and to search for the rare proximal fistula. A single-layered end-to-end interrupted anastomosis brings the ends of the esophagus together (Fig. 8.5). A nasogastric tube is passed through the anastomosis to ensure patency of the distal esophagus, and allow initial gastric decompression and eventual enteral feeds. A chest tube is placed in the retropleural space to control a potential leak. Some surgeons opt not to use a chest tube if the pleura remains intact. One advantage of the retropeural approach is that if the anastomosis leaks it will not soil the hemithorax and result in an empyema. A leak into the retropleural space will result in an esophagocutaneous fistula that will almost always close spontaneously.

Recently, thoracoscopic repair of esophageal atresia and tracheoesphageal fistula has proven feasible with similar outcomes to those seen with open repair [58]. Several large series

have been reported, including a multicenter series with 103 thoracoscopic repairs [59] and a single-institution series of 51 thoracoscopic repairs [60]. The left semi-prone position allows the lung to fall anterior and, along with CO_2 insufflation with 5 mmHg, provides an excellent view of the posterior mediastinum. Three or four trocars are used to disconnect the fistula and carry out the esophageal anastomosis. The purported benefits of the thoracoscopic approach include less pain from the incisions, less shoulder asymmetry and scoliosis, better cosmetic effect, and a magnified surgical view. The thoracoscopic approach requires advanced endosurgical skills because it is technically demanding.

After surgery (whether open or thoracoscopic) the infant returns to the Intensive Care Unit (ICU) and continues on intravenous nutrition and antibiotics. Special nursing care with frequent oropharyngeal suctioning and positioning with the head of the bed elevated 30–45° helps to prevent aspiration. Feedings may be started through a trans-anastomotic tube 2–3 days after surgery. Acid-suppressive therapy prevents irritation of the anastomosis and subsequent stricture formation. On postoperative days 5–7 esophagography can be used to check the integrity of the anastomosis. If no leak is seen, feedings are started orally, and the chest tube removed the following day. If a leak is present, conservative treatment with intravenous nutrition, broad-spectrum antibiotics, and chest-tube drainage continues. Another esophagram is ordered for the following week. These leaks will invariably close without further surgical intervention [61]. Only complete disruption of the anastomosis requires further intervention. A cervical esophagostomy drains the proximal pouch, the distal esophagus is tied off, and the mediastinum is drained widely.

8.8 Special Situations

Most cases of esophageal atresia and tracheoesophageal fistula can be handled routinely, but three situations require further discussion, i.e., infants with: severe respiratory disease in which the tracheoesophageal fistula contributes to ventilator insufficiency; long-gap esophageal atresia; an H-type tracheoesophageal fistula.

Infants with respiratory insufficiency and a tracheoesophageal fistula are often premature with lung immaturity and require a significant amount of ventilatory support. Breaths provided by the ventilator preferentially enter the distal esophagus through the fistula due to the high resistance in the airways produced by the non-compliant lungs. This allows a significant portion of each breath to enter the abdomen through the fistula and distal esophagus, producing abdominal distension and elevation of the hemidiaphragm, leading to further respiratory compromise. There are several options in this situation. High-frequency ventilation decreases the portion of the tidal volume lost through the fistula. Advancing the endotracheal tube distal to the fistula opening prevents further loss of ventilation, but is not always possible, and can be dangerous if the fistula is intubated [62]. A Fogarty catheter placed in the fistula bronchoscopically and inflated temporarily occludes the fistula but has a tendency to dislodge [63]. The Fogarty catheter may also be placed through a gastrostomy tube into the distal esophagus, or through the fistula into the trachea to prevent further runoff. The Fogarty catheter can then be secured well to the gastrostomy tube [64]. When a gastrostomy tube is present, it can be connected to a pleurovac and placed in an underwater seal to increase the resistance of the tract and reduce airflow through the fistula [50]. If these techniques fail, these infants require an urgent thoracotomy to ligate the tracheoesophageal fistula, prevent further respiratory decompensation, and ameliorate the risk of gastric perforation. Often the infant's respiratory status stabilizes in the operating room after fistula ligation, allowing completion of the repair [65]. If the infant remains unstable, the distal esophagus is secured to the prevertebral fascia, the chest closed, a gastros-

tomy tube placed (if not already present) and definitive repair delayed until the respiratory status stabilizes.

A long gap between the two esophageal segments comprises the next special situation. This often occurs with pure esophageal atresia or esophageal atresia with a proximal fistula. Both of these present with a radiographic picture of a gasless abdomen. On occasion, an infant with esophageal atresia and a distal tracheoesophageal fistula may have a long gap between the two esophageal segments. Initially, the infant requires a gastrostomy tube for enteral feedings while waiting for the two esophageal segments to grow adequately to allow a primary anastomosis. The stomach is quite small in these infants because it was unused during fetal life and has not yet stretched to its full capacity. During gastrostomy placement, care must be taken to avoid injury to the small stomach and its blood supply along the greater curvature. Careful placement will allow for future use of the stomach for an esophageal replacement if necessary. During placement of the gastrostomy tube, an estimation of the distance between the esophageal segments is obtained. Several methods utilizing metal sounds, dilators, contrast and endoscopy exist. The most accurate method uses fluoroscopy to measure the distance between a dilator placed in the upper esophageal pouch and an endoscope placed through the gastrostomy site and driven into the blind distal esophageal pouch [66]. If the ends of the esophageal segments are >3 vertebral-bodies apart they will not be easily connected. The infant should be fed *via* the gastrostomy tube with the head of the bed elevated 30–45° and a tube in the proximal pouch to control the secretions. During the first several months of life, the gap between the two segments of the esophagus shortens due to spontaneous growth of the atretic esophagus [67]. Stretching of the upper and (less frequently) the lower pouch twice a day by bougienage may help bring the two ends together [68]. The distance between the proximal and distal segments of the esophagus is measured every 2–4 weeks and, if they are within 2–3 vertebral bodies (which occurs in about 70% of infants [69]), a thoracotomy and attempted anastomosis are done.

There are several techniques that can be used to gain length on the esophageal segments during the procedure. These include complete dissection of the upper pouch to the thoracic inlet. A circular myotomy of Livadit is carried out on the upper pouch and produces approximately 1 cm of length for each myotomy [70]. Use of a circular myotomy is shown in Fig. 8.6. A tubularization graft of the upper pouch can be created and connected to the distal esophagus (Fig. 8.7) [71]. The distal esophagus can also be mobilized (despite its segmental blood supply) down through the hiatus to gain length [50]. If these maneuvers fail to provide an adequate anastomosis, other options include a staged esophageal replacement with a left cervical esophagostomy, or an immediate esophageal substitution with a gastric transposition, a gastric tube, or a colon interposition to replace the native esophagus. An immediate gastric transposition is our preferred approach. If the gap remains >3 vertebral bodies and the ends of the esophageal segments are no longer approaching each other, the infant may require a cervical esophagostomy and esophageal replacement at 9–12 months of age. Waiting >4 months rarely provides extra growth of the esophageal ends resulting in primary anastomosis. The esophagostomy allows sham feeds to prevent oral aversion and subsequent feeding problems without the risk of aspiration while awaiting esophageal replacement.

Two other surgical options to maintain the native esophagus include the Foker traction technique and the extrathoracic elongation technique of Kimura. The Foker technique involves placing traction sutures on both segments of esophagus and attaching them under tension to the prevertebral fascia if the gap is of moderate length, or bringing them out through the back and increasing tension on them sequentially over the ensuing 2 weeks. When the ends of the two segments of esophagus approach each other, a repeat thoracotomy with primary anastomosis completes the repair

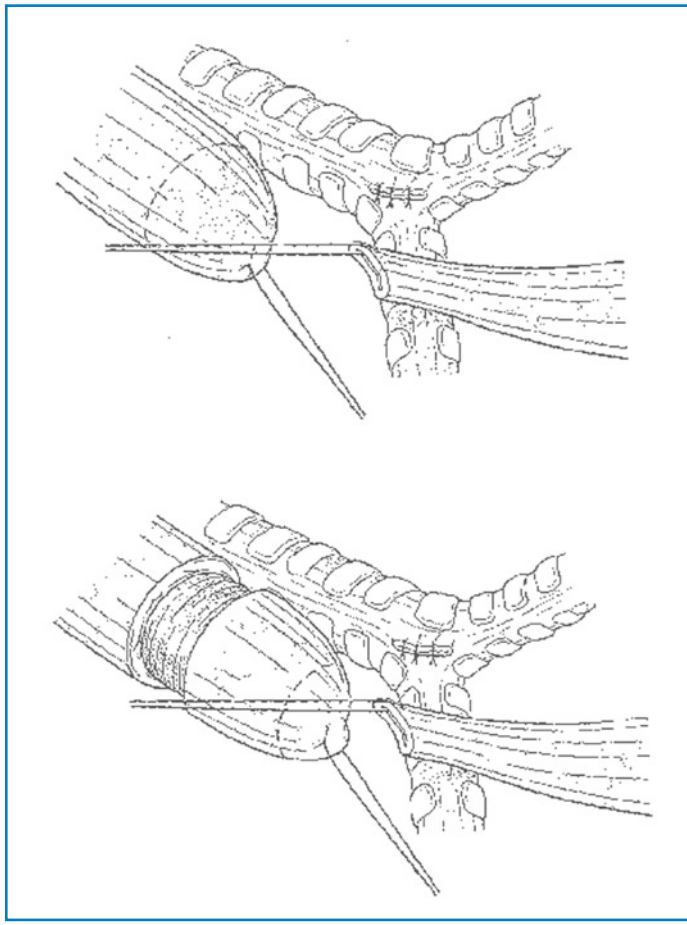

Fig. 8.6 A circular myotomy of the upper pouch extending its length by 1 cm

(Fig. 8.8) [72]. The Kimura technique involves mobilization of the proximal pouch and bringing it out as an end cervical esophagostomy. Then, every 2–3 weeks, the esophagus is mobilized and moved down the anterior chest wall until enough length is obtained to complete an end-to-end esophageal anastomosis *via* a thoracotomy [73].

The final special situation is the H-type tracheoesophageal fistula without esophageal atresia. To repair this fistula, a Fogarty catheter is placed across the fistula using rigid bronchoscopy and esophagoscopy. Exploration of the right neck through an incision just above the clavicle allows identification and division of the fistula. Palpation of the Fogarty catheter assists in finding the fistula (which is quite difficult without a catheter *in situ*). If possible, muscle or other vascularized tissue is placed between the suture lines to help prevent recurrence of the fistula.

8.9 Complications

Complications after repair of esophageal atresia and tracheoesophageal fistula relate to the anastomosis and the underlying disease. The anastomotic problems include anastomotic leaks, anastomotic strictures, and recurrent formation of a tracheoesophageal fistula. The issues related to the underlying disease include gastroesophageal reflux and tracheomalacia. The incidence of anastomotic problems seen after repair varies directly with the amount of tension used to create the anastomosis.

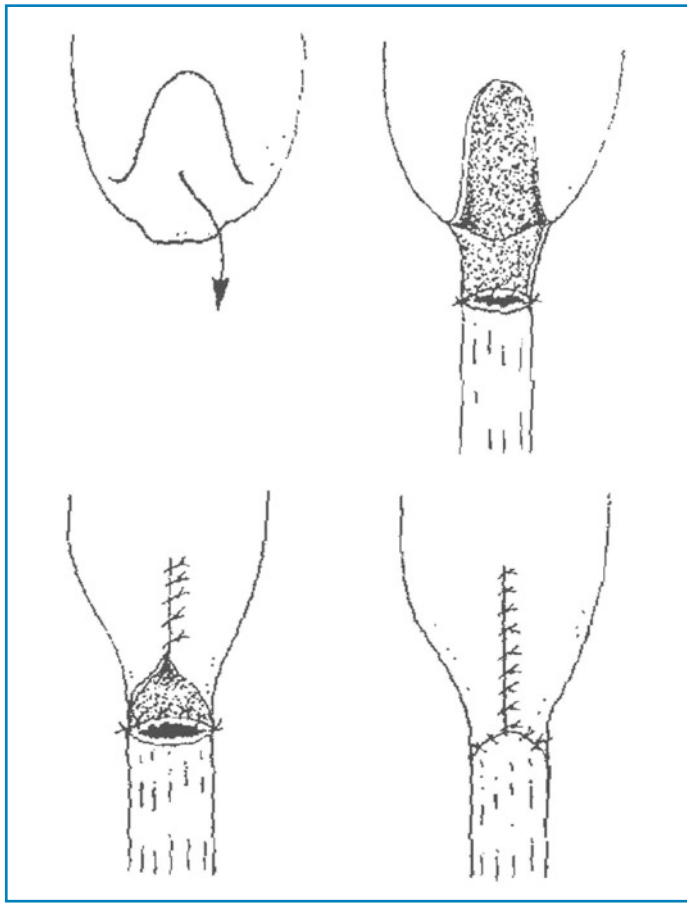

Fig. 8.7 Tubularization graft of the upper pouch

The incidence of leak at the anastomosis varies from 5% to 20% [45]. Most of these leaks seal in 1–2 weeks with conservative management, including parenteral nutrition, intravenous antibiotics, drainage, and withholding oral feeds. Complete disruption of the anastomosis, a rare complication occurring in <2% of cases, causes tension pneumothorax and significant salivary drainage from the chest tube. This scenario may require early thoracotomy and revision of the failed anastomosis, or cervical esophagostomy, gastrostomy, and subsequent esophageal replacement.

Anastomotic strictures occur in one-third to one-half of repairs [74]. Factors implicated in stricture formation include tension at the anastomosis, anastomotic leak, and gastroesophageal reflux [75, 76]. All repairs will show some degree of narrowing at the anastomosis, so dilations are reserved for symptomatic strictures, associated respiratory symptoms, foreign-body obstruction or those causing dysphagia. Most strictures require repeat dilation every 3–6 weeks over a 3–6-month period. Two recent series of esophageal strictures after repair of esophageal atresia revealed an average of 2.8–3.2 dilations required per stricture over an average of 7 months [75, 76]. Recalcitrant strictures often occur in association with gastroesophageal reflux and do not resolve until the reflux is controlled by medical or surgical means.

The prevalence of recurrent formation of tracheoesophageal fistulas ranged from <1% to 12% in various series [45, 77-80]. These children present with coughing, choking, and

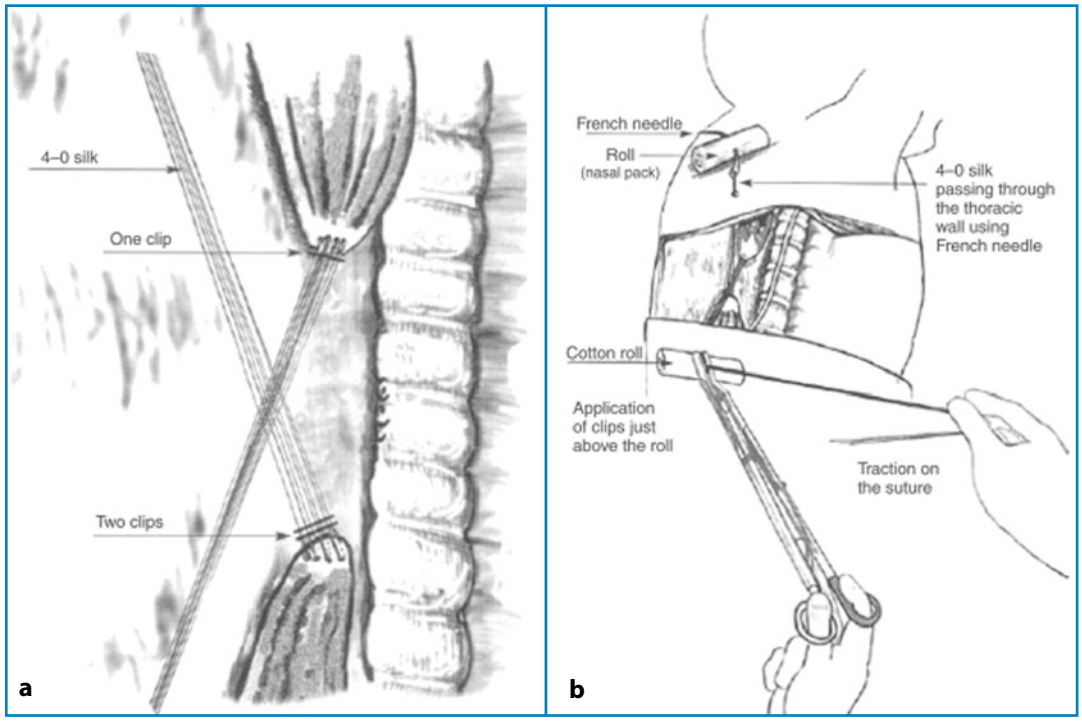

Fig. 8.8 Foker traction technique. Traction sutures are placed on each esophageal segment (**a**). The sutures are brought out the back of the infant and traction is increased incrementally until the two segments are close enough for anastamosis (**b**)

occasional cyanotic episodes with feeding, and with recurrent pulmonary infections. Recurrent fistulas are often associated with anastomotic leaks, but the possibility of a missed proximal fistula must also be entertained [81]. These fistulas are often small and sometimes difficult to diagnose. A prone, pullback esophagram combined with bronchoscopy with esophagoscopy are used to diagnose recurrent fistulas. A repeat right thoracotomy with closure of the fistula is a difficult procedure. Placement of a ureteral catheter in the fistula at bronchoscopy just before opening the chest improves the likelihood of identifying the fistula tract. After identification and division of the fistula, a viable piece of tissue (usually a vascularized muscle flap or a portion of pleura or pericardium) placed between the suture lines helps prevent recurrence of the fistula, which occurs in 11% to 20% of these repairs [79, 80]. Other techniques to close these fistulas have been attempted with varying success, including endoscopic diathermy [82], Nd:YAG [83] or KTP laser obliteration of the fistula [84], injection of sclerosing agents [85], and injection of fibrin glue [86]. If using these approaches, it is important to obliterate the mucosal lining of the fistula tract prior injecting agents to occlude the fistula. These techniques may be repeated, but if they continue to fail, surgical closure is required.

Gastroesophageal reflux commonly occurs in patients after esophageal atresia and tracheoesophageal fistula repair. Poor distal esophageal motility resulting in abnormal esophageal clearance accompanied with an altered angle of His due to the tension on the distal esophagus predispose these children to reflux. Using videomanometry with topographic analyses, Kawahara found two subgroups of patients after repair of esophageal atresia and tracheoesophageal fistula. Neither group had esophageal contractions at the anas-

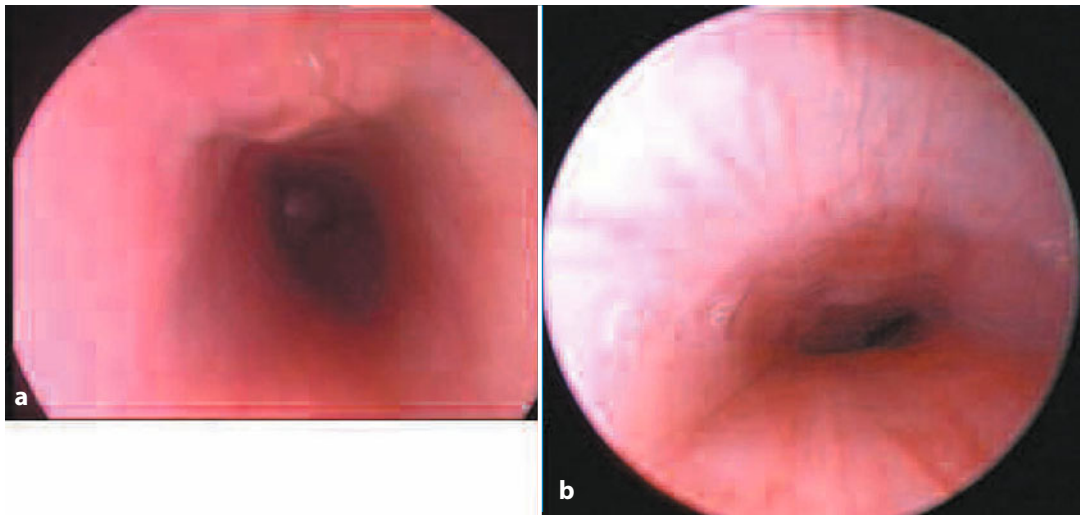

Fig. 8.9 Bronchoscopic view of the trachea in an infant with tracheomalacia. The trachea is open (**a**) during inspiration, and collapses on itself during expiration (**b**)

tomosis. One group had distal esophageal contractions and did not develop reflux, whereas the other group did not have distal contractions, and 15 of 17 developed symptomatic gastroesophagael reflux [87]. Significant gastroesophageal reflux occurs in 30% to 60% of children after repair of esophageal atresia and tracheoesophageal fistula [45, 77, 88]. In an adult series of patients born with esophageal atresia compared with normal controls, Sistonen et al. found symptomatic reflux in 34% compared with 8% of controls, dysphagia in 85% compared with 2%, and at endoscopy found more hiatial hernias (28%), strictures (8%), chronic esophagitis (8%) and Barrett's esophagus (11%) compared with controls [89]. Treatment begins initially with acid-reducing and prokinetic agents, but often patients require a fundoplication to control the reflux, especially if a stricture develops which is resistant to dilation, or if repeated pulmonary aspiration associated with reflux complicates the postoperative course. Careful consideration should be given to a partial fundoplication in these children because of their abnormal distal esophageal motility. The choice of a complete or partial fundoplication is left to the surgeon [90–92]. A comparison of fundoplications done in babies with and without esophageal atresia and tracheoesophageal fistula revealed that those with esophageal atresia had more intraoperative and postoperative complications and more problems with recurrent reflux, dysphagia and dumping after the fundoplication [93].

Significant tracheomalacia occurs in 10% to 20% of children with esophageal atresia and tracheoesophageal fistula [45, 94]. Tracheomalaciais a generalized or localized collapse of the tracheal lumen causing obstruction during respiration, and is considered pathologic if the obstruction is >50% of the lumen [95]. This results in expiratory stridor and episodes of desaturation, apnea, cyanosis, and bradycardia, and is often associated with feeds. The upper tracheal cartilage becomes weakened due to the pressure exerted from the fluid-filled dilated upper esophageal pouch during fetal life. Tracheomalacia, in its severe form sometimes prevents extubation after repair of the esophageal atresia and tracheoesophageal fistula. Determining the etiology of this symptom complex can be difficult because tracheomalacia and gastroesophageal reflux occur frequently in this population and produce similar symptoms. Rigid bronchoscopy in a spontaneously breathing patient provides the diagnosis. The trachea will flatten anteroposteriorly

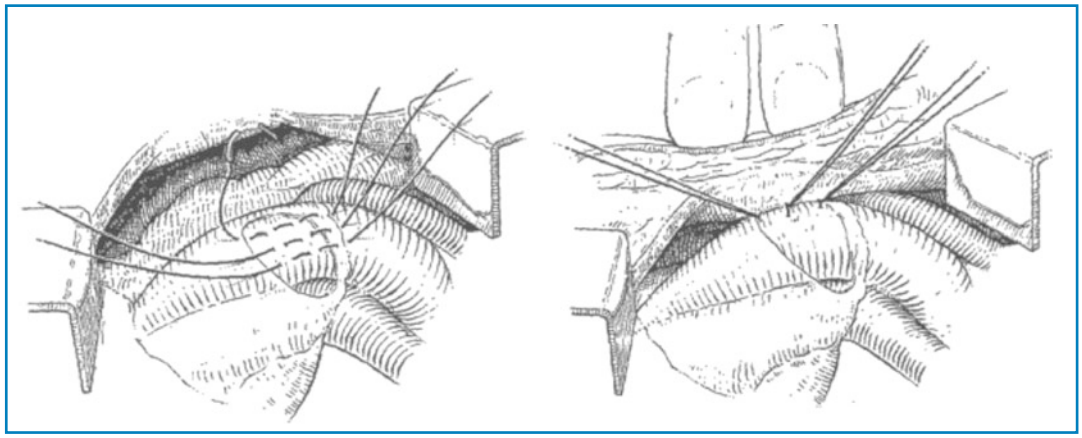

Fig. 8.10 Through an anterior second interspace thoracotomy, sutures are placed in the adventitia of the ascending aorta, fixing it to the posterior sternum, thus stenting the underlying trachea open. This is confirmed bronchoscopically during the procedure

("fishmouth") on expiration (Fig. 8.9). Tracheomalacia is often self-limiting, but may require intervention in children with severe life-threatening symptoms. If treatment with continuous positive-airway pressure is ineffective, then aortopexy [96] (Fig. 8.10) or tracheal stenting may be required [97]. Aortopexy fixes the adventitia of the aorta to the posterior sternum, thus stenting open the underlying trachea. Aortopexy remains the treatment of choice because the optimal tracheal stent for infants has not been developed [95]. Symptomatic tracheomalacia requires intervention in up to 5% of children with esophageal atresia [98].

8.10 Outcome

The outcome for infants with esophageal atresia and tracheoesophageal fistula has improved over time to the point where, unless the infant has major cardiac anomalies, significant chromosomal abnormalities, severe pulmonary complications, or a birth weight <1,500 g, he/she will survive. The long-term problems after esophageal atresia and tracheoesophageal fistula repair include pulmonary issues (especially reactive airway disease, bronchitis, and pneumonias) and upper gastrointestinal complaints of dysphagia and gastroesophageal reflux. There is a strong connection between the severity of the gastroesophageal reflux and the persistence of respiratory symptoms in these patients [99]. Pulmonary symptoms severe enough to require hospitalization occur in close to half of children after repair of their esophageal atresia and tracheoesophageal fistulas [100]. Although the pulmonary symptoms tend to persist into adulthood, they are mild and do not affect the activities of daily life [101]. The dysphagia and gastroesophageal reflux commonly seen in these children stem from the altered intrinsic innervation of the distal portion of the esophagus, leading to the dysmotility that contributes to the dysphagia and reflux. The dysmotility continues into adulthood. In manometric studies of adults with repaired esophageal atresia, the overriding long-term motility deficits are uncoordinated peristaltic activity and low-amplitude contraction of the distal esophagus. Interestingly, the swallow-induced relaxation of the lower esophageal sphincter remains normal. This abnormal esophageal motility results in dysphagia symptoms in up to 60% of adults and in gastroesophageal reflux. Symptoms of dysphagia occur more commonly in adults with pure esophageal atresia compared with those with esophageal atresia with a distal tracheoe-

sophageal fistula [102]. Using 24-h pH monitoring and esophageal biopsy data, the prevalence of gastroesophageal reflux has been documented in infants, in children up to age 10 years, and in adults after esophageal atresia repair. The prevalence of reflux was similar in the three age groups: 41% in infants, 45–50% in children up to age 10 years, and 40% in adults. In the group of children up to age 10 years, no new cases of histologic esophagitis or abnormal pH measurements occurred after age 5 years. The gastroesophageal reflux appears to develop early and persist after esophageal atresia repair [102]. Esophageal strictures are uncommon as a late complication. If a stricture does occur late in the course, it is usually associated with gastroesophagaeal reflux. Barrett's esophagus occurs in up to 11% of these patients [89]; how many of these progress on to esophageal adenocarcinoma remains uncertain [103]. Age, surgically treated anastomotic stricture in infancy, recurrent tracheoesophageal fistula, myotomy of the upper esophageal pouch, anastomotic stricture in adulthood, low distal esophageal wave amplitudes, and non-propagating peristalsis were found to be strong predictive factors for epithelial metaplasia in adults with esophageal atresia treated as infants [89]. There have been 6 reported cases of esophageal cancer in patients who had their esophageal atresia repaired at birth. Three of these were squamous cell carcinomas, and 3 were adenocarcinomas. These cases developed early between the ages of 20 years and 46 years [102]. However, a population-based, long-term follow-up study of 502 patients with repaired esophageal atresia over 50 years in Finland revealed 3 cases of cancer, none being esophageal or gastric [104]. Several quality of life (QoL) measures have been used to assess the long-term outcomes of adults after repair as an infant. A Dutch study of QoL in adults after repair of esophageal atresia and tracheoesophageal fistula compared with healthy subjects found no difference in overall physical or mental health between the two groups. However, former esophageal atresia patients reported worse "general health" and less 'vitality" than the healthy subjects because of continued gastrointestinal difficulties reported in up to one-quarter of the esophageal atresia group. Marital and family status did not differ from that of the general Dutch population [105]. A recent QoL study in patients aged 6–18 years with esophageal atresia revealed similar results: the general health was reduced compared with the reference population due to gastrointestinal symptoms and a high incidence of congenital anomalies [106]. The QoL of adults after a colonic interposition as an infant is not as good as it is for adults who had a primary repair. In addition, children with esophageal atresia and tracheoesophageal fistula have more learning, emotional, and behavioral problems than the normal population of children. This in part because of their associated anomalies, including varying degrees of prematurity, and their initial ICU course, which often involves mechanical ventilation for a period of time [107].

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Esophageal Malformations

9

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9.1 Laryngotracheoesophageal Clefts (LCs)

LCs are rare congenital anomalies consisting of a midline defect along the posterior portion of the larynx and trachea as well as the anterior portion of the esophagus, leaving a communication between these structures of varying lengths. Pattersson carried out the first successful repair of a LC in 1955 [1]. Benjamin and Inglis classified LCs into four types. Type I is a supraglottic interarytenoid cleft. Type II extends into (but not through) the posterior cricoid lamina. Type III extends through the cricoid and can involve the cervical trachea. Type IV extends below the thoracic inlet [2].

9.1.1 Presentation

In general, symptoms begin shortly after birth. Their severity correlates with the extent of the cleft. Some type-I clefts remain relatively asymptomatic, but most infants present with respiratory distress worsened with feeds, an absent or weak cry, hoarseness, stridor, inability to handle secretions, and aspiration pneumonia. Various congenital anomalies occur in association with LCs. Esophageal atresia and tracheoesophageal fistula occur in 20% to 37% of infants with clefts, and 6% of infants with esophageal atresia and tracheoesophageal fistula have a concomitant cleft. Other malformations include gastrointestinal (16–65%), genitourinary (14–44%), and cardiovascular anomalies (16–33%) [3].

9.1.2 Diagnosis

Contrast studies and bronchoscopy (often in conjunction) diagnose LCs in infants with suspicious symptoms. A LC is often picked up on a contrast esophagram. However, it is sometimes difficult to tell the difference between a small proximal cleft and contrast spillover from the pharynx and esophagus into the trachea. Although rigid bronchoscopy usually defines the defect, a high index of suspicion must be maintained during the bronchoscopy otherwise the small proximal cleft may be overlooked. Careful exploration of the posterior laryngeal wall is required because the mucosal folds in that area tend to obscure the clefts.

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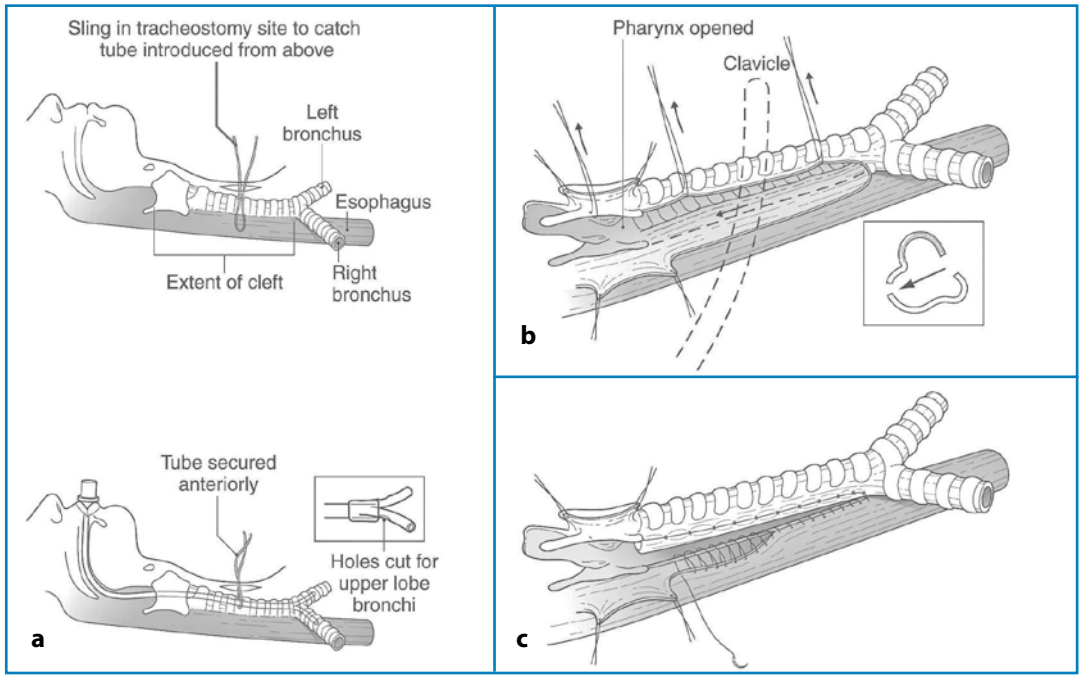

Fig. 9.1 Repair of a type-III laryngotracheoesophageal cleft. A bifurcated endotracheal tube held anterior against the trachea allows ventilation (**a**). A cervical and thoracic approach allows retropleural exposure of the cleft (**b**). The trachea and esophagus are separated, leaving ≈1 cm of esophageal wall attached to the trachea to allow adequate tissue to close the trachea. The trachea has been closed with interrupted sutures, and the esophagus closed

9.1.3 Treatment

Preoperative care focuses on avoidance of aspiration and stabilization of the airway. Depending on the severity of the cleft, some infants require a gastrostomy tube for feeds in addition to intubation to secure the airway prior to definitive repair. The type of repair depends on the severity of the cleft. Often, type-I clefts require no surgical treatment or may be repaired with endoscopic techniques [4]. For type-II and -III clefts, an anterior approach to the larynx and upper trachea is utilized. A lateral approach may be used which puts the recurrent laryngeal nerves at risk, but leaves less laryngeal instability and may avoid prolonged postoperative intubation. The lower (type IV) clefts require a right thoracotomy or a median sternotomy (Fig. 9.1). The tracheal and esophageal walls are divided along the length of the cleft. A small strip of esophagus remains with the trachea mimicking the posterior membranous portion of the trachea and allowing adequate closure of the trachea. The esophagus is closed over a nasogastric tube to complete the repair. Use of a special bifurcated endotracheal tube allows ventilation during repair [4]. Cardiopulmonary bypass and extracorporeal membrane oxygenation are sometimes used as adjuncts to ensure successful repair.

9.1.4 Outcome

Results are good for type-I, -II and -III clefts, but continue to be poor for type-IV clefts. Survival after repair is 75%, with anastomotic leaks occurring in ≤50% of repairs [3]. A review of the Great Ormond Street experience reinforced that the longer the cleft, the worse the prognosis. In their series, the 4 infants with

clefts ending proximal to the carina all survived, but all 5 infants with clefts extending to the carina died [5]. In addition, these infants had difficulty with pharyngoesophageal dysfunction, gastroesophageal reflux, and inability to wean from the ventilator after repair. Early recognition of the cleft and thus early treatment may reduce some of the secondary complications.

9.2 Esophageal Duplication Cysts (EDCs)

EDCs were first reported in 1711 by Blasius [6]. These duplications can occur in the cervical or thoracic esophagus, and on occasion the thoracic duplications will extend into the upper abdominal cavity. Cervical esophageal duplications are very rare. The first duplication cyst of the cervical esophagus was reported in 1964 by Bishop and Koop [7]. In an autopsy study by Arbona, the incidence of esophageal duplication cysts was 1 in 82,000, with a 2:1 male-to-female predominance [8].

EDCs are defined by three characteristics: a cyst attached to the esophageal wall, covered by two layers of muscle, and an epithelium that represents some level of the gastrointestinal tract [6]. The epithelium contained in the duplication is most often esophageal, but up to one-third contain gastric mucosa which may lead to ulceration, bleeding, or perforation. Up to 80–90% of esophageal duplication cysts do not communicate with the esophageal lumen. Sixty percent are located in the distal esophagus [9]. Some esophageal duplication cysts are referred to as "neuroenteric cysts". They connect to the spinal canal and are associated with vertebral anomalies [10]. In addition to their association with vertebral anomalies (scoliosis, hemivertibra, fusion), esophageal duplication cysts have also been described with small intestinal duplications, esophageal atresia and tracheoesophageal fistula, pulmonary abnormalities (e.g., congenital cystic adenomatoid malformations) and pericardial defects [11, 12]. A recent literature review identified 12 cases of esophageal duplication cysts associated with esophageal atresia. Of those, 5 were not identified at the original repair [13]. The embryology of esophageal duplication cysts is not known. Several theories have been described, including a failure of recanalization of the esophagus in the fifth to eighth weeks of embryonic life [14], and the split notochord theory [15].

9.2.1 Presentation

EDCs present in several ways depending on their location and the type of mucosa that lines the cyst. Some (especially those of small size) remain asymptomatic. Of those that become symptomatic, 70-95%, present before the age of 2 years [16]. The rare cervical esophageal duplication cysts most commonly present with respiratory symptoms due to tracheal compression [10]. However, they can also present with feeding difficulties or an enlarging neck mass due to infection, hemorrhage, or a build-up of secretions [14]. Thoracic EDCs can present with symptoms varying from respiratory symptoms, to dysphagia, to symptoms secondary to acid production of the gastric mucosa lining the cyst. The cysts in the mid-to-upper thorax generally cause respiratory symptoms due to tracheal compression. Cysts that lie in the vicinity of the mainstem bronchus can cause compression leading to hyperinflation of the ipsilateral lung that often requires resection in the neonatal period [17]. Most of the cysts are located in the distal third of the esophagus. Of these, 70% present with dysphagia, 20% with epigastric discomfort, and the remaining 10% with retrosternal pain [10]. A gastric mucosa is found in up to one-third of EDCs and can be responsible for a myriad of symptoms. Acid production from the gastric mucosa can lead to ulcer formation. The ulcer can bleed or perforate, causing different symptoms depending on the location of the cyst. If the bleeding occurs in the esophagus it may present as hematemesis or as melena. Bleeding in the

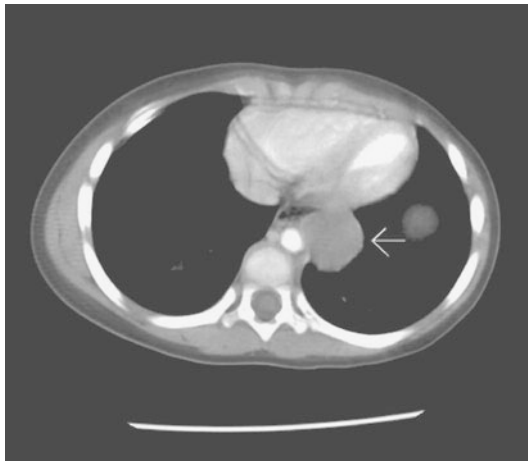

Fig. 9.2 Esophageal duplication cyst (*arrow*) seen extending into the left chest from the posterior mediastinum

trachea leads to hemoptysis that may be life-threatening. If the ulcer perforates into the pleural space it can cause chemical pleurisy, an empyema, or a pneumothorax [18]. Recently, EDCs are being discovered prenatally with ultrasonography or fetal magnetic resonance imaging (MRI) [19].

9.2.2 Diagnosis

Imaging studies confirm the diagnosis of an EDC. Plain radiographs may reveal deviation or compression of the trachea or esophagus by a soft tissue mass. Such esophageal deviation may be better seen with a nasogastric tube *in situ*. Esophageal contrast studies reveal extrinsic compression of the esophagus from the mass effect and may show communication between the cyst and esophagus on the rare occasion that it is present [14]. With the diagnosis suspected from the plain radiograph and contrast studies, further information regarding the size, exact location, and anatomic relationship to other mediastinal structures is useful prior to surgical intervention. Ultrasonography, computed tomography (CT), and MRI provide this information. Ultrasonography reveals a cystic mass with a typical gut signature of the walls consisting of inner hyperechoic mucosa and outer hypoechoic muscle. It may also identify debris inside the cyst, suggesting infection or hemorrhage. CT (Fig. 9.2) and MRI better identify the location and extent of the cyst, revealing extension into the abdominal cavity and mass effect on the airways if present. MRI rather than CT is utilized due to the lack of exposure to radiation. MRI is favored if one suspects a neuroenteric cyst [17].

9.2.3 Treatment

Treatment of EDCs is complete excision. The cysts must be separated from structures in the mediastinum, and then dissected away from the common wall with the esophagus. The esophageal muscular wall is opened, and an extramucosal dissection undertaken to remove the entire cyst while leaving the native esophageal wall intact. This may be done through an open thoracotomy, or minimally invasively using thoracoscopy [20–22] or a surgical robot [23]. One of the difficulties when carrying out this operation in a minimally invasive fashion is ensuring the esophageal mucosa remains intact during the dissection. The use of intraoperative endoscopy with insufflation during the procedure helps prevent esophageal injury [21]. The decision to remove the duplication cyst in a minimally invasive fashion should belong to the surgeon. However, some situations that may require a thoracotomy include compressive subcarinal cysts with secondary lung hyperinflation and mediastinal shift, and previously infected duplication cysts [19]. If for some reason the entire cyst cannot be removed, it is important to remove all of the mucosa so the cyst cavity does not recur.

9.2.4 Outcome

With appropriate treatment, children with esophageal duplication cysts should have excellent surgical outcome and overall quality of life.

9.3 Achalasia

Achalasia is an esophageal motor disorder resulting in increased lower esophageal sphincter resting pressure, incomplete relaxation of the lower esophageal sphincter after swallowing, and an absence of esophageal peristalsis. This leads to a dilated non-functioning esophagus with a functional obstruction at the gastroesophageal junction. Achalasia occurs infrequently in all ages, but only 5% of achalasia occurs in childhood. The incidence of achalasia in children has been on the increase. Large population studies of the incidence of achalasia in children have noted an increase from 0.11 to 0.18 cases per 100,000 children per year from 1988 to 2008 [24, 25]. In children, achalasia usually occurs in isolation during the teenage years, but has been associated in younger children with trisiomy 21 and Allgrove (triple A) syndrome (consisting of achalasia, alacrima, and adrenal insufficiency) and with familial dysautonomia [26]. Under the microscope, an esophagus affected with achalasia will have a reduction in the number of myenteric neurons (especially the inhibitory nitric oxide-releasing neurons in the distal esophagus and lower esophageal sphincter) [27]. This is thought to result from an autoimmume-mediated destruction of these inhibitory neurons in response to an unknown insult in genetically susceptible individuals [28].

9.3.1 Presentation

Although infants have been identified with achalasia, the symptoms most often develop in the early teen years. Several recent studies recorded the average age at diagnosis to be between 7.8 years and 13 years of age, with the earliest diagnosis at 1 month of age [25, 29–33]. Symptoms often continue for a prolonged period prior to the diagnosis, with average times from symptom onset to diagnosis varying from 7.2 months to 30 months [29–32]. The main symptoms include dysphagia, vomiting and regurgitation. In addition, retrosternal chest pain, recurrent respiratory symptoms (including cough or dyspnea after meals, and nocturnal cough), failure to thrive or weight loss, drooling, and food sticking have been reported. In a review of 40 children with achalasia, 72.5% presented with dysphagia, 60% with emesis, 30% with food sticking, 27.5% with cough, and 52.5% with weight loss [34].

9.3.2 Diagnosis

Achalasia is evaluated with a contrast esophagram, upper endoscopy, and esophageal manometry. Most often all three examinations are done to obtain the diagnosis, but some clinicians obtain manometry only if a question arises after the esophagram and endoscopy [29]. Contrast esophagography (Fig. 9.3) reveals a dilated esophagus with retained contrast,

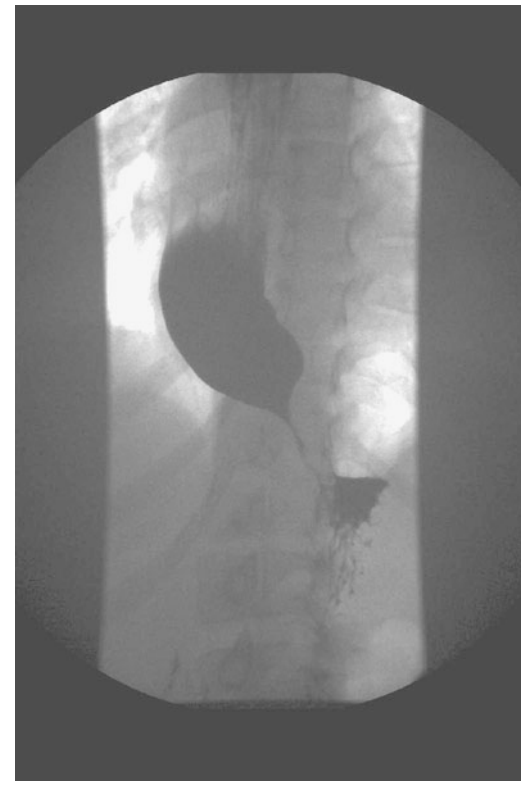

Fig. 9.3 Esophageal contrast study reveals a dilated proximal esophagus and the "bird's beak" appearance of the distal esophagus in achalasia

smooth tapering of the distal esophagus accounting for the "bird's beak" appearance, and a lack of peristalsis in the body of the esophagus. These are classic findings, but a normal esophagram does not necessarily exclude early achalasia [26]. Endoscopy reveals a distended esophagus with retained food or secretions, but no obstruction at the gastroesophageal junction. Endoscopy can also be normal in up to 44% of cases of achalasia [28]. Esophageal manometry has the highest sensitivity of the three diagnostic studies [28]. Manometry reveals aperistalsis of the smooth-muscle portion of the esophagus, incomplete relaxation of the lower esophageal sphincter, and an elevated lower esophageal sphincter resting pressure. Recently, high-resolution manometry of the esophagus (which displays manometric data as pressure contour plots) demonstrated the functional anatomy of the esophagus and could be obtained in children without sedation [35].

9.3.3 Treatment

The aim of treatment for achalasia is to relax or disrupt the lower esophageal sphincter. Three modalities are commonly used: pharamacological, endoscopic (including dilation and injection of botulinum toxin) and surgical myotomy with or without a fundoplication to protect against gastroesophageal reflux. The pharamacological agents used to achieve a reduction in lower esophageal sphincter pressure include calcium-channel blockers, nitrates, and phosphodiesterase-5 inhibitors. These agents provide an initial improvement in 50–90% of patients, but are short-acting and have a significant side-effect profile [36]. Pharmacolo-gical treatment should be limited to patients unwilling or unable to undergo other procedures. Pneumatic dilation involves placing a dilating balloon in the lower esophagus and expanding the balloon to rupture the muscle fibers of the lower esophageal sphincter. The main risk of dilation is perforation, which occurred in 1.6% of patients studied in a meta-analysis [37]. The long-term success ranges from 40% to 60% over 15 years [28]. Predictors of failure of dilation include younger age, male sex, pulmonary symptoms, failure to respond to 1–2 initial dilations, and manometric findings of a high initial lower esophageal sphincter pressure (>15–30 mmHg), or reduction in lower esophageal sphincter pressure <50% of baseline after the first dilation [28]. Botulinum toxin blocks the release of acetylcholine from excitatory motor neurons, thereby relaxing the lower esoph-ageal sphincter. Occasionally, the initial injection does not provide relief and, if this occurs, future injections rarely (if ever) are effective. Repeat injections are often needed because the prevalence of recurrence at one year is 50%, and patients are universally symptomatic at 2 years [28].

Given the need for long-term results in children, surgical myotomy is often the first approach in this population. A Heller myotomy consists of division and dissection of the muscular wall of the esophagus from the mucosa ≤4 cm from the gastroesophageal junction onto the esophagus, and 2–3 cm onto the stomach. This disruption of the lower esophageal sphincter may lead to postoperative gastroesophageal reflux and its complications, so a partial or complete fundoplication is often added to the myotomy. The procedure can be completed in an open or minimally invasive fashion from the abdomen or chest. The preferred approach is the laparoscopic abdominal approach. Adult data show that the risk of subsequent intervention for pneumatic dilation is 56% compared with 26% for surgical myotomy. Comparing pneumatic dilation to Heller myotomy with a Dor partial fundoplication at 5-year follow-up, 95% of subjects treated with a myotomy had a good result compared with 65% for pneumatic dilation. However, the success of surgery decreased to 75% at 15-year follow-up. Of the patients treated with a myotomy who had a poor result, 92% developed reflux that was the cause of the poor outcome, not an incomplete myotomy [28]. Addition of a Dor partial fundoplication to the Heller myotomy

decreased the prevalence of postoperative reflux from 47.6% to 9.1%. Comparing a Dor partial fundoplication to a Nissen complete fundoplication, the reflux was similar, but those treated with a Nissen developed dysphagia 15% of the time compared with a 2.8% in those treated with the Dor partial fundoplication [28]. At the time of surgery, endoscopy can be used to evaluate a perforation and the completeness of the myotomy. The endoscope is inserted, the distal esophagus is inspected, and gentle insufflation is used to open the lower esophageal sphincter. If the sphincter fails to open, a longer myotomy onto the stomach is required. Using this method, in one study, 3 of 5 patients required an extension of the myotomy after the endoscopy, and none of the 5 required further surgery for achalasia [33]. Postoperative manometry may help predict which patients will develop postoperative symptoms. If the lower esophageal sphincter pressure was <12 mmHg after the myotomy, patients had no recurrent symptoms, whereas those who had postoperative pressures >12 mmHg tended to develop symptoms [36]. If these modalities fail, esophagectomy and gastric pull-up remain an option.

9.3.4 Outcome

Less-than-acceptable outcomes with achalasia stem from three sources – the natural history of the disease, treatment-related complications, and late consequences of successful therapy. The natural history of achalasia can lead to problems related to aspiration, megaesophagus, and squamous cell cancer of the esophagus. Structural pulmonary disease thought to emanate from micro-aspiration occurs in 33% of patients with achalasia. A megaesophagus will develop in 10% of achalasia patients 18–21 years after the onset of symptoms. This may be related to a delay in the diagnosis or treatment, but can occur even after a successful myotomy. Treatment-related complications include perforation with pneumatic dilation and with laparoscopic Heller myotomy. A large meta-analysis found that pneumatic dilation carries a prevalence of perforation of 1.6% with a range of 0–8% in various series. The laparoscopic Heller myotomy had a prevalence of perforation of 0.7% with a range of 0–8%. The overall postoperative prevalence of complications with myotomy was 6.3% with a mortality of 0.1% [37]. The late consequences of successful therapy can also lead to morbidity. Overall, 10% of patients with achalasia undergoing pneumatic dilation or laparoscopic Heller myotomy will develop reflux esophagitis, and 43% will require acid-suppression therapy. Post-procedure reflux is more common in those treated with a myotomy (14% *versus* 5%) in those undergoing pneumatic dilation. Of these patients who develop post-procedure reflux, one-half will develop the late complications of reflux (most commonly a stricture) [28]. Two types of esophageal cancer develop in achalasia patients: squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma occurs more commonly, and is thought to develop from stasis that leads to bacterial overgrowth, production of nitrosamines, chronic inflammation, dysplasia and, eventually, cancer. Adenocarcinomas are thought to result from longstanding reflux. A prospective study following achalasia patients for a mean period of 15 years found a prevalence of 3.3% of esophageal cancer in the population. These cancers developed at a mean period of 11 years after the diagnosis of achalasia, and a mean period of 24 years after the onset of symptoms. The hazard ratio for achalasia patients to develop esophageal cancer was 28 [38]. Using a pediatric quality-of-life instrument, children with achalasia were found to have a quality of life after being treated with a Heller myotomy that was lower than those of healthy children and children with inflammatory bowel disease, but comparable with that of children with chronic constipation [39].

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Esophageal Strictures and Stenoses

10

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10.1 Introduction

The diagnosis and management of esophageal obstructions, namely strictures and stenoses, can be quite intimidating and challenging for the surgeon. We discuss in this chapter the many different types of esophageal obstructions and outline the major principles involved in their management. A careful understanding and thoughtful approach to the their treatment remains paramount to achieve optimal outcomes. Depending on the nature and etiology of the narrowing, the therapeutic options can range from pharmacotherapy alone to complex surgery, including esophagectomy with conduit reconstruction. More recently, endoscopic interventions have made a dramatic impact in many children previously thought to have a problem amenable only to major reconstructive esophageal surgery.

10.2 Epidemiology

Esophageal obstructions are relatively uncommon. The exact incidence within the pediatric population is not known. According to one estimate, there are >5,000 major caustic ingestions per year in the USA, of which ≈20–25% will result in an esophageal stricture [1]. Most caustic esophageal strictures occur in the setting of accidental ingestion, so most of these affected children are <5 years of age, with a peak incidence at 2 years of age [2]. Legislative efforts, including the United States Federal Hazardous Substances Act and the Poison Prevention Packaging Act of 1970, require that corrosive substances be packaged in such a way that it would be difficult for children <5 years to open them, yet not too difficult for adults to open them. Fortunately, such preventive measures have been effective in reducing the incidence of these tragic injuries. Nevertheless, in some "developing" countries, there continues to be an alarmingly high incidence of caustic esophageal injuries because of a lack of childproof containers.

Historically, the number of strictures secondary to gastroesophageal reflux disease (GERD), a common disorder in infants and children, has been estimated to occur in ≤15% of affected patients. However, more recent data suggests that this prevalence has probably decreased markedly with the widespread use of acid blockers, particularly proton pump inhibitors (PPIs) [3, 4]. Other causes of esophageal strictures and stenoses occur at a much lower frequency. For example, congenital esophageal stenosis is estimated to occur in 1 in 25,000–50,000 live births.

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10.3 Etiology and Pathogenesis

The more common disease processes (acquired and congenital) associated with esophageal strictures and stenoses are discussed below.

Caustic ingestion: Historically, caustic injuries have been the most common cause of esophageal strictures in children [5]. Many corrosive products contain sodium hydroxide or potassium hydroxide, and are therefore strong bases (pH >12). The usual alkaline agents include lye, caustic sodas, dishwashing detergents, disinfectants, degreasers, and drain cleaners.

Bases are particularly dangerous for young unsuspecting children because these substances are often tasteless and can cause extensive liquefactive necrosis, resulting in full-thickness esophageal damage and fibrotic strictures if ingested accidentally in small amounts. The consequences of these injuries, such as mediastinitis, tracheoesophageal fistula, and aortoesophageal fistula, are potentially lethal.

Acids (pH <1.5) can also be dangerous if ingested but are usually foul-tasting and cause less esophageal damage. The more common acidic agents are toilet-bowl cleaners, paint thinners, batteries, and metal cleaners. Most acids induce injury by coagulation necrosis, resulting in an eschar formation that is more superficial compared with injuries from bases. However, button batteries can cause significant esophageal damage, including tracheoesophageal fistula, from electrical discharge and direct pressure necrosis [6].

Gastroesophageal reflux (GER): Peptic esophageal strictures are the result of uncontrolled, chronic exposure of refluxed gastric acid onto the adjacent esophageal mucosa. Strictures of variable severity can develop over time secondary to recurrent inflammation with subsequent submucosal fibrosis. Most (but not all) of these strictures are located in the distal esophagus. Barrett's esophagitis, a potential precursor to esophageal adenocarcinoma, has been identified within some of these strictures in older children [7].

Eosinophilic esophagitis (EoE) has been an increasingly recognized cause of pediatric esophageal strictures over the last 15 years. In the past, many of these patients were thought to have GERD but showed a poor response to acid blockade medications. Pathology specimens of the esophagus in EoE are characterized by dense eosinophilic infiltrates with squamous hyperplasia.

Anastomotic strictures: The reported prevalence of strictures in neonates after repair of esophageal atresia is ≤37% depending on how these strictures are defined by authors [8, 9]. Known risk factors for stricture formation include increased tension, ischemia, acid reflux, and the use of silk sutures [10]. Additionally, stricture formation at the anastomosis is common after an anastomotic leak treated by non-surgical means.

Esophageal stenosis: Some infants are diagnosed with an intrinsic congenital stenosis of the esophagus. There are three histopathological subtypes of congenital stenosis: membranous webs, fibromuscular dysplasia, and ectopic tracheobronchial remnants [11]. The stenosis is usually located in the distal third of the esophagus, and is associated with esophageal atresia with tracheoesophageal fistula in about one-third of cases. Interestingly, the diagnosis of congenital stenosis is not commonly made during the neonatal period (Fig. 10.1). Instead, affected infants typically present with persistent vomiting, dysphagia, and/or failure to thrive, particularly with the introduction of solid foods between 4–10 months of age.

Mediastinal masses (e.g., esophageal duplications, bronchial duplications, leiomyomas) are rare but can cause local compression, thereby mimicking an esophageal stricture or stenosis.

Aberrant vascular anatomy: A vascular ring or an aberrant right subclavian artery can be a cause of proximal esophageal stenosis secondary to extrinsic compression. In the latter entity, children can present with dysphagia lusoria, described as such because of the unusual retro-esophageal course of the subcla-

vian artery. Contrast esophagography will often reveal a notching defect of the upper esophagus above the level of the aortic arch.

Epidermolysis bullosa (EB) represents a spectrum of rare, inherited blistering disorders secondary to a genetic defect in type-VII collagen. EB primarily affects the mucosa of the skin, pharynx, and esophagus. Although infants with EB rarely develop esophageal symptoms in early childhood, most affected individuals (particularly those with recessive dystrophic EB) will develop symptomatic esophageal strictures by 25 years of age. Many EB strictures are located in the proximal cervical esophagus [12].

Schatski ring is a very rare entity in children. Although most cases are seen in male adolescents, it is unclear whether this is the same entity as the membranous web subtype of congenital esophageal stenosis. The hallmark finding of a Schatski ring is formation of a thin, circumferential fold of mucosa that protrudes into the lumen at the gastroesophageal junction. Many cases have been identified in association with GERD or EoE.

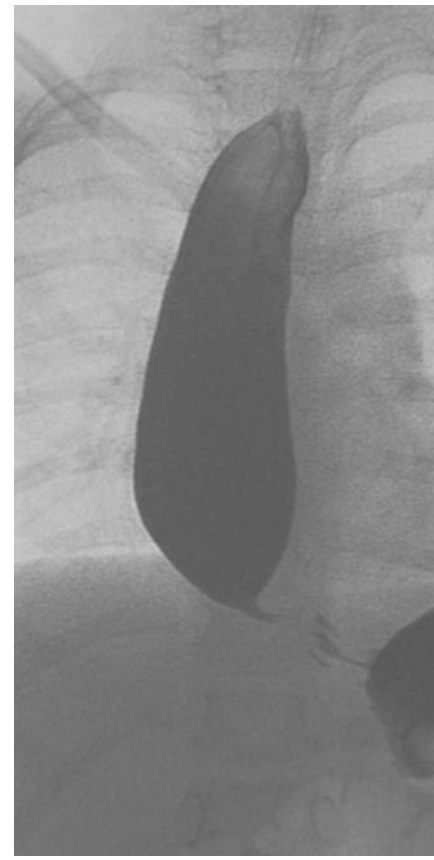

Fig. 10.1 Anterior contrast esophagram in a 6-month-old female with congenital esophageal stenosis showing marked dilation of the proximal esophagus with narrowing of the distal esophagus proximal to the gastroesophageal junction ("bird's beak" configuration)

10.4 Clinical Features

Although the presentation of an esophageal obstruction can vary depending on the etiology, most symptoms are specific to the upper alimentary tract. Most children will have some component of feeding intolerance, vomiting, dysphagia, or failure to thrive. Older children with GERD may experience heartburn. In young children with peptic esophageal strictures, it is important to realize that these symptoms can often be more insidious in nature, becoming more apparent over a 3–4 year period as they advance from a soft diet to more solid foods [3]. Children with EoE or Schatski ring often present with upper digestive tract symptoms complicated by impaction of a food bolus in up to 50% of cases [13, 14].

Extra-gastrointestinal tract symptoms may also be apparent in children with esophageal strictures and stenoses. For example, patients with a peptic esophageal stricture can be anemic secondary to chronic mucosal bleeding. Children with EoE often present with other associated manifestations of atopic diathesis (i.e., food allergy, asthma, eczema, chronic rhinitis, environmental allergies). Finally, because of the proximity of the esophagus to the airways, it is not uncommon for some patients with esophageal strictures or stenoses (particularly those secondary to GERD) to have concomitant respiratory symptoms because of chronic aspiration. Caustic ingestions may also cause acute and/or chronic injury to the larynx and trachea, leading to hoarseness, stridor, and dyspnea on presentation. All patients with suspected respiratory involvement should un-

dergo larynoscopy to fully assess the upper airway.

Children evaluated for a caustic ingestion in the acute setting should undergo immediate chest radiography if there is any concern for a possible esophageal perforation. Potential symptoms or signs of perforation include chest pain, fever, and tachycardia. Any radiographic evidence of a pleural effusion, pneumomediastinum, pneumothorax, or pneumoperitoneum mandates urgent esophagography with water-soluble contrast to further rule out perforation prior to undergoing esophagoscopy. Failure to recognize an occult esophageal perforation can be disastrous because insufflation during any esophagoscopy procedure may lead to worsening of the esophageal injury with the potential for mediastinitis, sepsis, cardiopulmonary arrest, and death.

10.5 Diagnosis

10.5.1 Esophagography

A contrast esophagram (often referred to as a swallow study) remains the "gold standard" for the diagnosis of an esophageal obstruction. During this test, water-soluble contrast (e.g., diatrizoic acid) or barium is delivered into the upper esophagus and followed distally past the gastroesophageal junction as it empties into the stomach. Barium gives superior mucosal detail but should not be used in a suspected perforation. In most cases, a carefully carried out study (including frontal and lateral projections) enables delineation of the precise location and length of the obstruction. Megaesophagus is highly suggestive of a chronic distal stricture. Evidence of dysmotility can often be ascertained from serial dynamic images. Based on the characteristics of the narrowing revealed by carefully carried out esophagography, a presumptive etiology for the stricture can often be made in conjunction with the clinical history.

10.5.2 Esophagoscopy

In addition to a contrast esophagography, complete endoscopic evaluation of the esophagus down to the gastroesophageal junction has an important and complementary diagnostic role in most types of esophageal obstructions. Although some surgeons prefer to use rigid esophagoscopes (which have a large operating channel), our preference is to use a flexible pediatric or neonatal endoscope for all but the most proximal cervical esophageal problems. We have found that modern, fiberoptic flexible endoscopes often give excellent visualization of the distal esophagus, induce less trauma to the oropharynx, and allow for evaluation of the entire stomach. The role of esophagoscopy is particularly vital in assessing obstructions in the settings detailed below.

10.5.2.1 Esophagoscopy in Caustic Ingestion

In the acute phase after ingestion, esophagoscopy serves as a useful tool for predicting the likelihood of a subsequent stricture. The absence of oropharyngeal burns on clinical examination or larynoscopy should never exclude the need for esophagoscopy in the presence of a good medical history [2]. The only major contraindication to endoscopic evaluation is esophageal perforation. Ideally, esophagoscopy should be done 12–48 h after ingestion. We discourage esophagoscopy done <12 h after ingestion because this may not allow sufficient time for full demarcation of the injury. We also do not advise delaying esophagoscopy for >72 h after ingestion because of the potential for encountering severe esophageal edema and early stricture formation, thereby increasing the risk of iatrogenic perforation.

During endoscopy, the entire esophagus should be assessed for the degree of injury according to a three-point grading scale modified from the more widely known classification system employed for thermal injuries to the skin [15]. First-degree injuries as demon-

strated by mucosal hyperemia and edema are superficial. Such findings predict a low likelihood of stricture formation. In contrast, second-degree injuries, characterized by patchy mucosal ulceration with vesicles, grayish exudates, and/or pseudomembranes, are suggestive of transmucosal (partial-thickness) involvement. Approximately half of all second-degree injuries will result in stricture. Findings of a third-degree esophageal injury include deep ulcerations with eschar formation. There can also be mucosal sloughing as well as thrombosis of submucosal vessels. The edema in third-degree injuries can sometimes be quite severe so as to obliterate the entire lumen. Signs of third-degree esophageal injury are consistent with transmural (full-thickness) damage and will therefore result in stricture formation in the vast majority of cases.

10.5.2.2 Esophagoscopy in GERD

Although peptic strictures classically occur in the distal esophagus, GERD-related strictures can also occur in the mid-esophagus at the anastomosis in patients after repair of esophageal atresia (Fig. 10.2). Evaluation of the esophageal mucosa by flexible esophagoscopy can be useful in confirming the etiology of the stricture. In older children, endoscopic biopsy of multiple areas within the distal esophagus can be done with minimal morbidity. Specimens will demonstrate chronic inflammatory changes within the mucosa. In older children with longstanding reflux symptoms, the surgeon should also look for salmon-red mucosa >2 cm above the gastroesophageal junction. Such findings are suggestive of Barrett's esophagus and merit endoscopic biopsy. Pathology specimens will show intestinal metaplastic columnar epithelium with goblet cells.

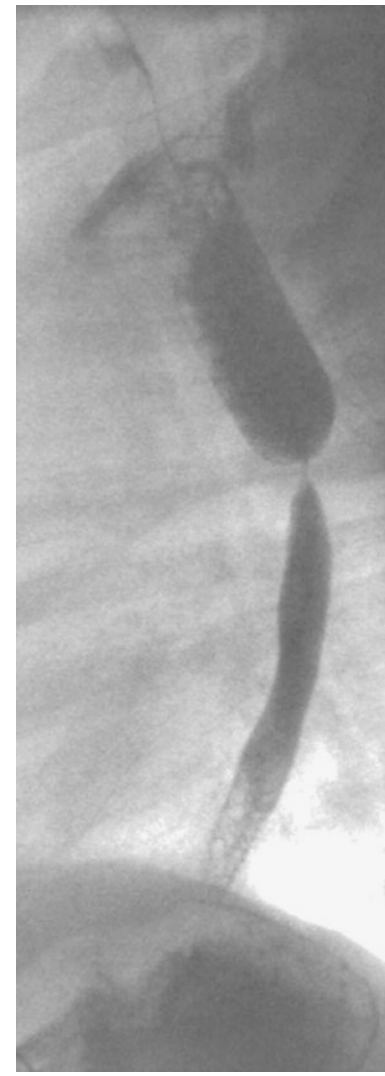

Fig. 10.2 Lateral contrast esophagram in a 4-month-old male after repair of esophageal atresia showing the interval development of a high-grade stricture at esophago-esophagostomy secondary to uncontrolled gastroesophageal reflux

10.5.2.3 Esophagoscopy in EoE

All children with a suspected esophageal narrowing secondary to EoE should undergo an endoscopic evaluation with possible biopsy. Findings on esophagoscopy consistent with EoE include a granular appearance of the esophageal mucosa with whitish exudates. A relatively specific finding of EoE is concentric mucosal rings, often referred to "trachealization" or "feline esophagus." However, not all patients with EoE will have obvious gross abnormalities, so a biopsy of multiple sites within the esophagus should always be done regardless of the appearance of the mucosa. Definitive cases of EoE will show >15 eosinophils per high-power field [16].

10.5.2.4 Other Diagnostic Studies

There are selected situations in which studies other than esophagography and esophagoscopy may be required to further delineate an esophageal stricture or stenosis. For example, angiography, computed tomography (CT) or magnetic resonance imaging (MRI) should be ordered to further evaluate patients with an obstruction secondary to a vascular ring. Similarly, an upper gastrointestinal contrast study and/or 24-h monitoring of esophageal pH may be indicated to help differentiate peptic esophageal strictures from esophageal stenosis or EoE. Prior to monitoring of esophageal pH, children need to temporarily discontinue all acid blockade medications to yield meaningful data that could guide further management. Finally, high-resolution esophageal manometry may be useful in some patients in whom achalasia or other functional disorders of the esophagus remain in the differential diagnosis.

10.6 Management

Appropriate management of esophageal strictures and stenoses depends largely on the underlying etiology. For example, in EoE, topical corticosteroids alone are the mainstay of therapy. For most other esophageal obstructions, endoscopic dilation is increasingly becoming the favored first line of treatment because of its minimal invasiveness and low prevalence of procedural morbidity. The specific management strategy based on etiology is detailed below.

10.6.1 Caustic Ingestion

In the acute setting after any suspected caustic injury, the patient should be placed on a strict *nothing per os* (NPO) diet. Blind placement of a nasogastric tube is contraindicated, and under no circumstances should the patient be given anything (including water) to dilute or neutralize the corrosive agent prior to diagnostic esophagoscopy. Such maneuvers may cause further esophageal injury by inducing an exothermic reaction and/or severe emesis.

First-degree injuries diagnosed by flexible esophagoscopy require no specific treatment because the risk of stricture formation is low. However, for all newly diagnosed second-degree injuries, the passage of a feeding nasogastric tube under direct visualization should be considered. In addition, all patients with second-degree injuries should be placed on a clear liquid diet as tolerated with esophagography ordered 2–3 weeks post-injury to assess for strictures. The indwelling nasogastric tube can serve as a guide for subsequent dilations if stricture formation occurs. If no stricture is present on follow-up esophagography, the tube can be removed and the child advanced to a regular diet as tolerated. There are surprisingly few data on the utility of any medication for a second-degree caustic injury. We advocate empirical parenteral antibiotics as well as chronic acid suppression in these patients. A seven-day course of piperacillin-sulbactam or a third-generation cephalosporin may be helpful in terms of protecting against potential direct bacterial translocation across the damaged esophageal wall and in diminishing the risk of aspiration pneumonia.

Third-degree caustic injuries should be treated initially with placement of a gastrostomy tube for two reasons. First, all of these patients are NPO, so the gastrostomy tube avoids the need for parenteral nutrition and provides stable access to the gastrointestinal tract for resumption of enteral feeds. Second, the gastrostomy tube facilitates placement of a transesophageal string guide that is passed through the gastrostomy site and one of the nares to maintain control of the esophageal lumen over the ensuing weeks of stricture formation. Commonly used guides include #3 braided silk suture, fishing wire, and silicone ventriculoperitoneal shunt tubing. The ends of the guide are then tied externally and taped on the child's back, leaving adequate laxity to prevent ulceration at the nose or gastrostomy sites while maintaining sufficient tension to keep

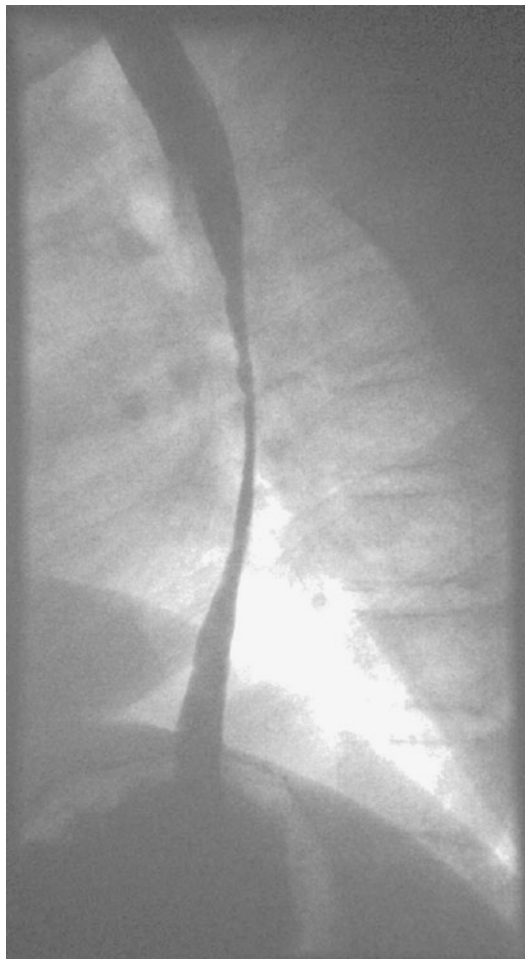

Fig. 10.3 Lateral contrast esophagram in an adolescent male 1 month after caustic injury demonstrating a long mid-esophageal stricture

from pulling out the guide. In the presence of a stricture on follow-up esophagography (Fig. 10.3), the guide allows for retrograde dilations through the site of the gastrostomy tube. Tucker dilators are specially designed for this purpose because they can be sequentially tied to the lower end of the string and passed through the stenosis in a retrograde fashion. String-guided retrograde dilation is associated with a lower prevalence of esophageal perforation and is therefore considered safer for high-grade and/or tortuous esophageal strictures [17]. One drawback of the retrograde approach is that the gastrostomy aperture is usually not well suited to accommodate larger-diameter bougies. However, in this situation one can simply reintroduce guided dilators in an anterograde fashion once a satisfactory lumen size has been established.

Since the 1950s, there has been considerable interest in the use of systemic corticosteroids to modify the inflammatory response and prevent stricture formation in high-grade esophageal injuries [15]. At present, its routine practice cannot be widely endorsed because the efficacy of corticosteroids in this setting has not been demonstrated in a randomized trial [12]. Nevertheless, proponents of corticosteroids suggest that most studies have included only a small number of patients and that corticosteroids may be beneficial if given at the appropriate dose and duration. For example, in one uncontrolled study, dexamethasone (0.5–1.0 mg per kg per day for 4–6 weeks was associated with a low prevalence of stricture formation [2]. Opponents of corticosteroids argue that the potentially deleterious effects of the drug (including the masking of septic complications and delays in esophageal wound healing) should not be underestimated. Although we do not routinely place patients with higher-grade corrosive injuries on corticosteroids, those who do receive corticosteroids should be placed on an antifungal agent in addition to a PPIs because of the known association between corticosteroid use with mycotic infections and peptic ulcer disease.

Management of a known caustic stricture remains highly dependent on the degree of narrowing as well as the length of the injured segment. In general, every reasonable effort should be made to preserve the native esophagus before resorting to resection, particularly if this involves esophageal replacement. Therefore, the initial approach includes serial endoscopic dilations every 2–4 weeks using an anterograde and/or retrograde approach based on the degree of injury. The optimal instrument used for dilation (i.e., hydrostatic balloon: Hurst–Maloney, Savary–Gillard, Jackson, Tucker) should be individualized based

on the nature of the stricture as well as the experience of the surgeon. Although somewhat controversial, dense fibrotic strictures involving a long segment of the esophagus tend to be more responsive to bougeinage as opposed to hydrostatic balloon systems.

Management of recurrent caustic esophageal strictures represents one of the most challenging problems in pediatric thoracic surgery. Prophylactic dilations to prevent strictures have been explored by several authors but their role remains undefined [18]. In many cases, perseverance is all that is required because some patients may require >20 dilation procedures until the stricture resolves. Management of short-segment strictures prior to dilation with endoscopic-assisted intralesional corticosteroids (1% triamcinolone) or topical mitomycin C (an anti-neoplastic agent that has been shown to reduce fibroblastic collagen synthesis by inhibiting DNA-dependent RNA synthesis) has shown promise in several reports [19, 20] Unfortunately, the efficacy of these agents has not been examined prospectively.

Long (>5 cm) esophageal strictures, particularly those that are persistent, circumferential in nature, and located in the mid-esophagus, are reasonable candidates for a temporary, covered esophageal stent. Esophageal stents are expandable and therefore designed to provide continuous, radially oriented force vectors sustained over a prolonged period of time. Unfortunately, few centers have extensive experience with esophageal stents in the pediatric population [21–23]. Moreover, the use of esophageal stents has been controversial because many of these devices are not well tolerated for more than several weeks, are prone to migration, and can be difficult to remove in a safe manner. Nevertheless, covered stents may serve an important role in esophageal strictures with a concomitant fistula as a temporary measure before definitive surgery. Even if the stricture responds to dilations or stenting, eventual esophageal shortening can occur with the subsequent development of GERD. All of these patients should be on long-term antacid therapy and some may eventually require a fundoplication with or without a Collis gastroplasty. Although the treatment plan should be individualized for every child with a persistent esophageal stricture, we would generally advise esophageal surgery if serial endoscopic dilation or stenting fails to remediate the stricture after 6–12 months.

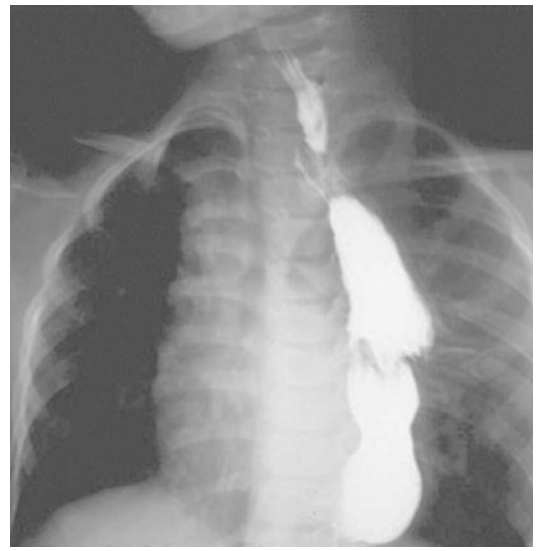

Fig. 10.4 Anterior contrast esophagram after esophagectomy with a gastric transposition placed through the posterior mediastinum

Short-segment strictures refractory to minimally invasive procedures can be considered for esophagoplasty or segmental esophageal resection. Colonic patch procedures have also been used with some success for less extensive disease [24]. Up to 60% of caustic strictures, particularly those that are long segment in nature, eventually require esophagectomy with conduit reconstruction. Based on our series of 9 patients with severe caustic strictures as well as our extensive experience with long-gap esophageal atresia, we favor the gastric transposition technique for esophageal reconstruction (Fig. 10.4) [25]. More recently, Javed reported similarly favorable outcomes in a large series of patients after gastric transposition when compared with other conduit procedures, including colon interposition [26].

Patients requiring esophagectomy are best cared for at major pediatric specialty centers with surgical expertise in the management of complex esophageal problems. A description of the surgical techniques involved in these procedures is beyond the scope of this chapter.

10.6.2 GERD

The initial principles of management for GERD-related strictures were established decades ago and include nutritional support, acid blockade, and serial bougienage [3]. Although some authors would recommend a primary anti-reflux procedure for peptic strictures, it may be technically more difficult to dilate the stricture just proximal to a fundoplication, and there have been additional concerns about causing trauma to the wrap itself after repeated dilations. Therefore, our research team as well as others advocate serial dilations while on a high-dose PPI (omeprazole 2 mg/kg/day) for several months [7]. Once the stricture has fully resolved and the child has been optimized from a nutritional and respiratory perspective, we would proceed with an anti-reflux procedure. Most children are excellent candidates for a Nissen fundoplication as definitive therapy to prevent further stricture recurrence [27]. Rarely, a Collis gastroplasty may also be required in conjunction with a fundoplication if there is significant esophageal foreshortening.

10.6.3 EoE

The mainstay of therapy for EoE includes elimination of all food allergens and initiation of topical corticosteroids. Topical corticosteroids are most easily delivered by ingestion of the medication (e.g., fluticasone proprionate) *via* a metered-dose inhaler [28]. Unfortunately, almost all patients will develop recurrent symptoms and esophageal eosinophilia after discontinuation of medical therapy [13]. Systemic corticosteroids should be reserved only for EoE patients with severe dysphagia or failure to thrive. PPIs may be helpful in a small subset of patients but should not to be considered as the sole primary therapy. Based on the literature in adult subjects, endoscopic dilation should be reserved for failure of medical management because dilation alone does not address the underlying inflammatory process, and there may be an increased risk of esophageal perforation in EoE when compared with strictures secondary to other disease processes [16].

10.6.4 Anastomotic Strictures

Although anastomotic strictures can be more difficult to treat compared with many other types of strictures, most are responsive to repeated anterograde dilation [29]. The frequency of these dilations should be individualized, but usually every 2–3 weeks in the initial period. At our institution, we favor serial dilations under combined endoscopic and fluoroscopic guidance using a hydrostatic balloon catheter filled with contrast reagent (Fig. 10.5). For high-grade strictures, a 0.035-inch guidewire can be used to position the balloon across the narrowing. Many patients with recurrent anastomotic strictures have undergone esophageal atresia repair in the neonatal period, so 24-h pH probe testing or an empirical trial of a PPI should also be considered. Recurrent strictures may also benefit from intramural injections of corticosteroid delivered using a sclerotherapy needle. Finally, placement of a temporary, covered esophageal stent may also be an option in selected patients (Fig. 10.6), although this may exacerbate pre-existing GERD and lead to worsening pulmonary symptoms in some cases. Overall, <5% of anastomotic strictures after esophageal atresia repair fail endoscopic management and require further surgical intervention such as segmental esophageal resection or esophageal substitution [10].

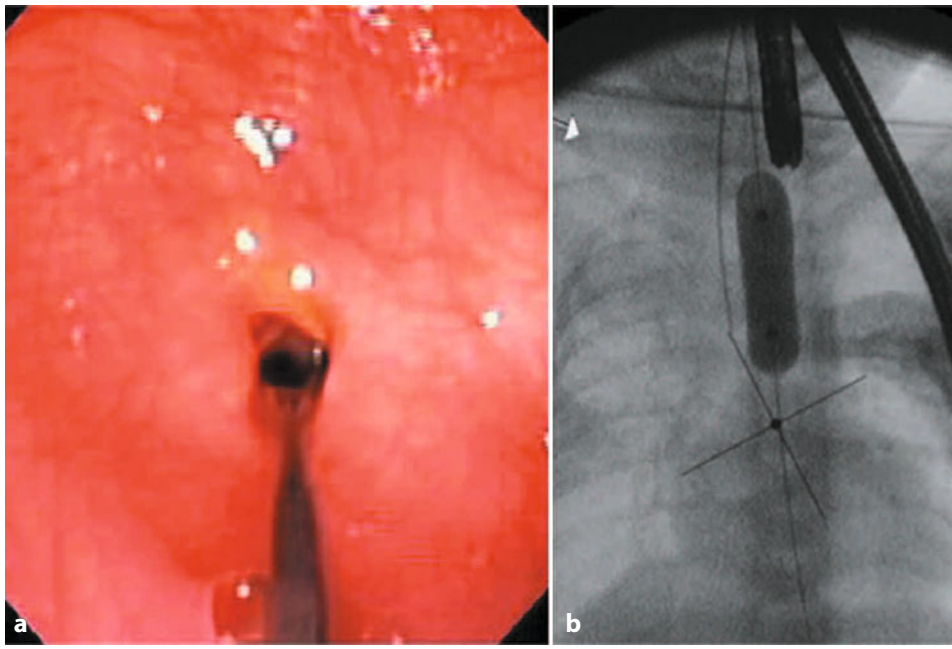

Fig. 10.5 Endoscopic view showing a high-grade anastomotic stricture after repair of esophageal atresia (**a**). A 0.035-inch guidewire is shown passing through the stricture at the 6 o'clock position. Anterior fluoroscopic image demonstrating successful dilation of the same stricture using a 10-mm hydrostatic balloon inflated with contrast medium (**b**)

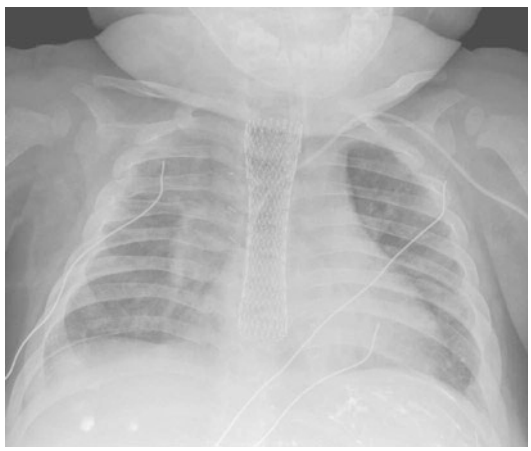

Fig. 10.6 Anterior chest radiograph of a fully covered esophageal stent (12 mm; Allimax) deployed in an infant referred for management of a recurrent esophageal stricture after repair of esophageal atresia

10.6.5 Esophageal Stenosis

The treatment of congenital esophageal stenosis remains controversial in large part because there are few large case series in the literature [11]. Historically, short, abrupt strictures were thought to contain rigid tracheobronchial remnants and were therefore not perceived to be amenable to endoscopic dilation without risk of perforation [30, 31]. In contrast, infants with stenosis secondary to fibromuscular dysplasia, as suggested by a short, tapered stricture within the lower esophagus, are considered to be excellent candidates for endoscopic dilation. In an effort to delineate the subtype of esophageal stenosis for further management guidance, the use of endoscopic ultrasound has been described but has not been studied extensively [11, 32].

More recently, our institution has favored empirical esophageal dilation using hydrostatic balloons or tapered, weighted (Hurst–Maloney) bougies as the first line of treatment in all cases of esophageal stenosis [11, 33]. Although the radial force induced by balloon dilators has some theoretical advantages with regards to wound healing, bougienage can provide greater tactile feedback, thereby reducing the risk of perforation. Depending on the de-

gree and duration of response after esophageal dilation, additional procedures can be done with potential long-term benefit. Iatrogenic perforations have been reported in ≤10% of cases, but many of these injuries can be treated medically depending on the size of perforation and clinical status [11]. Endoscopic ablation of a congenital membranous web represents another option that has been described recently [34].

If endoscopic maneuvers fail, the remaining treatment options for esophageal stenosis are segmental resection and esophagomyotomy. Resection of a congenital stenosis with primary esophago-esophagostomy *via* left thoracotomy or, more recently, left thoracoscopy, has been achieved with acceptable results [35]. However, segmental resection is recommended only if the stricture is <2.5 cm in length because longer resections often result in an intra-thoracic stomach and severe GERD that can be difficult to manage even with subsequent anti-reflux procedures. Postoperative anastomotic strictures after short-segment resections occur because of ischemia, tension, and/or untreated GERD. Fortunately, this complication usually responds to endoscopic dilation and anti-reflux medications. For distal lesions that involve the gastroesophageal junction, an anti-reflux procedure should be considered at the time of segmental resection. Esophagectomy for congenital stenosis is rarely, if ever, indicated.

10.6.6 EB

Historically, the management of EB esophageal strictures with dilations has been quite challenging because of the potential for creating severe iatrogenic mucosal sloughing. This can lead to significant chest pain and subsequent stricture formation after the procedure. Therefore, endoscopy and bougienage are now considered relative contraindications in the management of EB strictures, and hydrostatic balloon dilation under fluoroscopic guidance has become the preferred technique [36]. Balloon dilation allows for the application of uniform radial force at the site of the stricture while minimizing tangential forces that may cause inadvertent mucosal trauma to other areas of the esophagus. An added benefit of this approach is the potential avoidance of orotracheal intubation in this patient population.

10.6.7 Schatski Ring

Management of Schatski rings includes control of any underlying GERD using PPIs. For those who do not respond appropriately to acid blockade, recent data suggest that EoE should be considered with appropriate medical therapy such as topical corticosteroids employed in all cases in whom eosinophilia is identified on esophageal biopsy [37]. Endoscopic dilation of Schatzki rings has also been shown to be effective in refractory cases [14].

10.7 Outcome and Follow-up

Most children with successfully treated esophageal obstructions can resume complete oral nutrition with little or no dysphagia. Nevertheless, there are several long-term issues worth noting. For example, in children with significant residual scarring aftyer caustic ingestion who do not undergo esophageal replacement, there is an ≈1000-fold increased risk of esophageal carcinoma that can occur 30–45 years after caustic injury [38]. Because of the potential risk for malignant transformation, long-term endoscopic surveillance is advocated in this patient population. Similarly, most children managed by esophageal replacement require close follow-up because of significant short-term as well as long-term morbidities associated with esophagogastric anastomotic leak, recurrent stricture formation, and feeding intolerance [25]. These complications are yet another reason why esophagectomy patients are best cared for at major specialty centers equipped with surgical expertise and multidisciplinary care teams.

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Esophageal Perforation

11

Shaun M. Kunisaki, Steven W. Bruch
and Arnold G. Coran

11.1 Introduction

Of all the perforations of the alimentary tract, perforations of the esophagus are considered the most dire and life-threatening. Historically, esophageal perforations in children were treated with highly invasive procedures in similar fashion to those carried out in adults. However, we have learned that esophageal perforations in children are: (i) more often iatrogenic, (ii) more likely to occur within the cervical esophagus, and (iii) not generally associated with an underlying malignant disease process. These important distinctions have allowed for successful non-surgical treatment strategies in the pediatric population. Although there remains a clear role for surgical therapy in selected children with esophageal perforations, the management paradigm has clearly shifted towards less invasive treatment modalities as the first line of therapy in children who are otherwise clinically stable.

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11.2 Epidemiology

Esophageal perforations are relatively uncommon, but the exact incidence remains unknown. Based on the literature in adults and pediatric population, esophageal perforations occur after esophageal dilation procedures in 0.4% to 1.2% of cases [1]. The majority of these cases involve the thoracic esophagus, followed by injuries to the cervical esophagus and intra-abdominal esophagus [2]. Children with caustic strictures represent the highest risk for esophageal perforation due to the role of serial endoscopic dilation in their management.

11.3 Etiology and Pathogenesis

The esophagus has a thin wall with no adventitial layer, making it very susceptible to iatrogenic perforation. Based on several series, between 60% and 77% of esophageal perforations in children are iatrogenic [3]. The majority of these complications occur during bougie or balloon esophageal dilation for a wide range of problems, including strictures after caustic ingestion, severe reflux, or esophageal reconstruction for esophageal atresia [4], achalasia and congenital esophageal stenosis. Iatrogenic injuries have also been reported after endoscopic sclerotherapy and extraction of foreign bodies [5].

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Traumatic instrumentation of the oropharynx by nasogastric tubes, endotracheal tubes, and respiratory suction catheters is another important cause of iatrogenic esophageal perforation, particularly in neonates [6, 7]. These injuries typically occur at the pharyngoesophageal junction just proximal to the cricopharyngeus muscle. This area (referred to as Killian's triangle) is the narrowest part of the alimentary tract. It has also been hypothesized that the cervical vertebrae can further narrow this area if the neonatal neck is hyperextended [8].

Several less common causes of iatrogenic esophageal perforation that have been described [5]. For example, perforations have occurred while dissecting the intra-abdominal esophagus in preparation for a fundoplication or Heller myotomy, and after the ingestion of foreign bodies or corrosive substances. Spontaneous, post-emetic esophageal rupture (Boerhaave's syndrome) is less common in children but still accounts for ≈5% of reported cases [9]. Blunt or penetrating trauma may also result in esophageal perforation in the pediatric population.

The pathophysiological consequences of a thoracic esophageal perforation have been appreciated for decades. In untreated patients or in cases in which there has been significant delay in appropriate therapy, a severe inflammatory and infectious response within the mediastinum and pleural cavity ensues within hours, leading to sepsis, shock, and eventually death. This rapid deterioration has been attributed to a lack of a surrounding loose connective tissue adjacent to the esophagus. As a result, the body cannot wall off the perforation or to mount an adequate immune response within the mediastinum. The negative pressure within the pleural space results in increased spillage of digestive enzymes and bacteria from the esophageal lumen, leading to further contamination and the potential for sepsis.

11.4 Clinical Features

Careful history-taking and physical examination should be conducted in all children with a suspected esophageal injury. Chest pain, fever, tachypnea, or tachycardia after any endoscopic instrumentation of the esophagus should immediately raise suspicion for a perforation [2, 3]. Neonates and infants can present with drooling, increased oral secretions, and feeding problems. Mackler's triad (chest pain, subcutaneous emphysema, vomiting) has been associated with spontaneous esophageal perforations but its absence does not exclude the diagnosis. Neck or chest wall crepitus is worrisome for a proximal esophageal injury. Decreased breath sounds may suggest an underlying pneumothorax or pleural effusion. In contrast to adults, neonatal Boerhaave's syndrome tends to manifest itself as a right-sided pneumothorax, presumably because of the close adherence of the thoracic aorta to the left side of the esophagus in young children.

Spontaneous esophageal ruptures can result in substantial contamination of the mediastinum that can quickly progress to septic shock. Therefore, any critically ill child with unexplained mediastinitis or empyema should raise the suspicion for an esophageal perforation as its underlying etiology.

11.5 Diagnosis

Early diagnosis and management of esophageal perforations is associated with improved outcomes and lower mortality [10]. Therefore, it is imperative that all diagnostic testing to look for a possible esophageal perforation be conducted in a prompt and expeditious manner. Chest radiographs should be ordered immediately in all suspected cases. In one study, 82% of children with an esophageal perforation had pneumomediastinum on plain radiographs [3]. Other possible findings include gas in the soft tissue of the neck (subcutaneous

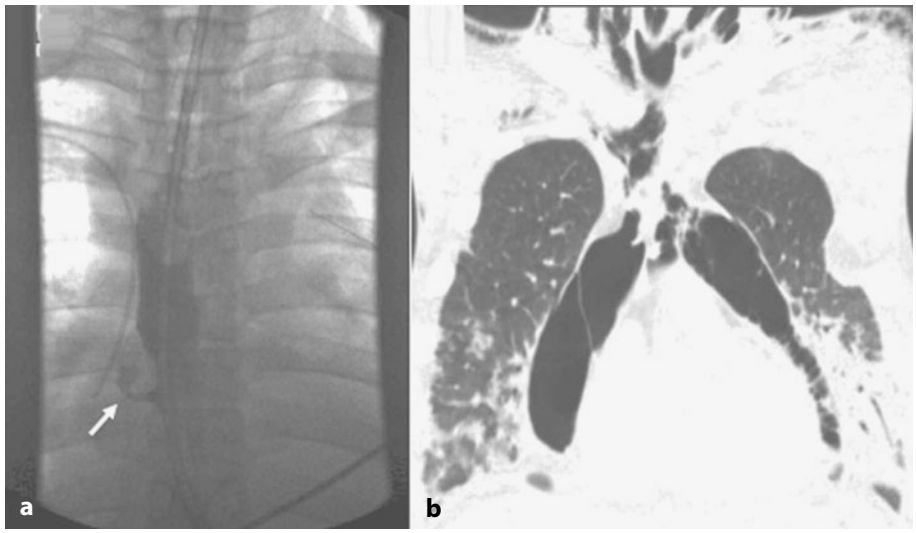

Fig. 11.1 Diagnostic imaging in a 16-year-old male with acute mediastinitis secondary to a spontaneous perforation of the esophagus. Anterior contrast esophagram demonstrating focal extravasation of contrast along the right lateral aspect of the mid-thoracic esophagus (**a**). Coronal CT showing massive pneumomediastinum and subcutaneous emphysema (**b**)

emphysema), pleural effusions, and pneumothoraces. Unfortunately, false-negative rates of ≤33% have been reported, and positive findings (including pneumomediastinum) can also be related to an isolated pulmonary disease process such as bronchospasm [11, 12]. Therefore, although plain radiographs can often be helpful, they are not sensitive enough to exclude the diagnosis of esophageal perforation (particularly in the early hours after an injury).

After review of the radiographs, all patients should undergo an emergency contrast esophagography (swallow study) because esophagography remains the "gold standard" for excluding the diagnosis of an esophageal perforation (Fig. 11.1a). Moreover, the study is often indispensable in terms of preoperative planning and for guiding further therapy. A water-soluble agent (e.g., diatrizoic acid, iohexol) is preferred over dilute barium because barium can be associated with granulatomous inflammatory reactions with subsequent pleuritis, mediastinitis, and mediastinal fibrosis. Moreover, water-soluble contrast is rapidly absorbed from the mediastinum in the presence of a leak, thereby leaving minimal residual contrast that would compromise interpretation of subsequent follow-up radiological studies. However, if no leak is found using a water-soluble agent, dilute barium should be administered to confirm the absence of an esophageal perforation. Barium has a greater sensitivity for detecting leaks because of its higher density as well as its ability to adhere to extraluminal tissues [13].

Two important aspects of an esophageal perforation revealed by esophagography are (i) its precise location and (ii) its degree of containment within the mediastinum. The cervical esophagus begins at the level of the cricoid cartilage and ends at the thoracic inlet. In neonates, a perforation in this area will often show a contained retropharyngeal pocket (pseudodiverticulum) on esophagography that can be mistaken for a proximal pouch seen in esophageal atresia [14]. Because of the course of the esophagus relative to the pleura within the mediastinum in young children, injuries involving the proximal thoracic

esophagus may affect the left thoracic cavity, whereas injuries in the distal thoracic esophagus may show findings in the right thoracic cavity even though the distal esophagus lies in the left pleural cavity [9, 15]. Submucosal dissections of the esophagus are always contained and can be visualized as a false lumen tracking in parallel with the true lumen of the esophagus.

The role of endoscopy in the evaluation of esophageal perforations remains undefined because there are no large studies of esophagoscopy for the diagnosis of esophageal perforation in children. However, in situations in which there is a high index of suspicion for an esophageal perforation with a normal barium esophagram, flexible esophagoscopy may be indicated [2]. The risks and benefits of the procedure must be individualized because endoscopic insufflation of the esophagus may convert a pre-existing partial-thickness esophageal wall tear into a large transmural injury.

In a small subset of clinically stable patients, chest CT with water-soluble oral contrast may be helpful if immediate expertise to conduct esophagography is not available or if further characterization of the mediastinum and pleural spaces is desired. Although several adult European reports have demonstrated the comparable sensitivity of chest CT with water-soluble contrast esophagography for the detection of esophageal anastomostic leaks [16], no such studies are available in the pediatric population. In many cases, the site of perforation can be more difficult to elucidate by CT, and pneumomediastinum will be the only sign of an esophageal injury (Fig. 11.1b).

11.6 Management

In the 1940s and 1950s, the preferred management of all thoracoabdominal esophageal perforations was immediate surgical repair. To delay surgical repair in favor of medical management, regardless of the clinical status, was equivalent to "surgical heresy" because the early adult experience found that delays in surgical management led to sepsis and were associated with a prevalence of mortality of >30% [17]. Nevertheless, in the 1960s and 1970s, several surgeons operating on adults began to report successful outcomes with non-surgical management of selected esophageal perforations [18, 19]. In 1979, Cameron proposed a non-surgical treatment strategy in adult patients who were clinically stable with contained intra-thoracic perforations [20]. Subsequent investigations in adults and children further validated that the finding that ≤80% of esophageal perforations, usually those that are contained and iatrogenic, can be treated by non-surgical management [3, 10, 21–25]. Unfortunately, all of these studies have been based on expert opinion from retrospective reviews of a heterogeneous group of patients, and there have been no randomized trials that have compared any of the different treatment modalities (Table 11.1). Therefore,

Table 11.1 Surgical techniques for the management of thoracic esophageal perforations

Reinforced primary closure (mobilization of pleura, muscle, pericardium, or pericardial fat)
Vascularized autologous patch repair
Wide decortication and drainage
Segmental resection with or without fundoplication
T-tube esophagostomy
Cervical esophagostomy with distal exclusion
Esophagectomy with conduit reconstruction (stomach, colon, or jejunum)
Endoscopic repair (esophageal stents, hemoclips, fibrin glue)

the decision of how to appropriately manage a pediatric esophageal perforation needs to be individualized based on clinical judgment.

11.6.1 Non-surgical Management

We favor a non-surgical management approach in clinically stable children with a contained iatrogenic perforation of the esophagus. The hallmarks of non-surgical therapy include nutritional support, broad-spectrum antibiotics, pharmacological blockade of gastric acid, cessation of oral intake, and catheter-based drainage of peri-esophageal collections. Whenever feasible, nutritional support using a post-pyloric feeding tube placed under fluoroscopic guidance can avoid the need for parenteral hyperalimentation. Broad-spectrum intravenous antibiotics are given because various organisms, including Gram-positive cocci, Gram-negative rods, and anerobes have been isolated from microbiological specimens [2]. The role of prophylactic anti-fungal coverage in esophageal perforations remains undefined. We routinely use intravenous H_2 antagonists and/or proton pump inhibitors to reduce gastric acidity, which may expedite healing of the esophageal injury.

A critical and often under-emphasized aspect of non-surgical management is the aggressive drainage of all peri-esophageal collections. Children should have a large-bore nasogastric or orogastric tube inserted distal to the perforation under fluoroscopic guidance to adequately decompress the stomach. Whenever possible, we also favor placement of a nasopharyngeal tube positioned proximal to the leak to minimize the anterograde flow of saliva across the perforation. One or more chest tubes should be placed (surgically or guided by interventional radiology) to address mediastinal or pleural collections. Some older studies have advocated placement of *per os* lavage catheters adjacent to the leak to allow for continuous antibiotic irrigation of the mediastinum [8, 15]. We have not used these lavage catheters because they are cumbersome and provide little marginal benefit.

11.6.2 Surgical Management

11.6.2.1 Thoracic Esophagus

For children with a thoracic esophageal perforation and any evidence of clinical instability, the treatment of choice remains immediate surgery. Because there are many ways to address an esophageal perforation intraoperatively (Table 11.1), it is imperative that the surgeon is familiar with the indications as well as relative advantages and disadvantages of the various procedures.

The side for the thoracotomy should be dictated by esophagography and other imaging studies. Once the hemithorax is entered, wide drainage and irrigation of the entire mediastinum and pleural space is done. If the injury is small, methylene blue can be instilled into the proximal esophagus to help localize the injury [15]. Other useful techniques to identify the perforation include insertion of an appropriately sized bougie dilator or flexible endoscope under direct vision. In the latter technique, the perforation may be more identified readily after transillumination through the esophageal wall.

For perforations that occur within 24 h of exploration, reinforced primary closure is the preferred technique for repair. In this approach, the site of the perforation is closed in a meticulous fashion with multiple interrupted sutures in 1–2 layers, and an autologous, vascularized flap of tissue is then mobilized over the suture line to reinforce the suture line. Options for local tissue flaps include intercostal muscle, pericardium, and pleura (Grillo patch) [17]. In adults without sepsis, pleural flap reinforcement has been associated with a very low prevalence of post-operative leaks [26].

Unfortunately, it is not uncommon to find an intra-thoracic esophageal perforation that is not be amenable to reinforced primary closure,

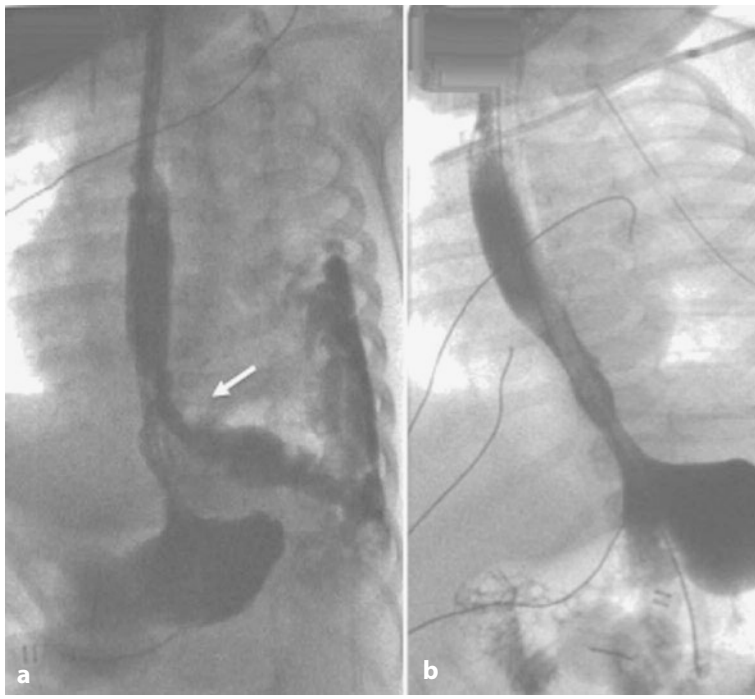

Fig. 11.2 Anterior contrast esophagram in a 10-month-old female with an esophageal perforation managed with thoracoscopic decortication and drainage. Initial film demonstrating massive extravasation of contrast into the left pleural space (**a**). No evidence of esophageal perforation on follow-up imaging undertaken 12 days later (**b**)

either because the tear cannot be readily visualized in the setting of significant mediastinal inflammation or because of extensive esophageal damage. In the former situation, decortication with wide mediastinal and pleural drainage remains a viable option in children. Our group, as well as others, has also carried out this procedure by thoracoscopy with favorable outcomes (Fig. 11.2) [27].

There are several options for the repair of the severely damaged esophagus. The first is to mobilize a local flap of vascularized tissue over the site (analogous to a Graham patch for perforated peptic ulcer disease). A second alternative is to place a 16-F soft biliary T-tube or trimmed percutaneous endoscopic gastrostomy (PEG) tube into the perforation [28]. In most cases, the goal of this approach is to establish an esophagocutaneous fistula that can close spontaneously or temporize until a more definitive procedure can be carried out. More recently, various endoscopic interventions, particularly covered esophageal stents, have been used successfully in adults with esophageal perforations [29–31]. Unfortunately, few pediatric centers have extensive experience with the deployment of these stents.

Another potential alternative for the management of focal esophageal injuries is to carry out a 1–2-cm segmental resection of the esophagus. Clinical scenarios in which segmental resection may be the best option for esophageal repair include the presence of a focal, non-dilatable caustic stricture. These procedures are generally well tolerated, but there can be anastomotic complications because of perioperative ischemia or, more commonly, postoperative gastroesophageal reflux within a foreshortened esophagus. Therefore, one should consider undertaking an anti-reflux procedure at the time of any segmental resection to minimize the risk of postoperative leak and stricture by recognizing that the fundoplication could partially obstruct a proximal fresh esophageal suture line.

Based primarily on the adult literature, several other surgical maneuvers have been described to deal with severe esophageal per-

forations. In a diverting cervical esophagostomy with distal exclusion, the esophagus is ligated at the gastroesophageal junction and just distal to the esophagostomy using absorbable sutures that will allow for subsequent recanalization of the esophagus in several weeks' time [32]. Although some surgeons have strongly advocated this approach in all unstable patients, the procedure is now rarely indicated given the success of less invasive approaches [2]. Esophagectomy with conduit reconstruction is another option for severe esophageal perforations but should be considered only in clinically stable children without sepsis for whom long-term salvage of the native esophagus (e.g., long-segment esophageal stricture, malignancy) seems unlikely. A variety of conduits, including stomach, colon, and jejunum, have been described for surgical reconstruction [5, 33, 34]. Given our own favorable experience with gastric transposition in patients with long-gap esophageal atresia [35] our preference has been to use the stomach as the conduit for reconstruction.

11.6.2.2 Cervical and Abdominal Esophagus

The majority of perforations of the cervical esophagus can be managed successfully in a non-surgical fashion because these injuries are rarely lethal, and adequate drainage will generally suffice [17]. However, if surgical therapy is indicated, a cervical perforation is best approached through a transverse neck incision. The esophagus can be easily visualized upon retracting the carotid sheath laterally and the trachea medially. The omohyoid muscle may need to be divided to improve exposure. The surgeon should be cognizant of the recurrent laryngeal nerve as it courses along the tracheoesophageal groove. Once the esophageal injury is repaired in a primary fashion using fine, interrupted sutures, the suture line should be reinforced with a local flap of strap muscle. Finally, a drain is sutured to the inferior aspect of the wound prior to skin closure.

For perforations of the intra-abdominal esophagus near the gastroesophageal junction, surgical repair is always indicated. Depending on the extent of the injury, the child should undergo primary repair or rarely a segmental resection of the distal esophagus. In either case, the suture line should be reinforced with a Nissen or Thal fundoplication. Although laparoscopic repair of these perforations has been described [36], a left subcostal or upper midline laparotomy with takedown of the left triangular ligament will usually be required to adequately visualize and repair these injuries.

11.7 Outcome and Follow-up

If surgical management is employed, placement of a central venous catheter and/or gastrojejunostomy tube at the conclusion of the procedure may help facilitate recovery in selected patients. Contrast esophagography is carried out 7–10 days postoperatively. All children are maintained on broad-spectrum intravenous antibiotics until the leak has resolved. We also routinely administer intravenous H_2 antagonists and/or proton pump inhibitors to minimize the potential damaging effects of refluxed gastric acid. Upon complete resolution of an esophageal leak, oral feeds can be initiated, and all catheters removed.

Persistent esophageal leaks lasting for more than several weeks are unusual and suggest a distal esophageal or gastric outlet obstruction. Formation of an esophageal stricture is the most common long-term complication after non-surgical treatment [15]. Fortunately, most of these strictures respond well to endoscopic dilations, which can be initiated in several weeks once no leak is identified on esophagography. Contemporary series of children with esophageal perforations have shown a median length of stay ranging from 11 days to 29 days, and a prevalence of mortality of <5% [2, 3, 15, 24].

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Esophageal Replacements in Children

12

Olivier Reinberg

12.1 Introduction

For historical reasons, Lausanne University Hospital (Lausanne, Switzerland) has always been involved in esophageal replacements. In 1907, Cesar Roux successfully carried out the first total esophageal replacement on a 12-year-old child in Lausanne. The child suffered from caustic stenosis. It was a presternal jejunoplasty (also called "esophago-jejuno-gastrostomosy"), a new procedure for untreatable esophageal stenosis. That patient died at age 53 years. Since then, many surgical procedures have been used to replace the injured or abnormal esophagus [1–4].

12.2 Epidemiology and Indications for Esophageal Replacement

The indications for esophageal replacements differ according to the native country of the child. However, in high-income countries, despite laws stating that containers must have child-resistant lids, ingestion of corrosive substances (e.g., alkalis or acids) is the most common indication for esophageal replacement.

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The true prevalence of these injuries is not known. According to one report on pediatric trauma by the World Health Organization and UNICEF in 2008, >120,000 children under 6 years of age suffered caustic injuries in the USA in 2004 [5]. Chemicals around the house to which children may have access contribute significantly to unintentional poisonings in childhood in high- and low-income countries, only the substances differ. In high-income countries, bleach, dishwasher detergents and ammonia are common. Dishwasher tablets are the household products most frequently involved in esophageal injuries. Dishwasher detergents are highly corrosive, causing potentially life-threatening injuries and ongoing morbidity. In most countries, dishwasher tablets are not included in the regulations for child-resistant closures. In low-income countries, sodium hypochlorite or sodium hydroxide (lye, caustic soda) is used to make soap and textiles. It is also used: as a bleaching agent; for the washing or chemical peeling of fruits and vegetables; for cocoa processings for the softening or blackening of olives; or to prepare "medicines". All of these items can be accessed by children. Most exposures to cleaning agents result in mild poisoning, but strong alkalis and acids can lead to severe tissue damage. In the pediatric group, 90% of burns are caused by alkaline substances and 10% by acidic substances [6].

Other indications for esophageal replacements are uncommon. Our team (which I will

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now refer to as 'we') has been involved in the treatment of isolated cases of: post-infectious strictures; fungal (candida) or viral (herpes) causes; malformations (long congenital strictures or long duplications of the esophagus); tumors (giant leiomyoma); stenosis post-radiotherapy or related to epidermolysis bullosa.

Since 1987, we have never carried out an esophageal replacement, either for a peptic stricture or for esophageal atresia. Peptic strictures are released with dilatations after anti-reflux procedures. Most anastomoses of "long-gap esophageal atresia" can be done as delayed procedures, waiting sometimes for several months with a gastrostomy, as long as cervicostomy has not been done. The native esophagus is the best, and everything must be done to preserve it. There is a strong correlation between precipitated procedures and complications including graft necrosis, anastomotic leaks and sepsis [7,8].

12.3 Etiology and Pathogenesis

Acids and bases can be defined as "caustics", which cause significant tissue damage upon contact with the esophagus. Caustic ingestions in children are in general accidental, but some may result from neglect and/or abuse.

Most acids produce coagulation necrosis by denaturing proteins, inducing a coating coagulum that protects the underlayers from deeper penetration. Bases induce more severe injuries known as "liquefaction necrosis", i.e., protein denaturation together with fat saponification, which penetrate deep through the esophageal wall (and can perforate).

The severity of damage is related to the pH, concentration and volume of the agent ingested. The contact time is of little relevance because a lesion occurs within a few seconds. The physical form of the agent plays a significant part. Ingestion of solid pellets results in prolonged local contact time with the esophagus, resulting in deep, localized burns; liquids generate superficial but more extensive lesions. Hence, it is of major importance to refrain from drinking after pellet ingestion because it may induce both types of lesion.

Like skin, the long-term effect of caustic esophageal burns is a hypertrophic scarring process which can result in stricture formation. Mucosal re-epithelialization is a slow process that is usually not complete before 4–6 weeks. Inflammation continues and granulation tissue matures until complete re-epithelialization occurs. Thus, stricture formation is detectable as of the second week, and is definite by the fourth week. This is the best time to start dilatations.

The caustic burn induces a shortening of the esophagus and motility disorder. These actions result in poor esophageal clearance and reflux, which adds a peptic stenosis to a caustic one. Hence, all of our patients undergoing conservative treatment with dilatations receive proton pump inhibitors [Reinberg, unpublished observation].

12.4 Diagnosis and Initial Treatment

About 1 month after ingestion of a caustic material, the diagnosis of stenosis can be assessed by esophagography and endoscopy once the edema has resolved. Then, according to the severity of the stenosis, a dilatation program can be started which is continued every 3 weeks for 6–12 months. The rate of stricture formation reported in the literature varies from to 2% to 63%. Subsequently, indications for esophageal replacements and their timing vary widely. As a result, children are often subjected to prolonged courses of dilatations before esophageal replacement or, conversely, may be exposed to unnecessary surgery [7]. A strong predictor of poor outcome is the delay from ingestion to the beginning of dilatations [7, 8].

Isolated short stenosis of the esophagus (i.e. 1–2 cm) can be treated by dilatations with good results. Long ones (>3 cm), multiple stenosis (>2), or those with a tracheo-esophageal fistulae cannot be solved by dilatations and require esophageal replace-

ment [7]. However the decision should not be precipitated.

The scarring process of the esophagus is long, and the persistence of a stenosis must be confirmed by repeated esophagography. An apparent severe stenosis related to the inflammatory process can last for months before its disappearance. Conversely, a dilatation program without significant improvement after 1 year can be considered to be a failure. For these reasons, a stenosis is considered persistent after 6 months without improvement and we do not continue a dilatation program after more than 1 year [9].

Benign esophageal strictures usually produce dysphagia for solids, liquids or both, with slow and insidious progression of weight loss and malnutrition. If the stenosis is important with subsequent dysphagia lasting for >1 month, a gastrostomy should be done (see below for gastrostomy placement). Most patients, even those with a gastrostomy, are referred to us in poor condition, and must be placed under a refeeding program before surgery.

A preoperative evaluation of the oropharynx and larynx (including vocal-cord movements) must be done. The aim is to document possible scarring processes and the status of the recurrent laryngeal nerves before surgery in the neck. The level of a pre-existing tracheoesophageal fistula must be defined by tracheoscopy. The length of the intact proximal esophagus above the first stenosis should be measured carefully to anticipate swallowing problems. The day before surgery, we recommend bowel preparation because we do not know which transplant will be used.

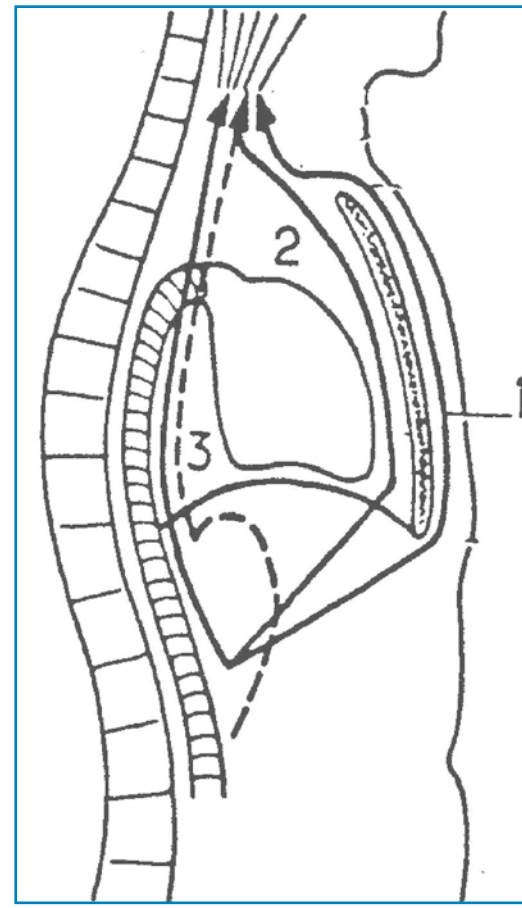

Fig. 12.1 Routes for substitute placement: presternal (historic) (*1*); retrosternal (*2*); and orthotopic mediastinal posterior (*3*)

12.5 Therapeutic Management

12.5.1 Where Should the Esophageal Substitute Be Placed?

Choosing the appropriate route for esophageal replacement is an important decision. Historically, the route was presternal (Fig. 12.1) because, at that time, the thorax could not be open. Then, the transplant was placed in the retrosternal position in a first step and the native esophagus was removed in a second step (Fig. 12.1). We introduced the one-stage procedure in 1989, placing the transplant in the orthotopic position (i.e., in the posterior mediastinum) after a closed-chest esophagectomy (Fig. 12.1) [10]. The path for an orthotopic plasty is straighter and shorter than that of the retrosternal route, but requires removal of the native esophagus. It avoids the two kinks at the upper cervical opening and at reentry into the abdomen. It is our favorite procedure because it seems that peri-esophagitis limits dilatation or the redundancy of the transplant [2, 10–12].

However, in some circumstances, the retrosternal route must be used. It is easy to create a path behind the sternum in a space with very few adhesions. However, with time, any transplant placed in this space will widen, especially if there is a narrowing at the distal end where it reintegrates the abdomen. This is more common in colonic transplants than in gastric tubes. Colonic transplants placed retrosternally have a strong tendency to become redundant, and we have had to tailor some of them. A gastric tube is more appropriate if the transplant is placed in the retrosternum.

12.5.2 Should we Remove the Native Esophagus and, if so, how?

There are two reasons to remove the native esophagus before an esophageal replacement: (i) to place the transplant in the orthotopic position (as mentioned above) and (ii) the oncologic risk induced by the burned esophagus. The prevalence of malignancies (mostly carcinoma) is not known, but has been shown in several reports to range from 1.8% to 16%, and the malignancies are known to take decades to develop. No one knows the fate of a disconnected, burned esophagus. However, some cases of carcinoma in a native esophagus after replacement have been reported [9, 13]. We believe that a demucosed, short segment of an abandoned disconnected esophagus is an acceptable risk.

In 1978, Orringer and Sloan were the first to describe a blind esophagectomy without thoracotomy [14]. In 1989, we introduced the one-stage orthotopic esophageal replacement after a closed-chest esophagectomy [10, 15]. The esophagus is removed through a left cervical incision after its transhiatal dissection by laparotomy without thoracotomy. A blind dissection by digitoclasy is undertaken in the middle part of the esophagus. At this site, scarring adhesions to the major vascular structures and bronchi are the most severe, and can lead to serious, life-threatening injuries [15]. Some anatomical considerations on the vascularization of the esophagus are particularly useful if carrying out the hemostasis from the cervical opening and hiatus [16]. A greater danger remains at the level of the aortic arch and left bronchus, where the more important adhesions are, and which is the farthest point from the skin incisions during blind dissection. When total esophagectomy becomes too dangerous, we abandon certain esophageal remnants at the level of the aortic arch after removal of the mucosa without subsequent narrowing of the esophageal substitute. Even after >200 cases we consider this step to be the most dangerous part of the procedure, showing a prevalence of 16% for various complications. It allows the esophagus to be completely removed in 71% of cases and to be partially removed in 16% of cases [17].

During this step of the procedure, two complications related to anesthesia can occur: (i) displacement of the endotracheal tube during blind dissection of the esophagus (which requires tractions on it and through it) and (ii) obstruction of the endotracheal tube or of the bronchi (mainly the left bronchus) because of mobilization of mucous plugs from the lungs during esophagectomy.

For these reasons, we have tried to achieve esophagectomy under visual control without opening the thorax. Since 2006, we have used a standardized procedure through a laparoscopic transhiatal approach [18, 19]. Some cases of esophageal dissection in children using thoracoscopy [20], or a combination of thoracoscopy and laparoscopy, have also been reported [21–23].

During the laparoscopic procedure, the child lays supine at the foot end of the operating table. The legs are wrapped in the “frog position” (as for an anti-reflux procedure). The operating table is tilted to a 30° anti-Trendelenburg position. To allow good access to the esophagus, the right-hand port is placed in relation to the position of the gastrostomy (i.e., slightly inward and inferior to it). This will not only help dissection of the esophagus (especially during dissection in the mediastinum) but also allow easier insertion of

instruments by giving the appropriate direction to the mediastinum through the open hiatus. The esophageal diaphragmatic hiatus is enlarged by a 2–3-cm incision at 10 o'clock. Two large (0 or 2) transparietal monofilament threads are passed through the two crura from both sides of the patient, and taken out through the skin. They allow a wide opening of the crura (similar to the raising of a stage curtain). Transhiatal dissection of the esophagus is pursued under direct vision in close contact with the esophageal wall using a sealing device (LigaSure™ Dolphin Tip Laparoscopic Instrument (LS1500) made by Covidien). Once the distal third of the esophagus has been freed, the liver retractor can be introduced into the mediastinum below the heart to allow a wider view of its major anatomical structures. A 30° rotation of the camera provides with a better view of both sides of the esophagus. This approach provides a clear view of the vagus nerves and facilitates their preservation. Should a pleural tear occur, a drainage tube is inserted under direct vision. The anatomical structures which run the greatest danger of being damaged during dissection are the left bronchus (whose soft posterior membrane usually adheres firmly to the esophagus) and the left brachiocephalic vein (innominate vein). The esophagus can be freed as far up as possible (usually 2 cm below the clavicle). Using this technique, no vascular or bronchial wound occurred, and the prevalence of total removal of the esophagus increased up to 89% without producing complications [18, 19].

Cervical dissection of the esophagus requires the greatest care in both techniques to avoid a tracheal tear or a lesion to the left recurrent laryngeal nerve. Preserving the most proximal centimeters of the native esophagus is crucial to avoid swallowing disorders.

A pre-existent or preoperative tracheoesophageal fistula must be identified and occluded. The healing of such a suture requires good vascular coverage because of the firm and poorly vascularized scarring processes in the mediastinum. For this purpose, a pericardial flap can be used (or a muscular flap taken from the intercostal muscles or from the latissimus dorsi in the most severe cases). However, in some cases, we have left part of the native esophagus after removal of its mucosa and used it as tracheal or bronchial coverage with success.

12.5.3 Which Transplant?

The esophagus may be replaced by a segment of colon, the entire stomach, a gastric tube or a part of the small bowel. However, none is perfect or can operate as a normal esophagus.

12.5.3.1 Colonic Transplant

The colon is the most frequently used conduit to replace the esophagus; the transverse, ascending or descending colon has been used in an antiperistaltic or isoperistaltic fashion. It offers the advantage of a segment of bowel with several possible vascular supplies that is long enough to be mobilized. Its width is approximately the same as that of the esophagus. Its length can be adjusted to the specific requirement [8, 9, 12]. This procedure requires meticulous attention to technical details for a successful outcome.

The procedure is carried out through a midline incision from the xyphoid process to the umbilicus. The best transplant is taken on the transverse colon, vascularized by the left colonic artery and placed isoperistaltically (Fig. 12.2). Before ligating the unused vascular bundles, it is wise to generously mobilize the colon from the right to the left, severing the gastrocolonic ligament and to explore carefully its arteries. An efficient left colonic artery is missing in about 10% of patients, and the anastomotic transverse colonic arcade can be absent. We check the quality of the chosen arterial supply by clamping the unused arteries during 10–15 min with atraumatic vascular bulldog artery clamps. The superficial arteries must be pulsating (especially those at the farthest end from the vascular supply) and peristaltism must be present. Once an appropriate

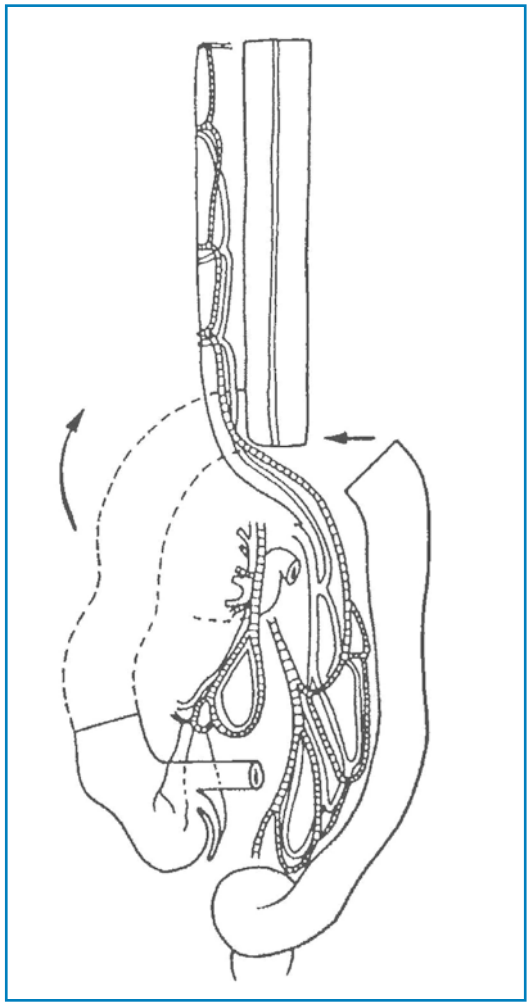

Fig. 12.2 Isoperistaltic transverse colon vascularized by the left colonic artery

length is chosen, the transplant is prepared by severing the unused vessels while preserving long arcades. We use conventional ligatures and never coagulate them to prevent vascular spasms. Once freed, the transplant is cleaned and preserved in warm cloths, avoiding tension on its vascular supply.

The colonic transplant has no efficient propulsive contraction and empties by gravity. However, it was demonstrated by Jones et al. in 1971 on animals [24] and since then in humans [25] that acid reflux in the transplant can induce a contraction which protects the colonic mucosa against acid aggression. If reflux occurs, this intrinsic contraction (which can be reproduced with the amplitude of 15–20 mmHg for 45–50 s) can rapidly clear the colon. For this reason, we believe that colonic transplants should be placed (if possible) in an isoperistaltic position to benefit from this self-protection.

If the right colon is used, it can be placed in an isoperistaltic fashion using a vascular supply from the middle colonic artery or antiperistaltically on the ileocolic artery. The right colon is shorter than the transverse colon, so the distal ileum is used with sacrifice of the valve to gain some extra length.

In some cases, we use an interesting artifice suggested in 1974 by Papahagi and Popovici. When carrying out the gastrostomy, these authors ligated the middle colonic artery and sometimes the right one to stimulate development of the left one, anticipating transverse isoperistaltic colonic replacement [26].

To bring the transplant to the neck, we use a large (40 mm) Penrose drain, the proximal end of the transplant being placed inside and sutured to it. This avoids any friction to its proximal edge when pulling it up. We check the arterial pulse with Doppler ultrasonography, but also the venous return.

We always perform the proximal end-to-end anastomosis using single-layer, full-thickness interrupted resorbable sutures with a V-shape incision of the proximal esophagus to make the colon width fit to its diameter (if needed). In some cases, if a short stenosis is present in the upper part of the native esophagus, we widen it using the Mikulicz procedure to avoid the anastomosis being too close from the upper esophageal sphincter.

The distal cologastric anastomosis is undertaken on the anterior wall of the stomach by the upper third of the small curvature. The suture is done using two layers of resorbable stitches, with disrupted stitches on the seromuscular suture and a running stitch on the mucosa.

As we placed the colons in an orthotopic position, we experienced frequent reflux and/or stasis in the transplants. Thus, we felt

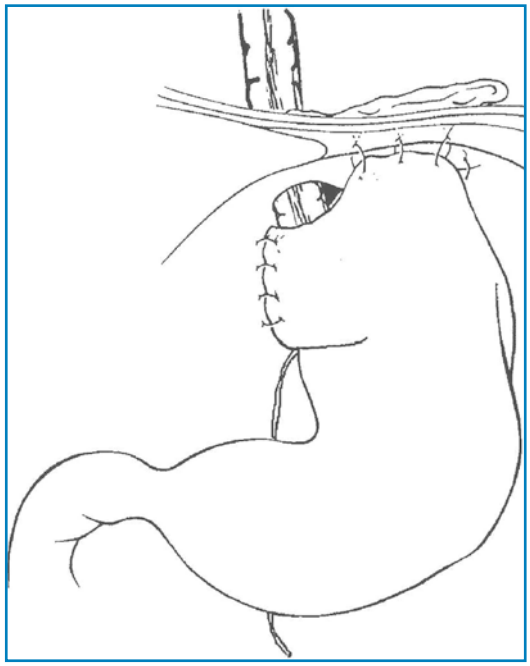

Fig. 12.3 Anti-reflux wrap for colonic transplants

the need of a new anti-reflux procedure because the standard procedure (Nissen, Toupet) was too efficient on the weak wall of the colon. We described in 1993 a new anti-reflux procedure for colonic transplants using an anterior wrap similar to the one described by Dor that was made out of the fundus but fixed to the right crus [27] (Fig. 12.3). It covers 3 cm of the distal transplant. The wrap must be loose enough not to compress the vascular pedicle located behind the transplant. The opening of the hiatus behind the transplant is never closed. This loose anterior wrap is efficient enough on a colonic transplant to prevent reflux (as shown by esophagography on day 10). It reduces the reflux from 48% to 7.5% using the anti-reflux wrap and from 40% to 21% on later esophagograms. A long-term prevalence of stasis of 25% in the transplant is not increased with this valve [27].

We have never carried out gastric drainage or a Mikulicz pyloroplasty even if damage to the vagus nerves was suspected. We have observed some stasis in the stomach and in the transplant, but they have all resolved spontaneously within a few days or weeks. Some children have delayed gastric emptying before surgery, so we believe that the vagus nerves have suffered transparietal burns because it is in the scar of the peri-esophagitis.

12.5.3.2 Gastric Tube

The concept of a gastric tube comes from experiments on gastrostomies undertaken during the second half of the nineteenth century. The first use of a gastric tube as an eseophageal substitute was by Daniel Gavriliu from Romania in 1951. Heimlich claimed he did it first but, in 1957 after visiting him, he paid tribute to Gavriliu. The first gastric tube procedure in the USA was by the Canadian James Fallis. Dan Gavriliu built two tubes using the greater curvature vascularized by the gastroepiploic artery. The first one was a reversed gastric tube, the pre-pyloric antrum being brought to the neck and vascularized by the left gastroepiploic artery; the second tube was isoperistaltic and supplied by the right gastroepiploic artery. At that time, both required a splenectomy [2,3]. Today, most gastric tubes are reversed, built from the greater curvature of the stomach and with blood supply from the left gastroepiploic artery without splenectomy (Fig. 12.4). It brings the antrum to the neck, this part of the stomach producing less acid than the fundus.

The procedure involves first the division of the gastrocolic ligament, preserving the gastroepiploic artery from the pyloroduodenal artery to the splenic one. Usually, the short gastric vessels can be preserved. The free edge of the tube should be taken at about 3 cm from the pylorus. The gastric curvature is molded around a 24-F tube using 2–3 shots of a 75 mm-long GIA™ stapler or is hand-sewn. It is brought to the neck in the same manner as for a colonic transplant. Care must be taken to the hinge between the tube and the stomach, and some reinforcement stitches can be useful. The upper anastomosis is done in the same way as for the colon. A gastrostomy is carried out on the anterior wall of the stomach. A

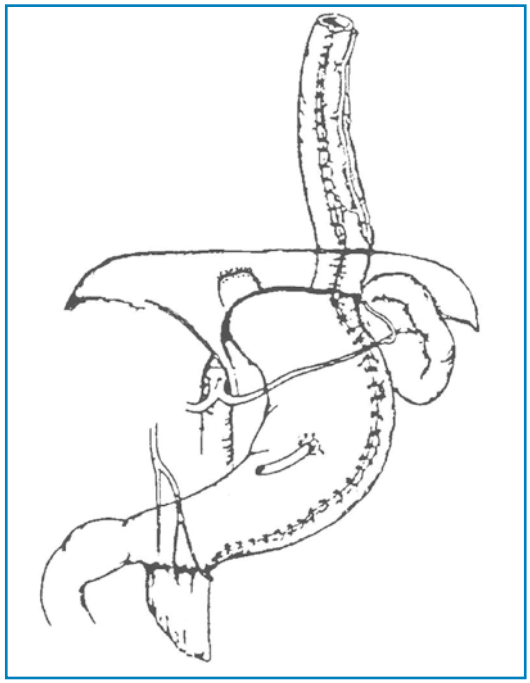

Fig. 12.4 Reversed gastric tube vascularized by the left gastroepiploic artery

decompression tube into the transplant, a gastrostomy tube and a jejunal feeding tube are placed through it [8].

The gastric tube is an excellent substitute to the esophagus with a reliable blood supply, better than the colon. However, a major problem is related to the position of a previous gastrostomy along the great curvature, which interrupts the gastroepiploic artery. We had to deal with several redo esophageal replacements for severe stenosis of the upper part of gastric tubes because the surgeons had closed gastrostomies along the curvature to build their tubes. When carrying out a gastrostomy for caustic stenosis, it is wise to place it far away from the great curvature, just in case a tube should need to be created. Even with an apparently intact gastroepiploic artery, defects in its continuity have been shown in cadaver studies by Koskas et al. and Ndoye et al. [28, 29].

Because a part of the stomach has been used, an anti-reflux wrap is not possible. Thus, the gastric tube has the disadvantage of an associated gastroesophageal reflux with the possibility of an ulcer later on. The long suture carries the risk of a leak and progressive dysfunctional propulsion. It appears to act purely as a passive conduit. The volume of the stomach reduced at the beginning grows with time. The gastric tube keeps its tubular shape without developing dilatations.

12.5.3.3 Gastric Pull-up

In the last two decades, the gastric pull-up became predominant. This has been due to the works of Sweet in adult patients with esophageal cancer [30] and Spitz in children [31]. Discouraged by the long-term results of colonic transplants at his institution, Spitz reintroduced it for esophageal atresia at first [9].

The gastric pull-up involves mobilization of the entire stomach, creating a space in the mediastinum and achieving only one anastomosis in the neck with the cervical esophagus. The patient is positioned supine with the neck, chest and abdomen prepared and draped. A midline laparotomy is done and the gastrostomy is taken down and closed. The stomach should be totally freed from adhesions: the gastrocolic ligament with the short gastric vessels should be carefully divided as well as the gastro-hepatic omentum. The right gastroepiploic artery is preserved and the left one divided. This may imply removal of the spleen. The gastroesophageal junction is closed with two layers of sutures. The stomach must be completely freed, preserving the blood supply *via* the right gastric artery and right gastroepiploic vessels. The stomach is brought to the neck through the mediastinum. Extra length can be obtained by addition of a Kocher maneuver or by other improvements of the technique (e.g., additional Collis procedure) [32]. The esophagus is sutured to the fundus of the stomach using a single layer of full-thickness interrupted sutures. This gives the longest possible conduit [33].

The vagus nerves are divided bilaterally during gastric pull-up, so most authors recommend a Mikulicz pyloroplasty. However, Cowles and Coran advocate an extramucosal pyloromyotomy considering that a formal

Mikulicz pyloroplasty is placed under tension when the conduit is pulled into the neck and a pyloromyotomy is suitably efficient. A feeding jejunostomy should be done for the postoperative period [33].

The gastric pull-up requires a single cervical anastomosis and the conduit has an excellent blood supply. However, the closures of the gastrostomy, esogastric junction and the pyloric procedure are at risk of leakage in case of gastric distension [8].

Hirschl et al. found no deaths in 41 patients who underwent surgery between 1985 and 2002, but a high prevalence of leaks (36%) and strictures (49%) was noted [34]. In a large, single-center updated series of 192 gastric pull-up procedures over a 25-year period, Spitz reported no instances of transplant failure but deaths in 5.2% of cases. Morbidity is not unusual, and can include cervical fistulae (12%), anastomotic strictures (19.6%), swallowing dysfunctions (30.6%), and delayed gastric emptying (8.7%) [35].

For the sake of comparison, from 1989 to 2012 we undertook 280 esophageal replacements using the colon or a gastric tube (but no gastric pull-up): no deaths were observed and no transplant lost. The complications were cervical leaks in 12% (all of which resolved spontaneously within a few days), proximal stenosis requiring 1–12 dilatations (and two enlargement surgeries, see below) in 35%, and <20% refluxes in the transplants.

In 2009, Tovar et al. reviewed a series of 33-year median follow-ups of 65 patients with colonic interpositions, and reported deaths in 9% of cases. Patients experienced mild symptoms of reflux (43%), scoliosis, (22%) and other complications [9].

Gastroesophageal reflux is a major problem encountered by 25–30% of patients with gastric transplants with acid and/or biliary reflux even if pyloroplasty is not carried out. The prevalence of reflux esophagitis in the upper native esophagus if the stomach is used as a substitute is 30–78%. The gastric conduit is aperistaltic and surgically denervated even if studies have shown mass contractions of the body of the stomach without obvious rhythmic peristaltic contractions [36].

Another major problem is related to the volume of the stomach in the chest of small children, which compromises lung function and the venous return. We were involved in undoing gastric pull-ups for life-threatening events and possibly some of the reported deaths were related to that. According to Newman and Anderson, reports suggest that several patients undergoing gastric pull-up in the 1960s required colon transposition in the 1980s because of lung problems associated with chronic acid reflux, aspiration pneumonia and compression by a dilated intrathoracic stomach [37].

12.5.3.4 Small Bowel Interposition

Several techniques of small bowel interposition have been tried using the jejunum or ileum on their pedicles [38, 39] or as free grafts [40].

Jejunal interposition is seldom used because the blood vessels of the jejunum are thin and frequently compromised after anastomosis. According to its vascular disposition, the jejunal transplant requires withdrawal or a greater length than needed to divide the vascular arcades and to allow curves in the jejunum to be straightened [2, 38]. Furthermore, the jejunum is fragile to the erosion of acid, so the jejunum should not be the first choice. However, we have used the jejunum as a rescue transplant for referred patients after failure of a colonic and/or gastric transplant. Nevertheless, the jejunum can be used in the neck as a free graft with microvascular anastomosis on the facial or superior thyroid arteries. We used it successfully in short stenosis of the cervical esophagus or in 2 cases after recurrent stenosis of the proximal anastomosis in transplants.

12.5.4 Pharyngeal-associated Burns

Burns from the ingestion of caustic agents may also include the oral, pharynx and larynx. Combined lesions of the esophagus and phar-

ynx are unusual but represent a challenging problem. Among 281 esophagoplasties undertaken for caustic burns since 1989, 20 children had associated pharyngeal burns with partial or total destruction of the epiglottis, pharyngolaryngeal stenosis, and/or obstruction of one or both pyrifom sinuses with variable severity (including total closure of the airways in 4 cases). In spite of severe narrowing of the airways related to subglottic diaphragm with respiratory impairment, only 3 cases had tracheostomies when referred. However, they all had intact vocal cords. The closure reflex of the laryngeal vestibule during accidental ingestion of caustic materials acts as protective measure at the level of the larynx [41]. With the help of ENT surgeons, we totally resected the pharyngo-epiglottic stenosis with a CO_2 laser under suspension micropharyngoscopy at the beginning of the procedure. This allowed resection of the two pyriform sinuses with excellent homeostasis and located exactly the place where the transplant should be brought.

Then a one-stage esophagoplasty is done using isoperistaltic colonic interposition or a gastric tube associated with an endocopic pharyngoplasty, the proximal anastomosis being done at the level of the arythenoids on the larynx and higher in the oro-pharynx posteriorly. Thus, the proximal end of the transplant is 3–5 mm from the vocal cords. A long stay in the Intensive Care Unit (ICU) is needed after surgery because of possible pharyngeal and pulmonary complications, in spite of tracheostomies.

In all but one child we were able to recover normal swallowing within 2–6 months. After this time they did not present with broncho-aspiration during the day once the tracheostomy was closed. It took 3–12 months until they stopped coughing at night. During this period, pulmonary aspirations were frequent and a high prevalence of pneumonia episodes (1–5 per child) noted. With a follow-up of 1–10.6 years all children are healthily eating and breathing normally.

We believe that very proximal pharyngeal anastomosis of esophageal replacements can be attempted as long as children do not have impairment of mobility of the vocal cords by glottic scars or lesions in the recurrent laryngeal nerve. However, the rehabilitation takes time, during which aspirations and subsequent pneumonia occur. Regardless of the transplant used, there is an important difference in those in which the proximal anastomosis is done a few centimeters below the upper esophageal sphincter or if it has been destroyed.

12.6 Outcome, Complications and Follow-up

12.6.1 Immediate Follow-up

Patients leave the operating theater with several pieces of equipment. We place a low-pressure suction tube into the transplants to avoid postoperative distension. We believe that most vascular problems are not related to the arterial supply but due to venous stasis. Deflating the transplants improves venous return.

The children cannot eat postoperatively (sometimes for an extended period), so we avoid total parenteral nutrition, placing a gastrostomy in all cases. It is used to deflate the stomach while the gastric sutures heal, and a jejunal tube is placed through it to feed the child promptly.

Intraoperatively, we always place a non-resorbable, never-ending thread through the nose, throat and transplant, and it is exteriorized through the gastrostomy. This never-ending thread is left *in situ* for months. It can be used to replace a probe in the transplant without the risk of perforation related to blind introduction in a tortuous conduit. Furthermore, it has the advantage of safe dilatations, and Rehbein bougies are used for the same reasons.

12.6.2 Postoperative Period

Postoperative care demands a stay in the ICU because of potential pharyngeal and pul-

monary respiratory complications. Hence, we intubate patients for 2–5 days. We ask intensivists to administer adequate fluids and sometimes amines during the first 24 h to maintain as high a mean arterial pressure as possible, thereby avoiding poor perfusion in the transplant.

12.6.3 Stenosis and Leaks

The most frequent short- and long-term complications of esophageal replacements are leaks and stenosis of the proximal anastomosis. Leaks at the proximal anastomosis occur even if the transplant is well vascularized and the suture line free of tension on an intact proximal esophagus. We believe they are related to ischemia of the farthest end of the transplant. Slight ischemia seems to be related to venous stasis rather than poor arterial supply, as evidenced by the fact that a straighter transplant gives better results with less leakage and stenosis than a tortuous one.

The same explanation can be ascribed to stenosis of the proximal anastomosis but may follow persistent ischemia. We noticed that all patients with a leak of the proximal anastomosis require dilatations. Two children developed cervical stenosis 3 months after the replacements, and 2 others developed cervical stenosis 3 years and 5 years after surgery even though the radiological, endoscopic and surgical aspects were normal and they were already eating. These findings were probably related to a recurrent hypertrophic healing process induced by the surgical procedure and/or by subsequent oral feeding. These recurrences raise the question of how long these children should be kept under observation.

12.6.4 Long-term Follow-up

Patients in our series had a mean long-term follow-up of 8.6 years. All patients are eating normally, with no failure to thrive and no growth retardation. Most children or parents have no complaints. Those who are now adults lead a normal life. Nevertheless, many children experience noisy breathing, coughing refluxes, and have acquired strange eating habits (e.g., drinking between each bite).

12.7 Conclusions

According to Cowles and Coran, the "ideal" esophageal replacement conduit for children should: (a) be long-lasting; (b) be associated with minimal reflux; (c) be technically feasible; (d) not affect cardiac or pulmonary function; and (e) allow oral consumption of nutrition [33]. With experience of >280 esophageal replacements during 24 years, we still do not know the best procedure.

When intending to replace an esophagus the surgeon does not know which transplant can be used: if the gastrostomy has been placed too close from the great curvature he/she may face an interruption of the gastroepiploic artery, and a gastric tube cannot be achieved. If the surgeon plans a colonic transplant, a missing artery could make it impossible. Therefore, the surgeon must be able to adapt his/her technique to the patient's condition, and so must be aware of several techniques.

Our belief is that a successful esophageal replacement does not behave as a normal one. The best esophagus for a child is his/her own one. Everything must be done to preserve it, and esophageal replacement should be the last resort.

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Gastroesophageal Reflux

13

Juan A. Tovar

13.1 Introduction

Gastroesophageal reflux (GER) is the retrograde passage of gastric contents into the esophagus. GER is so common in infancy and childhood that it is difficult to distinguish "normal" spitting or regurgitation from gastroesophageal reflux disease (GERD). In most infantile cases, GERD has a benign clinical course with a spontaneous tendency to improve over time. However, occasionally it can evolve into a severe (or even lethal) condition requiring aggressive treatment. In these cases, important therapeutic decisions are needed because surgery is often required.

13.2 Anatomical and Physiological Basis of GER

The esophagus transports the alimentary bolus from the pharynx to the stomach. For this purpose it generates organized peristaltic movements that are particularly active during meals. In contrast, the esophagus lacks any digestive or absorptive function. Its mucosal lining is not prepared for prolonged contact with digestive juices and, because the nature of gastric secretion is particularly harmful, an efficient barrier with several components is interposed between both organs [1]. The main components are the lower esophageal sphincter and the diaphragmatic crural sling that overlap anatomically and work synergistically to close the esogastric junction permanently except during deglutition, when passage of the bolus into the stomach is required [2]. The circular layer of smooth muscle of the distal esophagus constitutes the sphincter that maintains a permanent tonic contraction and which relaxes only during deglutition. Conversely, the striated muscle fibers of the crural sling that surround the distal esophagus contract rythmically and displace downwards the gastroesophageal junction during each inspiratory movement, when the intrathoracic negative pressures are stronger and accentuate the abdomino–thoracic gradient [3]. Other components of the gastroesophageal barrier are the intra-abdominal esophagus compressed by permanently positive pressures, the air chamber of the gastric fundus, and the angle of His.

In addition to the barrier and peristalsis, the esophagus has other defense mechanisms: saliva and the fluid secreted by the esophageal submucosal glands are alkaline and buffer the acid present into the lumen [4, 5]. The structure of the mucosa is the result of a permanent balance between desquamation of the outer cells and regeneration from the basal layers.

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Physical or chemical aggressions increase desquamation, but the mucosa can react by increasing proliferation [6]. The high concentration of epidermal growth factor (EGF) in the saliva suggests that stimulation of proliferation is, to some extent, related to salivary secretion [7].

Swallowing triggers primary peristaltic waves that progress caudally along the esophagus. Simultaneously, the upper and lower esophageal sphincters relax, making propulsion and passage of the bolus into the stomach possible. If the closure mechanism of the barrier fails, allowing reflux of the gastric fluid into the esophagus, non-deglutory secondary peristaltic waves are triggered to achieve clearance [8]. All of these actions are mediated by the intrinsic neural network of the esophagus and regulated by vagal and sympathetic nerve fibers. The normal esophagus undergoes occasional simultaneous tertiary non-propulsive waves that are definitely more frequent in GERD (9).

The anatomical position of the esophagus favors GER: the stomach is located in the abdominal cavity and contracts strongly. For these reasons, it is under permanently positive pressures. In contrast, the esophagus is a predominantly thoracic organ exposed to strong negative inspiratory pressures. This anatomical arrangement creates a positive abdomino–thoracic pressure gradient that facilitates GER, particularly during inspiration [10]. The recumbent position further aggravates the gradient, and this explains (at least in part) why GER is so common in infancy and why it improves with acquisition of the standing position.

13.3 Reflux Mechanisms

The barrier may be anatomically distorted (as in hiatal hernia) or functionally abolished (thereby facilitating GER). However, there is manometric evidence of non-deglutory relaxations of the sphincter as the main cause of episodes of GER in children as well as in adults [11]. Abolition of sphincter tone for longer or shorter periods of time creates a common gastroesophageal cavity in which the unfavorable pressure gradient acts without restriction. The causes of these relaxations are unknown, but they are certainly related to failures in the neural or humoral regulation of the mechanisms of closure [12].

In addition to these non-deglutory relaxations, there are some comorbidities in which the barrier mechanisms are absent or modified, thereby facilitating the appearance of GER. These conditions are particularly relevant for pediatric surgeons because they constitute the main indications for surgical treatment.

Neurologic impairment: Children with neurologic disease of various origins have abnormal neural regulation of the gastrointestinal (GI) tract, spasticity, constipation, scoliosis, and are often in the recumbent position, These factors distort the anatomy of the barrier and interfere with its function, leading almost constantly to GERD [13].

Neonatal malformations in which the barrier itself or its functions are abnormal: Babies surviving neonatal surgery for esophageal atresia (EA), congenital diaphragmatic hernia (CDH) and anterior abdominal wall defects (AAWDs) frequently suffer GERD. In EA, the more or less tight anastomosis achieves reconstruction of an esophagus that is shorter than normal and that has abnormal innervation [14–16] and Cajal's cells [17]. The intra-abdominal segment of the esophagus is often absent and the angle of His is obtuse. A failing barrier and damaged peristalsis means that GERD is likely in this patient group [18, 19]. In CDH, closure of the hernial orifice puts the hiatus under tension while increasing abdominal pressure and exaggerating negative thoracic pressure [20]. The increased abdomino–thoracic gradient facilitates GER, which is further aggravated by an inefficient peristaltic pump. The esophagus is often dilated and atonic (21) probably because it is poorly innervated [22, 23]. Conversely, abnormal rotation of the gut, which is almost constant in

CDH, further facilitates GER. Finally, neonatal closure of AAWDs such as omphalocele and gastroschisis increases the intra-abdominal pressure [24, 25] and the almost constant association with malrotation also facilitates GER [26].

Infra-esophageal obstruction: pyloric stenosis, duodenal or jejunal stenosis and malrotation delay gastric emptying and facilitate GER.

13.4 Natural History of GER in Childhood

In contrast to adults in whom GERD is a more or less permanent condition, children (and particularly infants) have a marked tendency to improve to the point that all diagnostic and therapeutic approaches should be tailored to this evidence.

Immaturity of the gastroesophageal barrier was supposed to be present in newborns and infants, and this was accepted as a good explanation for the frequency of GER at this age. Following this line of thought, progressive maturation of the mechanisms of barriers would explain the tendency to improve with time [27]. There is no strong manometric evidence to maintain this explanation because infants [28, 29] and even premature babies [30, 31] have adequate sphincteric pressures. Most probably, the recumbent position, the relative sizes of the esophagus and the stomach, and high-pressure gradients between the abdomen and the thorax facilitate GER in young infants. Acquisition of the upright position and changes in the relative sizes of the body compartments contribute to decrease GER-facilitating conditions, and most patients are asymptomatice by the age of 12–18 months. After 2 years, only a minority of patients remain symptomatic [32]. They belong probably to a select population in which the factors leading to GER persist. This group is particularly relevant for pediatric surgeons because most of the surgical indications are in this group. However, the disappearance of symptoms means that the babies stop vomiting and gain weight; it is not known if some of them undergo silent reflux and become symptomatic much later. GER is extremely common in adults, and many of these patients have a history of vomiting during infancy.

Children with GER and neurologic impairment or previous surgery for EA, CDH or AAWDs do not tend to improve over time. Hence, it would be a serious mistake to tailor their treatment following the guidelines imposed to the generally favorable natural history of the disease in other cases [33].

13.5 Clinical Features

GER may manifest itself in children through three pathogenic pathways that may concur in the same patient.

Vomiting is the key symptom of GER in neonates and toddlers. It is non-bilious, frequent, rarely complete and often (but not always) post-prandial. These children stop thriving and may become malnourished after some months. Regardless of the severity of reflux, vomiting decreases in frequency and volume over time and usually resolves when the child starts walking. Children aged >2 years in whom GER persists vomit rarely or only if they have concurrent diseases. Refluxing adults do not vomit and older children are in this respect very similar to them. Other consequences of the frequent presence of refluxate into the esophagus are foul breath (halitosis) that is obvious for the relatives, and deterioration of dental enamel.

Esophagitis: Repeated or prolonged exposure of the esophagus to acid and/or alkaline refluxate harms the mucosa, which desquamates and becomes infiltrated by neutrophils and eosinophils. Active regeneration from below thickens the basal layer and lengthtens the papillae. If desquamation takes over regeneration, the papillar vessels are exposed and bleed. In severe cases, the inflammation reaches the deeper layers of the wall, leading to ulceration and fibrosis.

Hemorrhage is more often microscopic and may be undetectable except by stool tests. However, it may lead to iron-deficient anemia, which stops mucosal regeneration and further aggravates esophagitis. The hemorrhage is manifested by hematemesis or melena only rarely.

Esophagitis is painful and these patients show their disconfort in different ways. Older children may describe it as heartburn or retrosternal pain but more often, particularly younger ones, complain of "abdominal pain" which is frequently periumbilical or cry bitterly without apparent explanation. These infants may be agitated during the night and are often "irritable" or "unfriendly".

Inflammation of the esophageal wall may also cause dysphagia, which is a rare complaint during childhood. A few cases (in general, untreated refluxers with brain damage) have peptic stenoses that make swallowing progressively difficult or impossible and which require aggressive treatment.

Occasionally, GER is accompanied by torticollis or vicious neck positions without osteomuscular causes. This condition is known as Sandifer's syndrome and is sometimes the only symptom of esophagitis and dysphagia [34].

Respiratory tract disease involves an important group of symptoms that are known to be associated with reflux but which are often attributed to other origins. GER may cause chronic laryngitis and edema in the upper airway [35]. It can also permit aspiration of the gastric content into the airway, leading to sudden death (Mendelson's syndrome), asphyxia with apparent life-threatening events (ALTEs), missed sudden infant death (rare), repeated pneumonia or atelectasis (frequent) and recurrent bronchitis or infection of the respiratory tract (very frequent) [36]. Sometimes the bronchitis is of a spastic or constrictive nature, mimicking asthma. GER may cause bronchial constriction by local eso–bronchial reflexes or by microaspiration. This in turn may help to sensitize the respiratory epithelium to some alimentary allergens. Conversely, medications such as xanthines that are known to relax the lower esophageal sphincter, together with an increased gastroesophageal pressure gradient by expiratory efforts, facilitate reflux in children with atopic asthma. The consequences of the uncertainty of these pathogenetic pathways are relevant because, if GER comes first, its treatment will alleviate or cure the respiratory tract disease but, if it is secondary to respiratory triggers, the control of GER will be achieved only after treating these effectively [37].

Familial history, evidence of atopy, increased immunoglobulin (Ig)E or positive skin tests should be taken into account as indicative of a primary respiratory origin when trying to determine the association of GER with respiratory symptoms. Conversely, a history of vomiting during infancy or some pH-metric features (see below) are more consistent with primary GER inducing respiratory tract disease in a secondary manner.

13.6 Diagnostic Tests

13.6.1 Methods

GER is, to some extent, a normal phenomenon that happens in all of us, particularly after meals. Therefore, its diagnosis cannot be based on its detection alone but rather on some form of quantification. To estimate how much GER is harmful is difficult, and this explains the apparently excessive variety of tests used for this purpose.

Radiology: Barium meals are still used for the diagnosis of GER. They provide morphologic information (hiatal hernia, esophageal stenosis, absence of the His angle, delayed emptying, malrotation) (Fig. 13.1) that can be crucial for carrying out treatment. However, for assessing GER itself, radiology generates too many false-positive diagnoses and has poor specificity [38].

Scintigraphy: Using an isotope-tagged meal instead of barium allows detection of

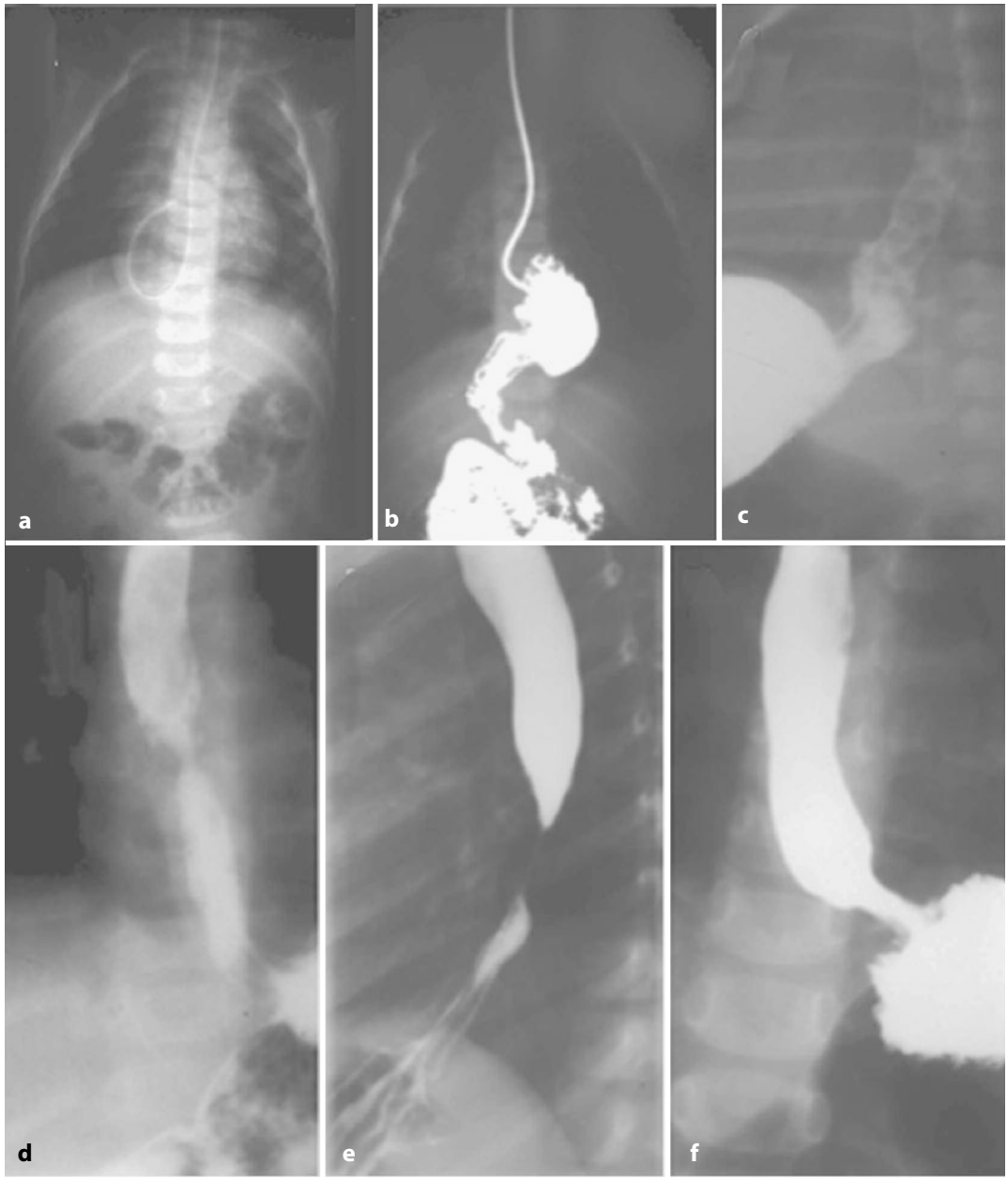

Fig. 13.1 Plain radiograph of the thorax and abdomen (**a**) and plain radiograph of the thorax and abdomen after a barium meal (**b**) in a baby with hiatal hernia. An air bubble above the diaphragm is seen in (**a**) and as an ectopic stomach is observed in (**b**). Images **c-f** are different barium studies in an infant with GER without gastric displacement (**c**). She was under antacid therapy for years before developing peptic stenosis in the mid-esophagus (**d**). One year later, she was barely able to swallow and the esophagus had shortened (**e**). The barium meal after repeated dilatation and successful Nissen fundoplication is shown in (**f**)

GER episodes over long periods of time with minimal irradiation. Scintigraphy also allows assessment of gastric emptying. However, the morphological information obtained is quite approximate, and the equipment is scarce and expensive. Hence, it is not suitable for routine diagnosis of such a common condition [39].

Ultrasonography has the advantage of being harmless even during prologed use. Widening of the junction and flow through it can be detected by expert observers. Although it is operator-dependent, it will probably be used increasingly frequently in the future [40].

Fiberoptic endoscopy and biopsy: Modern endoscopes allow direct observation of inflammation of the esophageal mucosa and exudates, stenosis or ulcers. Biopsies can be taken to assess esophagitis (papillary lengthening, basal thickenning, leukocyte infiltration, ulceration or Barrett's columnar dysplasia). However, esophagitis is only one of the pathogenic pathways of GERD and although not very often, patients may even die of reflux without esophagitis. Nevertheless, the finding of esophagitis is an important adjunct to the diagnosis.

Prolonged measurement of esophageal pH is the best method for quantifying reflux. An antimony or glass electrode is placed in the lower esophagus and connected to a pH meter that allows recording of the pH in the lumen every few seconds, together with other information (e.g., timing of meals, position) in a portable Holter-type device. A pH of 4 is the threshold to mark the onset of abnormal exposure to acid. The number of falls below this level, the proportion of total time below pH 4, the number of episodes lasting >5 min and the duration of the longest episode are measured [41]. Other variables (such as the area under the curve or scores that put all these data together) can also be measured. However, in our experience the four "classical" parameters and a thorough analysis of the trace give the best information.

However, prolonged measurement of esophageal pH has limitations. The pH meter measures only pH and not reflux; if the gastric content is not acid, the esophageal electrode will not read any episode of reflux. This is particularly bothersome in young children who receive 5–6 feeds every day. The gastric pH is buffered for ≥2 h after each meal, so the esophageal electrode will remain "blind" for 12 h out of 24 h.

The same artifact might occur if alkaline duodeno-gastric reflux occurs. In these cases (well known in adults and not very well studied in children), bile and pancreatic secretions activated by HCl and pepsin neutralize acid while creating a harmful refluxate that cannot be detected by a pH electrode located in the esophagus. Simultaneous use of gastric and esophageal pH electrodes allows better assessment of the nature of the refluxate and pH within the esophagus [42].

Impedance: Prolonged multichannel intraluminal impedance (MII) measurement is a relatively non-invasive procedure that allows detection of the changes of volume at different levels of the esophagus and hence displacements of contents in either direction. If coupled with one or more pH electrodes, it provides a complete view of acidic, non-acidic or alkaline episodes of reflux and provides information about clearing capacity. However, its acceptatance as a new "gold standard" is limitred because: of its expense; of its time-consuming nature; and difficulty in interpretation of data [43, 44].

Manometry: Direct measurement of the pressures within the lumen of the esophagus allows assessment of the sphincter as well as peristalsis. It therefore permits evaluation of the status of the barrier and clearing ability of the esophagus.

Manometry also requires multichannel probes with lateral orifices perfused with pneumohydraulic pumps capable of creating constant high pressures within low-compliance systems. These are in turn connected to transducers that deliver the information continuously to recording devices.

Previously, sphincteric manometry was undertaken by pulling the probe through the gastroesophageal junction or high-pressure

zone. Gastric pressures were first recorded followed by a pressure *plateau* corresponding to the sphincter and then by thoracic pressures. Introduction of perfused sphincteric sleeves allowed stationary study of the sphincer and revealed that non-deglutory relaxations were at the origin of most episodes of GER. Manometry is not very popular because measurement of the pressure is valuable only when it is very diminished and because non-deglutory relaxations are difficult to record [11].

Assessment of peristalsis using stationary perfusion manometry in children is difficult for obvious reasons. However, it has been facilitated to some extent by the introduction of non-perfused solid-state probes, but they are quite thick, making the procedure applicable only for older children.

Manometry has contributed appreciably to understanding of the phenomenon of GER and the physiology of the esophagus. However, it cannot be considered to be a routine diagnostic method in children.

13.6.2 Application of Methods

The application of the different diagnostic methods must be limited by reasonable suspicion of the severity or particular nature of GER in each particular patient. When dealing with young vomiting infants, no diagnostic procedure is indicated until a first-level therapeutic trial has been proven to fail. This approach makes these relatively invasive and expensive tests non-eligible for the vast majority of babies with reflux symptoms. In those in whom the symptoms are of late onset or persist beyond 2–3 years, measurement of esophageal pH is indicated. Scintigraphy or ultrasonography can also be used as first-level tests. Esophagoscopy is indicated in children only with symptoms suggestive of esophagitis [45]. Stationary or ambulatory manometry is justified only in children in whom motor disorders of the esophagus are suspected. In respiratory patients, measurement of esophageal pH is particularly useful and other tests such as the recovery of lipid-ladden phagocytes [46] from tracheal aspirates are poorly specific.

13.7 Treatment

Treatment of GERD in children is approached in a rather conservative manner on the basis of the generally favorable natural history of the disease. Most babies suspected of having GER are treated initially with minimal measures even before diagnostic tests. Twenty-four-hour maintenance of the upright supine or prone position, decreased volume with an increased number of feeds, and the use of milk thickeners if the baby is bottle-fed may stop symptoms. A semi-upright position is attained in older children (as in adults) by elevating the head of the bed. A light and early dinner avoiding fat and chocolate is advisable at this age. Alginates and other absorbants (e.g., sucralfate) are used but, if these medications are required, it is probably better to give H_2-receptor inhibitors such as cimetidine (30 mg/kg/day) or ranitidine (10–15 mg/kd/day). If symptoms persist, a prokinetic drug is indicated. Cisapride (0.8 mg/kg/day in three doses) is a non-dopamine receptor blocker that improves esophageal peristalsis, strengthens the sphincter and facilitates gastric emptying. Cisapride was used for a long time with some success until side effects on heart conduction were reported. Domperidone (1 mg/kg/day), metoclopramide (0.5 mg/kg/day) and other prokinetics are used instead. The results have been reported to be satisfactory but evidence of their benefits in children is weak [47].

If there is evidence of esophagitis or if the symptoms are not controlled, energetic inhibition of the secretion of gastric acid with proton pump inhibitors (omeprazol, esomeprazol, pantoprazol) is indicated, and can also be used successfully in children [48–50]. After a few months, if the symptoms disappear, treatment can be stopped. If they recur, surgery should be discussed. If the symptoms do not disappear with treatment, this is considered to be failed treatment

and surgery should be considered. The recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) [51] and European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) [52] on the management of GERD in children were based on all aspects of the diagnosis and non-surgical treatment of GERD. These guidelines limited surgical indications to cases: refractory to optimal treatment; with intractable erosive esophagitis; with intractable asthma; of ALTEs with convincing evidence of a temporal relationship between the episodes and reflux. However, these recommendations did not take into consideration some of the comorbidities that are particularly relevant for pediatric surgeons [33].

In general, pediatric surgeons rarely propose surgery for patients before the age of 2 years to allow spontaneous improvement to occur. Only patients in whom conservative treatment fails undergo surgery, but this rule has some important exceptions.

Patients with respiratory symptoms and demonstrable GER should be treated surgically if they have a history of vomiting during infancy and repeated non-obstructive bronchial or parenchymal disease, or if they have prolonged nocturnal episodes of reflux upon measurement of esophageal pH [36, 53]. Under these circumstances, a favorable outcome can be predicted if a previous energetic course of medical treatment resulted in temporary relief. Nevertheless, some atopic asthmatic patients may also improve after anti-reflux surgery in terms of less dependency on drugs or fewer crises.

There are some rare circumstances in which the surgical indication should be made primarily. Children with brain damage and symptomatic reflux should also undergo surgery without much expectancy of a favorable natural history because the causes of GER will persist irrespective of the duration or nature of the treatment.

Children with symptomatic reflux in the context of previously treated malformations such as EA, CDH or AAWDs often require surgery because a favorable natural history cannot be expected. After ruling out malrotation or delayed gastric emptying, the surgical procedure should be planned.

A few babies with ALTEs or a near-miss sudden infant death syndrome may require early surgery. There are many other causes for these episodes, and every effort to exclude them should be made before surgical decisions are made. However, whenever GER is documented (and particularly if there are ALTEs in temporal coincidence with episodes of GER), there should be no hesitation. These children may die of GER and it is better to overindicate a relatively simple surgical procedure than to regret a preventable catastrophy [54].

Anti-reflux surgery aims at reconstructing an effective anti-reflux barrier while maintaining free passage of the bolus through the gastroesophageal junction. In the Nissen procedure, the gastric fundus serves to construct a periesophageal wrap that acts as a highly efficient pneumohydraulic valve. The wrap should be loose and not too long to avoid gas bloating and dysphagia. This is the most efficient anti-reflux procedure and should be considered the gold standard for other techniques to match. Anterior fundoplications have been proposed by Thal-Dor, Roy-Choudhury and Ashcraft [55] and Boix Ochoa [56] and posterior fundoplication has been introduced by Toupet [57] (Fig. 13.2). Other procedures such as anterior gastropexy may be less effective.

All these procedures are undertaken laparoscopically and have approximately the same outcomes and less discomfort that their open counterparts [58]. However, if local conditions interfere with the minimally invasive procedure (e.g., GER in low-weight infants or if EA is associated or peptic stenosis), an open approach remains appropriate.

Delayed gastric emptying should be suspected in children with large stomachs (rare in regular refluxers) or if prolonged post-cibal gastric neutralization is detected upon simultaneous measurement of gastric and esophageal pH. Isotopic assessment of emptying time is

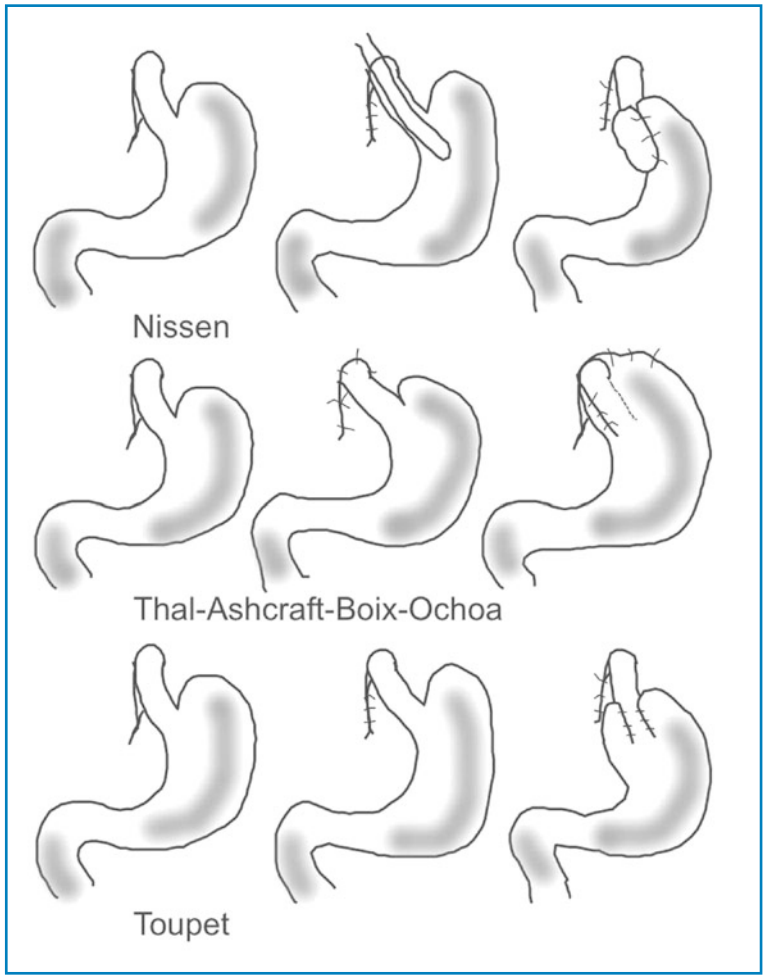

Fig. 13.2 The Nissen fundoplication is the gold-standard surgical treatment of GERD. The distal esophagus is replaced below the diaphragm, and the posterior wall of the fundus is passed behind the esophagus and sutured to the anterior wall in front of it. The one-way pneumohydraulic valve should be loose. A thick dilator within the esophagus during plication is convenient. The Thal–Ashcraft–Boix Ochoa anterior plication (middle drawing) or Toupet posterior plication can be as effective as the Nissen fundoplication

then indicated and, very rarely, a pyloroplasty or antroplasty is carried out to avoid undue pressure within the stomach caused by bipolar closure [59]. Evidence regarding the participation of delayed gastric empying in GERD in children is controversial.

Peptic stenoses should be first dilated until adequate esophageal caliber is re-established and, under vigorous acid supression, fundoplication should be done. Acquired brachyesophagus in these cases may make the laparoscopic procedure particularly difficult, and an open approach might be better in such cases.

Anti-reflux procedures are often highly effective but have some unpleasant side effects or complications that should be known by patients and families. For instance, use of the fundus for confectioning the wrap reduces gastric compliance transiently to the point of making large meals impossible during the first postoperative weeks. Also, long and/or tight wraps cause entrapment of gas into the stomach ("gas bloat") that may be very uncomfortable and which should be prevented by strict-

ly adhering to a policy of loose and short wraps. In addition, dumping syndrome is possible after fundoplication, particularly if a pyloroplasty or antroplasty are undertaken simultaneously to facilitate gastric emptying. This situation is rare and generally transient, but may be considerably bothersome and require dietary treatment.

Wrap failure should not be a very frequent problem in children undergoing surgery for GER alone. However, it is very common in neurologic patients and in those who previously underwent surgery for EA, CDH or AAWDs. This is because all of the mechanisms leading to GER persist postoperatively, and interposition of the wrap alone does not always maintain the situation for years.

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Esophageal Achalasia

14

Marcello Carlucci, Girolamo Mattioli
and Vincenzo Jasonni

14.1 Introduction

Esophageal achalasia (EA) is a functional disorder characterized by abnormal motility of the esophageal body associated with delayed (or absent) mechanical (but not neurogenic) relaxation of the lower esophageal sphincter (LES) during deglutition. Subsequent dilation of the overhanging esophagus, together with the primary hypoperistalsis, results in ineffective propulsion. EA in the pediatric population is rare, but several cases in late childhood have been described [1–8].

14.2 Epidemiology

Idiopathic EA is a rare primary motility disorder of the esophagus with an estimated incidence in the general population of 1 case per 100,000. The highest incidence is seen in those aged 30–40 years. It is more common in males (M:F=4:1) and is very rare in childhood. Pediatric EA is observed 4–5% of all cases, and is seen particularly in late childhood or early adolescence [2, 5, 9–11].

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14.3 Etiology and Pathogenesis

The etiology of EA is not known. It is considered to be an acquired disorder [12], but several studies have suggested that the genetic background may have a role in the pathogenesis. Primary and secondary forms have been defined. Evidence of a progressive disturbance in the intrinsic innervation of the esophagus characterizes the primary disorder. These motor abnormalities are probably the result of autoimmune-mediated destruction of inhibitory neurons by an unknown trigger in genetically susceptible individuals [13, 14]. Nitric oxide (NO) is a non-adrenergic, non-cholinergic neurotransmitter involved in the relaxation of smooth muscle. NO seems to play a part in the pathogenesis of primary esophageal achalasia: reduced (or absent) activity of nitric oxide synthase (NOS) inhibits the relaxation of the LES [15–16]. Secondary EA may be due to vagal nerve lesions, neuritis, esophagitis, infections (encephalitis, scarlet fever, Chagas disease). Chagas disease is caused by the parasite *Trypanosoma cruzi*. Classically, it presents as progressive degeneration of intrinsic esophageal innervation, leading to a dilated proximal esophagus ("megaesophagus") [17]. EA can be associated with syndromes such as Allgrove's (adrenocortical insufficiency, alacrimia, esophageal motor dysfunctions), Rozycki's (deafness, vitiligo, esophageal achalasia) or Down's [18, 19].

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14.4 Clinical Aspects

Symptom onset in EA is variable. Almost all patients present with progressive dysphagia until they complain of paroxysmal dysphagia (fluid dysphagia), retention, and regurgitation of undigested food retained in the esophagus. These findings should not be confused with vomiting. Retrosternal pain and pyrosis are described in ≤40% of cases. Failure to thrive, weight loss and foul breath are associated symptoms along with respiratory symptoms (nocturnal cough, repeated pneumonia because of frequent micro-aspirations). Syndromic patients can present with other symptoms (adrenocortical insufficiency, alacrimia, deafness, vitiligo, neurologic deficit) [7].

Classically, EA evolves in three major steps: stage 1: very mild dysphagia; stage 2 (compensation): decrease or disappearance of symptoms due to esophageal muscular hypertrophy; stage 3 (decompensation): resumption of dysphagia, regurgitation, and pain. Macroscopically, the esophagus is considerably dilated with variable thickening of the wall. Microscopically, a hypertrophic muscular layer associated with various fibrocellular degenerative phenomena is present. Inflammation of the submucosa and lamina propria, as well as epithelial hyperplasia, may be present.

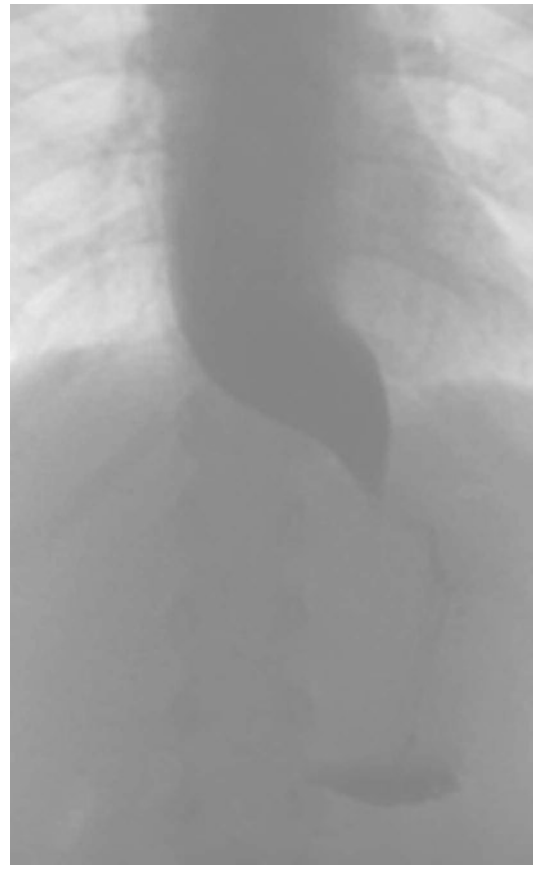


Fig. 14.1 Barium swallow test showing the esophagus to be dilated with slow emptying. A typical "bird's beak" pattern is evident

14.5 Diagnosis

Several diagnostic tools are available to confirm a suspicion of EA to guide treatment and identify complications. If EA is suspected, the patient should undergo the barium swallow test. Classically, patients with EA show a megaesophagus containing stagnant fluid above the barium column, smooth tapering of the distal tract of the esophagus ("bird's beak") and a lack of peristalsis during fluoroscopy (Fig. 14.1). Contrast fluid progresses into the stomach after a considerable time period and most of it is retained in the esophagus for hours [7]. Magnetic resonance imaging (MRI), computed tomography (CT) (Fig. 14.2) or transabdominal ultrasonography can be used as adjuncts to the barium swallow test to evaluate esophageal dilation and to exclude infiltrative processes that can be the cause of pseudoachalasia (a condition more often seen in adults) [20].

In addition to contrast studies, esophagogastroduodenoscopy (EGD) is an essential part of the diagnosis. EGD can be used to exclude the presence of strictures, detect mucosal lesions, and to demonstrate esophageal dilation and retention of food or liquid (although findings are usually normal in the early stage of the disease). EGD can be useful for the detection and treatment of late complications resulting from the disease (megaesophagus, Bar-

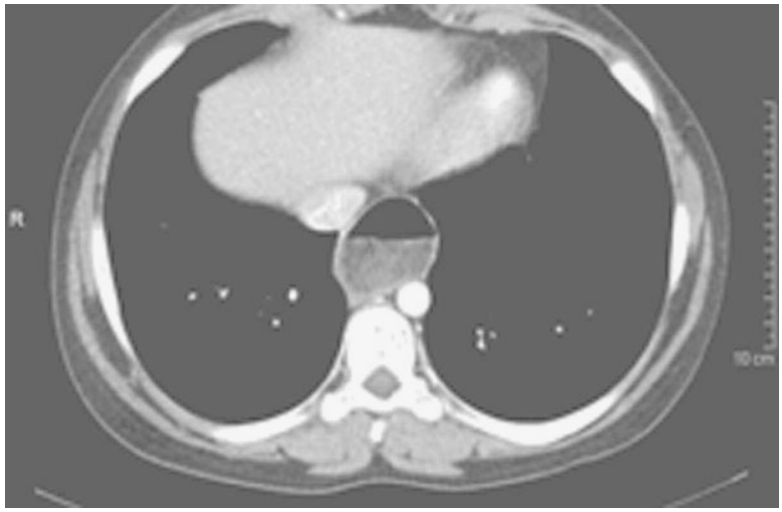


Fig. 14.2 CT of the thorax showing a dilated esophagus containing stagnant fluid

rett's esophagus) or of successful treatment (reflux esophagitis, peptic strictures). Radionuclide scintigraphy may depict a lack of progression of esophageal content. Twenty-four-hour monitoring of esophageal pH excludes gastroesophageal reflux disease (GERD), which can result in dysphagia in ≤37% of patients. Esophageal manometry (standard or 24-h) is the "gold standard" method for the diagnosis of EA and shows three cardinal features: aperistalsis of the smooth-muscle portion of the esophagus; incomplete relaxation of the LES; and increased pressure in the LES [3, 6, 21]. Pandolfino et al. described three distinct variants of achalasia in adult patients based on manometry findings: type 1, classic achalasia with minimal esophageal contractility and low intraesophageal pressure; type 2, absence of peristalsis and panesophageal elevation in pressure; and type 3, lumen-obliterating esophageal spasm [22].

EA is a progressive disease that does not resolve spontaneously. Hence, in general, treatment is required as soon as the diagnosis has been confirmed. The aim of treatment is to: preserve esophageal motility; prevent the onset of complications (failure to thrive, weight loss, inhalation); and reduce the risk of the need for partial esophagectomy [23, 24].

14.6 Management

Several therapeutic options have been proposed, but treatment of EA remains strictly palliative. Treatments aim to: reduce distal esophageal obstruction; facilitate esophageal emptying; improve dilation of the esophagus; and reduce the risk of inhalation. Treatment may reduce dysphagia, regurgitation and weight loss. Treatment options can be pharmacological, endoscopic or surgical.

14.6.1 Pharmacological Treatment

Pharmacological treatment represents the least effective of the available therapeutic options for EA. Pharmacologic treatment aims to reduce pressure in the LES by relaxation of smooth muscle. Calcium-channel blockers (e.g., nifedipine) [25], long-acting nitrates (e.g., isosorbide dinitrate) [26] and phosphodiesterase-5 inhibitors (e.g., sildenafil) [27] can alleviate spasm in some cases but they are considered temporary measures at best. The main limitations of these agents are their short duration of action, limited clinical efficacy, and frequent occurrence of adverse effects (edema,

vertigo, headache). Pharmacological therapy is mainly temporary and reserved for patients who cannot tolerate more invasive interventions. Pharmacological therapy cannot be relied upon as long-term treatment in children [28].

14.6.2 Endoscopic Treatment

Two methods can be applied by endoscopic means: botulinum injection and pneumatic dilation. Botulinum toxin is a potent neurotoxin that leads to blockade of the release of acetylcholine from excitatory motor neurons, thereby reducing pressure in the LES by >50% [25]. A single injection may be successful but, usually, more than one treatment is needed. It has been demonstrated that such injections can improve esophageal emptying in about two-thirds of patients at 1-year follow-up [29]. However, symptoms relapse in 50% and ≈100% of patients at 1-year and 2-year follow-up, respectively.

Pneumatic balloon dilation of the distal end of the esophagus is often successful in adult patients but it is seldom permanently effective in children. However, it is considered to be the most effective non-surgical treatment for EA. Graded and serial esophageal dilation with fluoroscopic monitoring of balloon position is the standard procedure, though balloon position monitoring can be done *via* endoscopic means to avoid radiation exposure. After dilation, an esophagogram with contrast can be helpful to exclude the possibility of complications such as esophageal perforation. Follow-up is usually by manometry: a post-dilation LES pressure <10–15 mmHg is a favorable predictor of the success of long-term treatment [30]. Possible complications of this treatment are esophageal perforation and intramural hematoma.

New endoscopic methods have been proposed but evidence of their efficacy in the pediatric population is lacking. Peroral endoscopic myotomy (POEM) [31] enables dissection of the esophageal submucosa with CO_2 insufflation to gain access to the muscle fibers of the LES so that dissection of the circular fibers can be initiated, leaving the longitudinal muscle layer intact. Another therapeutic approach is temporary esophageal stenting using self-expanding metal stents [32].

14.6.3 Surgical Treatment

Extramucosal myotomy is the first-line treatment. It can be done through a thoracic or abdominal approach, but the laparoscopic extramucosal Heller myotomy is first-line treatment because of its feasibility and safety [2, 3, 6, 7, 33–36]. A fundoplication must be associated with the myotomy to avoid long-term complications associated with gastroesophageal reflux and to protect the herniated mucosa to prevent leakage [2, 3, 5, 6, 33, 37]. A Nissen fundoplication may not be appropriate because of the large diameter of the thickened esophagus, and could result in significant postoperative dysphagia. An anterior hemifundoplication (as described by Thal-Dor et al.) or a posterior fundoplication (as described by Toupet) are preferred because they have been shown to reduce reflux symptoms from 47% to 9.1% [3, 37]. Compared with 360° fundoplication, Thal-Dor or Toupet fundoplications result in a lower prevalence of postoperative dysphagia (2.8% *versus* 15%, P=0.001) [38]. Surgical treatment can be undertaken after unsuccessful pneumatic dilation or botulinum injections but, in these scenarios, worse outcomes should be expected [39]. A second myotomy can be repeated if the first one did not show sufficient improvement in symptoms. In these cases, myotomy must be done at the opposite site to the initial intervention. Incomplete myotomy or strictures can be treated by repeated endoscopic dilations [33]. In cases of failure of endoscopic procedures, recurrence, or a very dilated esophagus, a segmental esophageal resection with gastric or colonic transposition can be carried out [40, 41].

14.6.3.1 Surgical Procedure for Laparoscopic Modified Heller–Dor Esophageal Anterior Myotomy and Fundoplication

The patient is fed only with fluids the day before surgery. A nasogastric tube is introduced to clean the dilated esophagus and stomach and to reduce the risk of inhalation. A clean esophagus is essential to minimize spillage of contents in the event of inadvertent perforation. Enemas are administered to reduce the risk of colonic distension.

The patient is placed supine in the lithotomy position with a reverse Trendelenburg. The surgeon stands between the legs of the patient. The monitor is placed on the left side of the patient, at the head of the table. Five cannulas are inserted in a semicircular pattern (Fig. 14.3a). After retracting the distal esophagus and opening the parietal peritoneum, anterior and lateral esophageal sides are freed to proceed cranially in the mediastinum (Fig. 14.3b). A single longitudinal anterior myotomy (modified Heller myotomy) is undertaken (Fig. 14.3c). The landmark for esophageal myotomy in the proximal direction is the cross-section of vagal nerve on the anterior dilated esophageal wall; in the distal direction, the transverse esophageal vessels at the esophagogastric junction is the landmark. Complete myotomy is demonstrated by mucosal herniation (Fig. 14.3d). Mucosal integrity is confirmed by insufflating air inside the esophagus through a nasogastric tube. Myotomy is then protected using a 180° anterior fundoplication. Using non-absorbable sutures, the anterior surface of the stomach is fixed to the two muscular edges of the myotomy to keep it open, and to the right portion of the left crura (Fig. 14.3e) [33–35, 42]. On the first postoperative day, a barium swallow test is undertaken to exclude mucosal perforations, and feeding is started progressively.

14.7 Outcome and Follow-up

Despite good understanding of the pathophysiology of EA, its treatment remains palliative because the esophageal motility disorder seems to be irreversible. The treatment goals are relief from gastroenteric and respiratory symptoms as well as prevention of long-term complications. The Heller–Dor procedure seems to be the most effective treatment of EA due to the durability of the myotomy and the association of a fundoplication to prevent GERD complications. Medical or endoscopic treatments seem to have a role in patients with significant comorbidities who cannot undergo surgery. Patients treated for EA should undergo follow-up at an early stage to confirm treatment success, detect recurrence (Fig. 14.4) and to prevent/recognize late complications. Despite successful treatment, the esophagus remains dilated for months (or even years) and its function rarely returns to normal. After surgery, esophageal peristalsis remains very poor despite the lower pressure in the LES and symptoms could reappear.

Several scoring systems have been proposed to evaluate the quality of life and symptom relief of patients treated by medical, endoscopic or surgical approaches [43]. A barium swallow test should be done early after surgery to exclude the possibility of mucosal perforation; delayed imaging studies or esophageal manometry permit deterioration and disease progression to be identified. Endoscopic evaluation should be done to evaluate and prevent long-term complications (megaesophagus, GERD, esophagitis, Barrett's esophagus, esophageal tumors). Predictors of treatment response should be considered when the type of treatment has been chosen (Table 14.1) [30, 44]. Major complications of surgical and endoscopic procedures are bleeding from esophageal vessels, mucosal perforation (5% for myotomy and 1–6% for balloon dilation), residual GERD (about 10–20% of endoscopic dilation procedures).

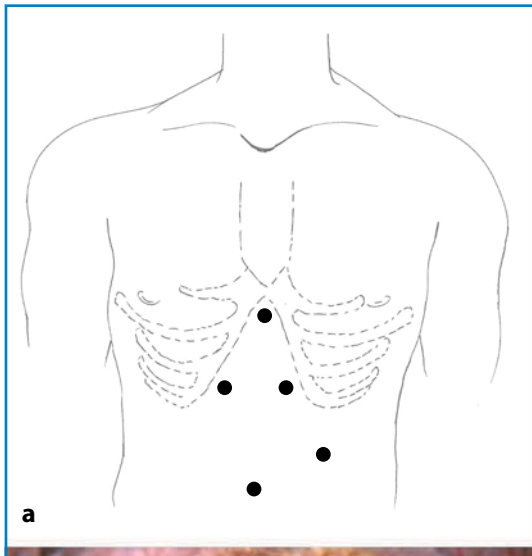
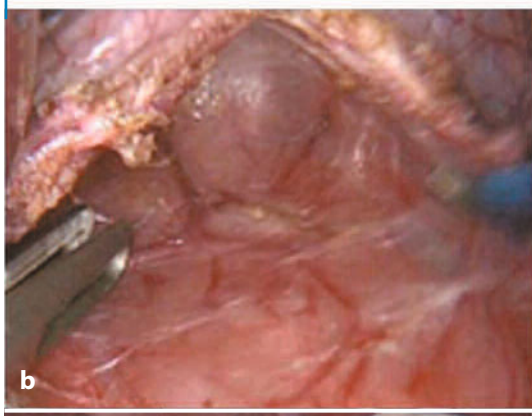
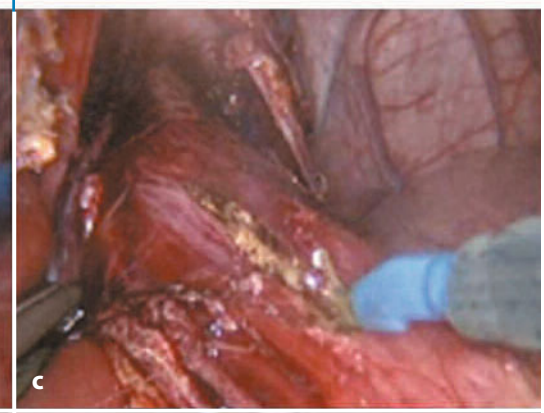


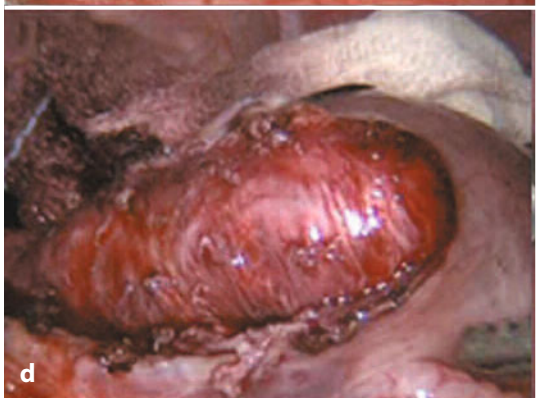
Table 14.1 Predictors of outcome of surgical treatment in patients with esophageal achalasia

Positive predictors	Negative predictors
Young age	Previous ineffective treatments
Early disease	Type-1 or -3 achalasia on manometry
Type-2 achalasia on manometry	Advanced disease
LES pressure <10 mmHg after treatment	LES pressure >15 mmHg after treatment

LES, lower esophageal sphincter.







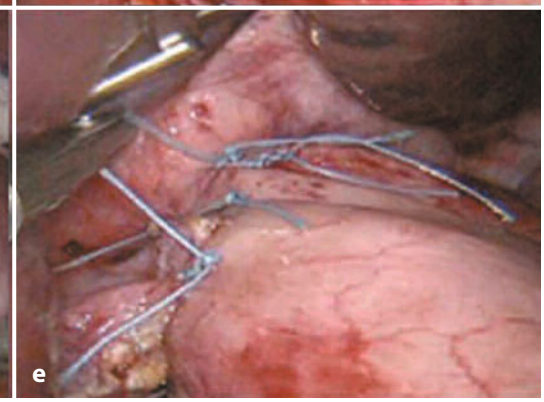


Fig. 14.3 Position for laparoscopic access (schematic) (**a**) and intraoperative images (**b**-**e**) for the modified Heller–Dor myotomy and fundoplication (see text for details of each stage)

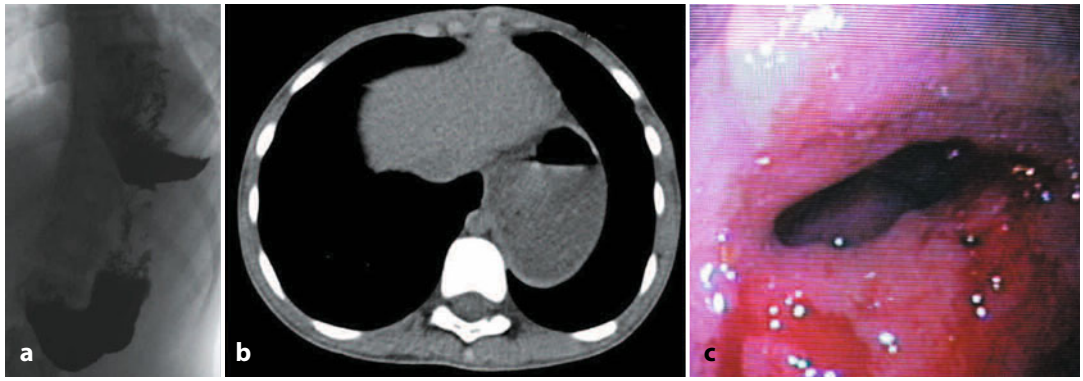


Fig. 14.4 Barium swallow test, CT of the thorax, and endoscopy in a 14-year-old patient with recurrence of esophageal achalasia after surgery. A very dilated esophagus (7 × 6 cm) (**a** and **b**) and a stricture at the esophageal–gastric junction (**a**,**c**) are shown. Esophagectomy and esophageal replacement were undertaken

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Part III

Larynx and Trachea

Airway Endoscopy

15

Francesca Masciopinto, Andrea Gentili,
Amedeo Bianchini and Simonetta Baroncini

15.1 Introduction

Endoscopic management is often required for thoracic surgery for diagnostic and therapeutic purposes. Rigid or flexible endoscopes are selected depending on the age of the child and the particular disease being treated. Flexible endoscopes are indicated for dynamic evaluation of the airways, one-lung ventilation, and for obtaining microbiological samples. Rigid endoscopes are used for diagnostic and surgical procedures.

Laryngoscopy and airway management stimulate the sympathetic reflex. This can result in tachycardia, arrhythmias, systemic and intracranial hypertension, and catecholamine release. General and topical anesthesia protect the child from these responses [1–3].

15.2 Informed Consent

If endoscopic management is planned, the benefits and risks of the procedure must be explained to the parents and, if possible, to the child. Written informed consent must be obtained from the former.

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15.3 Equipment

Each team member must be skilled in the management of all endoscopic instruments and devices. Endoscopic instruments and devices must be available and assembled in a cart (Fig. 15.1). Back-up equipment must be readily available. Imaging documentation (photographs and videos) is important in all cases to ensure reviewing of the case, for comparisons, and for teaching purposes [4, 5].

15.4 Procedural Steps

Before starting the endoscopic procedure, the patient's medical history and imaging (chest radiography, ultrasound, CT, MRI) must be known. Each procedure should be scheduled and the entire Endoscopy Team should be informed.

Monitoring: Guidelines on patient safety recommend standard monitoring:

- electrocardiography (ECG);
- saturated oxygen ($SatO_2$);
- end-tidal carbon dioxide ($ETCO_2$);
- temperature;
- non-invasive blood pressure (NIBP);
- end-tidal levels of anesthetic halogenates;
- airway pressure.

During anaesthesia, it must be clear to all present that a rigid endoscope allows ventila-

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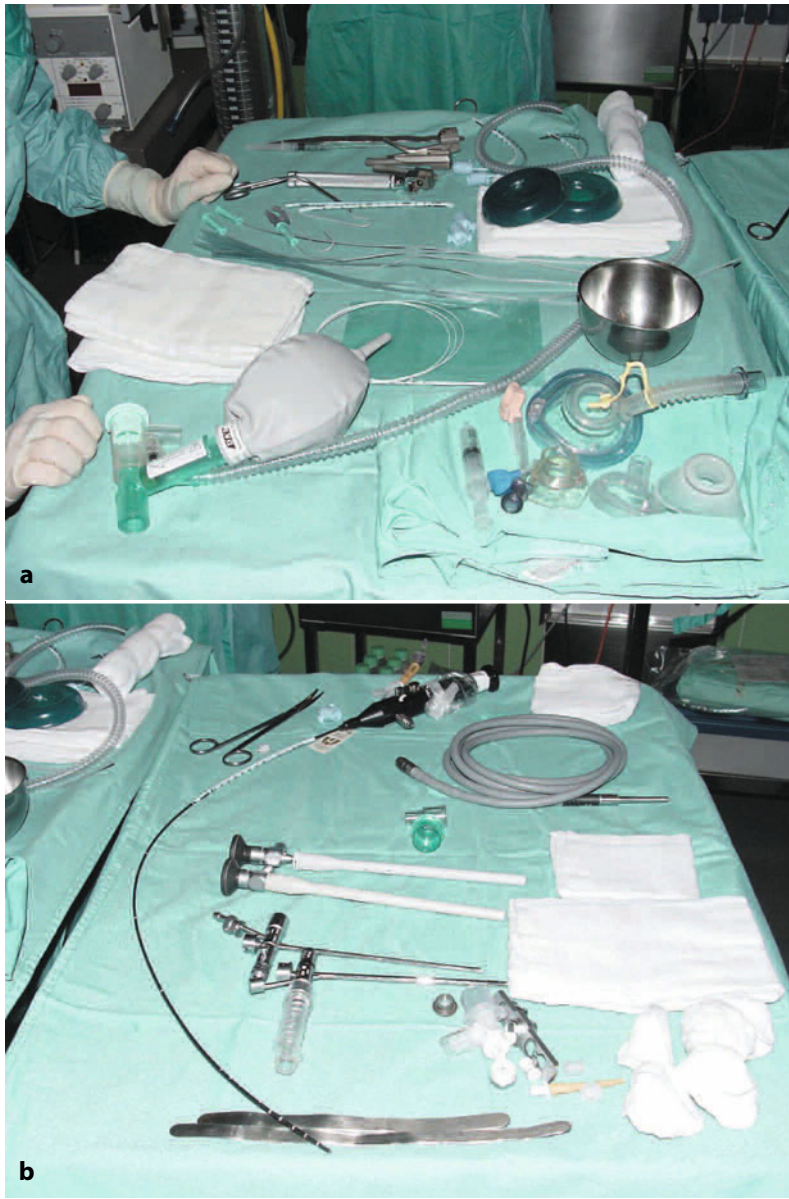

Fig. 15.1 Endoscopic instruments

tion and oxygenation, whereas a flexible endoscope determines airway obstruction [6].

Pre-oxygenation using a face mask: Inhalation of 100% oxygen for 5 minutes ensures denitrogenation before prolonged apnea is induced. Spontaneous ventilation is essential.

Sedation general anesthesia-local anesthesia: Sedation or general anesthesia (inhalatory anesthesia or total intravenous anesthesia, TIVA) combined with topical anesthesia is the best choice to maintain spontaneous ventilation. In our experience, topical anesthesia with lidocaine (3–5 mg/kg in progressive steps) affects the tongue, hypopharynx, epiglottis, larynx and trachea [7–9].

Patient positioning is dependent upon the choice of method. Flexible endoscopy can be undertaken with the head and neck in the neu-

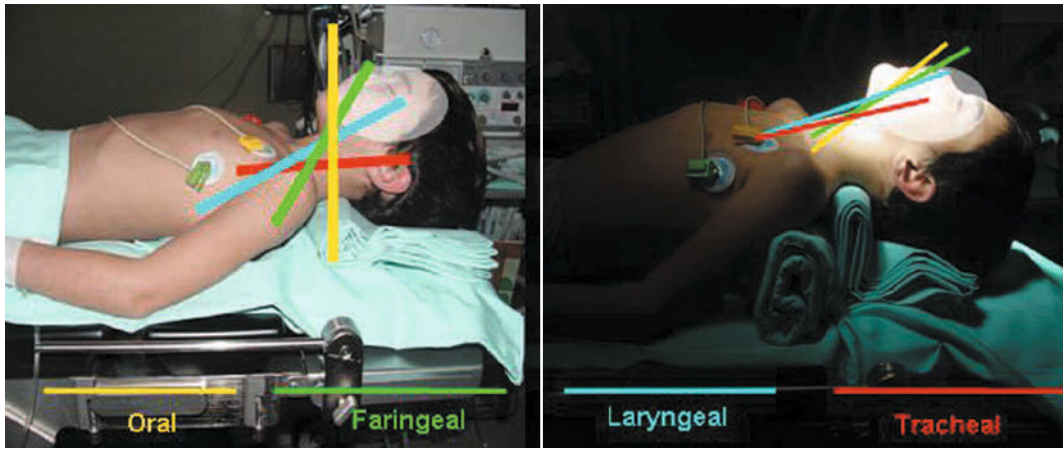

Fig. 15.2 Position of the head and neck for rigid endoscopy

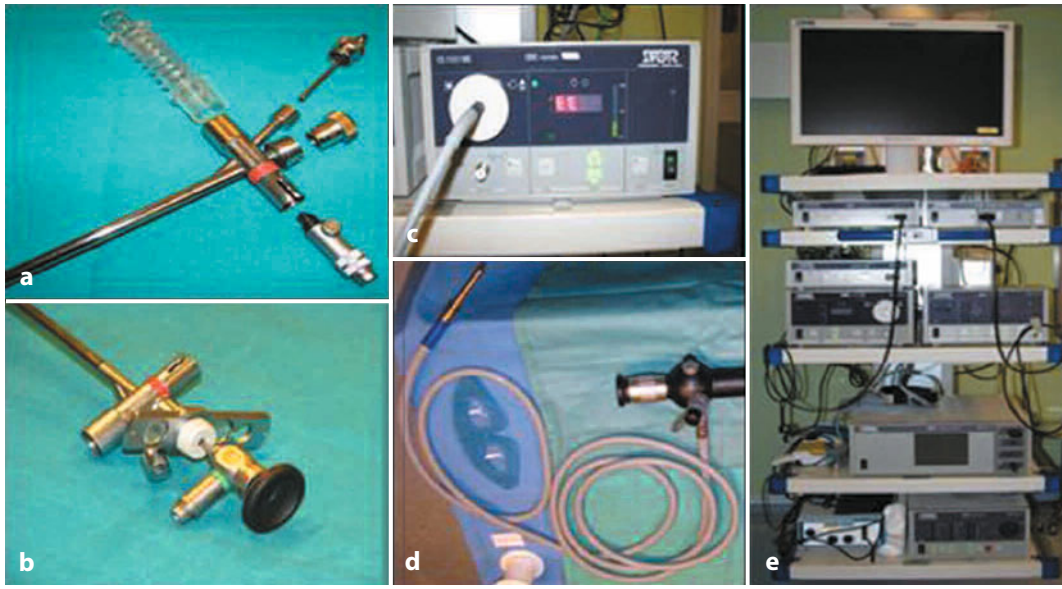

Fig. 15.3 Endoscopes and endoscopic system used for image acquisition. **a**,**b** Rigid endoscope. **c** Light source. **d** Flexible endoscope. **e** System for image acquisition

tral position. Rigid endoscopy requires correct alignment of the head and neck to introduce the instrument while avoiding airway trauma (Fig. 15.2). All instruments should be handled aseptically. Before starting, the endoscope, suction tube and the focus view must be checked. The possibility of image recording must also be considered (Fig. 15.3). Each member of the endoscopy team must occupy the planned position.

Flexible endoscopy: The flexible endoscope may be introduced *via* the nasal or oral routes through specific face masks that provide respiratory assistance, a laryngeal mask or an endotracheal tube (Fig. 15.4). The endoscopist should advance the instrument gently, atraumatically and slowly, recognizing the anatomical landmarks, avoiding trauma and, above all, bleeding. The endoscope is rotated and flexed to maintain the central field of vision [10].

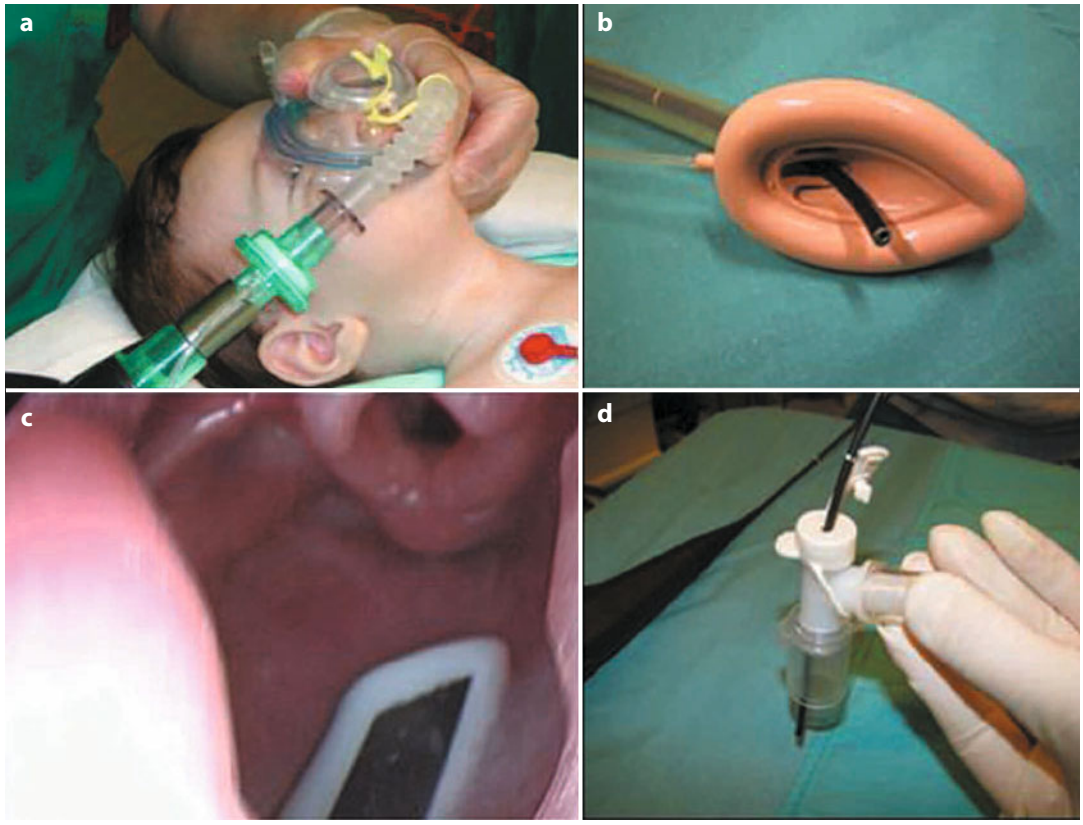

Fig. 15.4 Systems used for the introduction of flexible endoscopes. **a** Ventilation with specific mask. **b** Flexible endoscope through LM. **c** Position of pharyngeal tube. **d** Flexible endoscope through the connection for the endotracheal tube

Rigid endoscopy: Laryngoscopy using a 0° Hopkins Rod Laryngoscope should be done before introduction of a rigid instrument that has an optic rod inside. The choice of bronchoscope size is dependent upon several factors, but an indication can be given by the subglottic (cricoid) diameter, which is related to the age of the child (Table 15.1).

15.5 Complications

In experienced hands, complications are rare but nevertheless possible. Complications include: trauma to the nose, lips, tongue, vocal cords, teeth or tracheobronchial tree; bleeding; pneumothorax; and pneumomediastinum. Hy-

Table 15.1 Choosing the bronchoscope dimension according to the age of the child

Age	Cricoid diameter (mm)	Bronchoscope size	Internal diameter of bronchoscope (mm)	External diameter of bronchoscope (mm)
Newborn	4.0	2.5–3.0	3.2	4.0
Term newborn	4.5	3.0–3.5	4.2	5.0
6 months	5.0	3.5–4.0	4.2	5.0
1 year	5.5	4.0–4.5	4.9	5.7
2 years	6.0	4.5–5.0	4.9	5.7
3 years	6.5	4.5–5.0	5.9	6.7
5 years	7.0	5.0–5.5	7.0	7.8

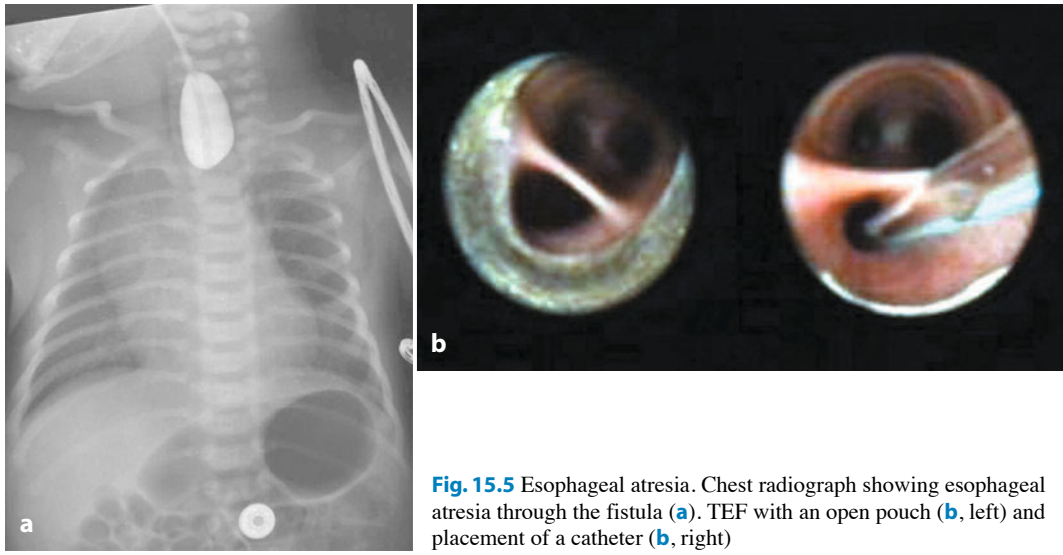

Fig. 15.5 Esophageal atresia. Chest radiograph showing esophageal atresia through the fistula (**a**). TEF with an open pouch (**b**, left) and placement of a catheter (**b**, right)

poxia may occur for reasons related to airway occlusion, excessive suctioning and atelectasis, laryngospasm/bronchospasm, or post-traumatic edema. Prolonged hypoxia can result in bradycardia and the need for prompt reoxygenation. A late complication, at the end of the procedure, is stridor related to post-traumatic subglottic edema. This complication can be treated successfully with nebulization using epinephrine (1:1,000 dilution in 0.25 mL/kg) plus dexamethasone (0.2–0.5 mg/kg, i.v.).

15.6 Principal Airway Anomalies and Thoracic Diseases

15.6.1 Tracheoesophageal Fistula (TEF) and Esophageal Atresia

Endoscopy of the airways enables determination of the: type of esophageal atresia (Fig. 15.5); presence, characteristics, and size of the fistula; anatomical relationship with the esophageal pouch. It also allows the fistula to be cannulated which, in the case of distal TEF, provides direct access to the stomach. With cannulation, the stomach can be drained, thereby reducing the risk of aspiration pneumonia and improving mechanical ventilation. Chest radiography will show the upper end of the esophagus. Examination using a rigid endoscope will show a pouch fistula and allows passage of a fine catheter to guide the surgeon to the correct site of repair [11, 12]. There is considerable variability in TEFs, but careful endoscopy can identify the position (Fig. 15.6). Tracheal bronchus (carinal trifurcation) is a differential diagnosis (Fig. 15.7).

15.6.2 Recurrent TEF

After surgical correction of esophageal atresia, cough, recurrent pulmonary infection and lobar atelectasis could appear, so a plan for diagnostic endoscopy may be necessary. For example, a 2-month-old child with symptoms suggestive of recurrent TEF underwent rigid endoscopy (Fig. 15.8). During the procedure, a recurrent TEF was diagnosed. As another example, a 2-month-old child with persistent cough during enteral feeding underwent rigid endoscopy that showed a second TEF in a distal fistula that had already been corrected. A catheter was placed in the upper fistula (Fig. 15.9).

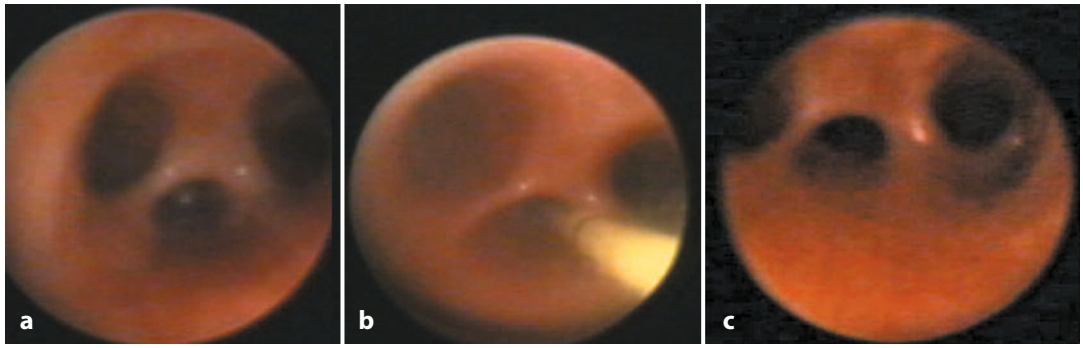

Fig. 15.6 Different types of TEF. TEF in carina: trifurcation (**a**). Trifurcation: catheter placed through the fistula (**b**). Trifurcation and tracheal bronchus (**c**)

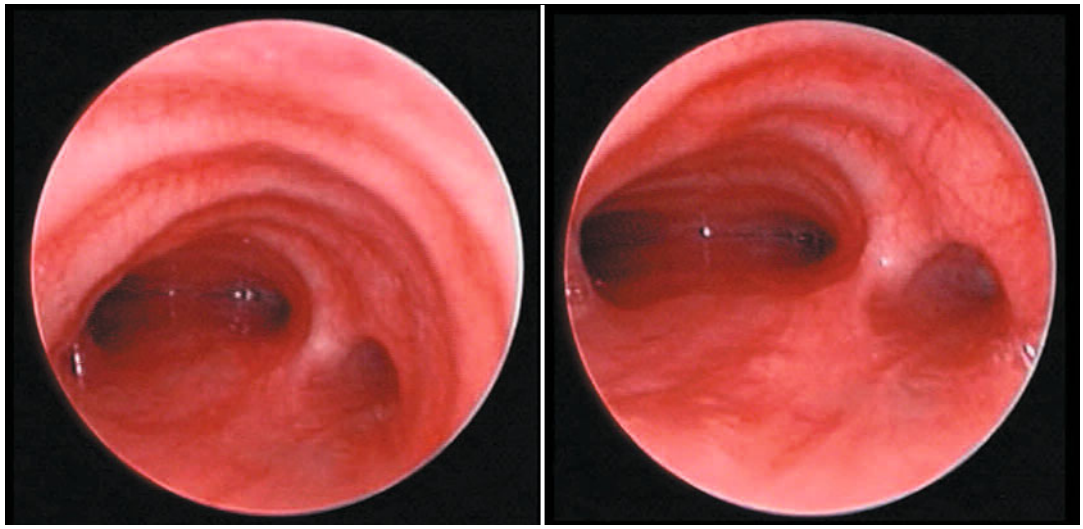

Fig. 15.7 Tracheal bronchus

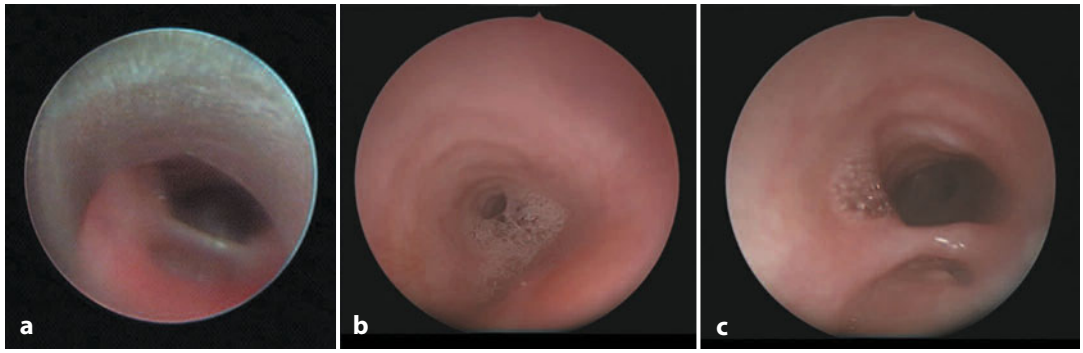

Fig. 15.8 Endoscopic images of a 2-month-old child with symptoms suggestive of recurrent TEF who underwent rigid endoscopy. An open pouch is shown in (**a**), gastric juice is shown bubbling up the fistula in (**b**) and the situation after aspiration is shown in (**c**)

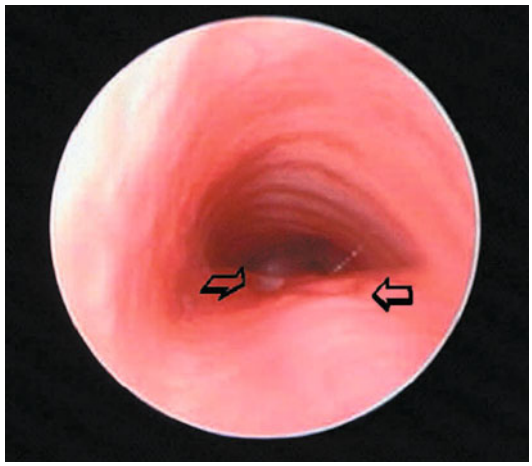

Fig. 15.9 Double TEF in esophageal atresia. A distal pouch fistula and upper fistula are shown (*arrows*)

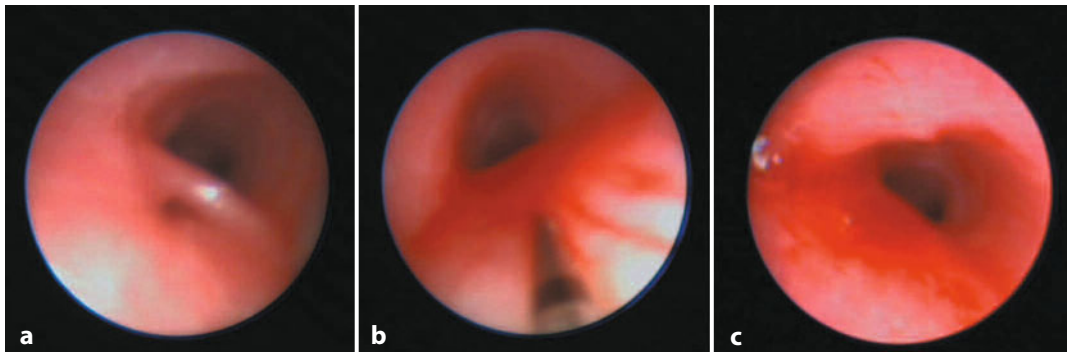

Fig. 15.10 Endoscopic sequence for obliteration of recurrent TEF in esophageal atresia. TEF (**a**). A needle is used to inject glue into the submucosal pouch (**b**). Obliteration of TEF (**c**)

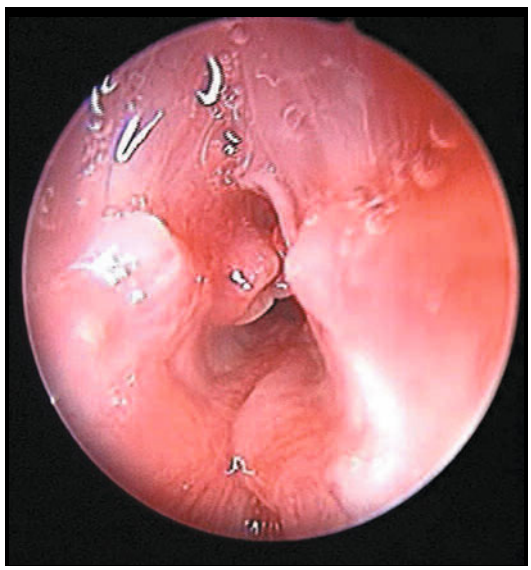

Fig. 15.11 Complication of prolonged tracheal intubation: laryngeal granulations

If a recurrent fistula is suspected, endoscopy must be carried out and, if confirmed, two strategies are available. Surgery is a possible treatment but endoscopic therapy can be applied [13]. For example, a 15-month-old child underwent injection of glue in the submucosal pouch of an open fistula (Fig. 15.10). Obliteration of the TEF was followed up 1-year later and a good outcome was documented.

15.6.3 Laryngotracheal Diseases

Granulations after prolonged intubation: The example of a 6-month-old child who was extubated under endoscopic control after prolonged intubation is shown in Figure 15.11.

Lymphangiomatosis: *Intra-utero* diagnosis of airway obstruction and planned *ex-utero* in-

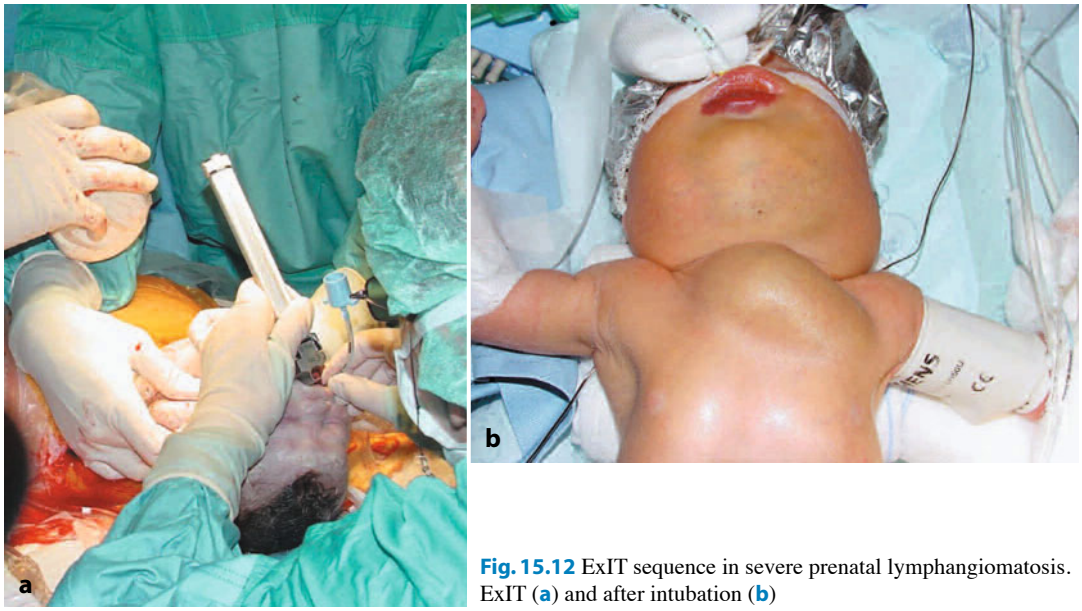

Fig. 15.12 ExIT sequence in severe prenatal lymphangiomatosis. ExIT (**a**) and after intubation (**b**)

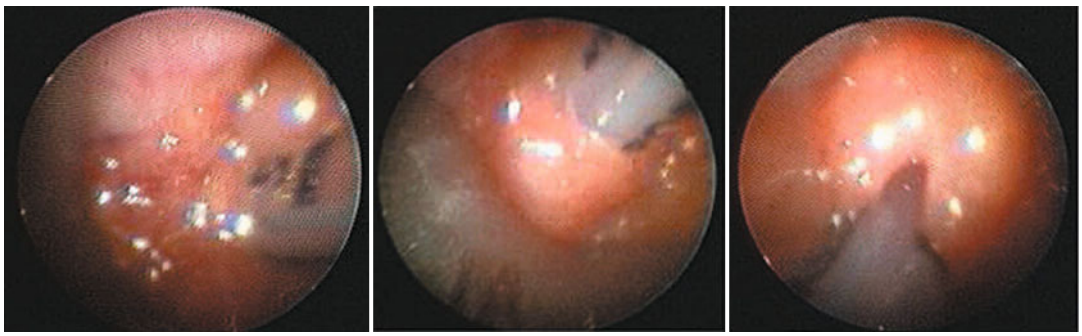

Fig.15.13 Rhinotracheal fiberoptic intubation at birth

trapartum treatment (ExIT) at birth are shown in Figure 15.12. The endoscopic view for intubation during ExIT is shown in Figure 15.13.

Laryngotracheal agenesis: A newborn who could not undergo tracheal intubation for laryngeal agenesia (Fig. 15.14) was oxygenated using a face mask [14]. A tracheoesophageal fistula was cannulated, thereby permitting ventilation (Fig. 15.15).

Tracheomalacia: A 5-month-old child with severe respiratory insufficiency is shown in Fig. 15.16. After endoscopy, aortopexy was carried out and the critical clinical condition resolved.

Tracheal stenosis is a possible consequence of prolonged tracheal intubation. However, it may also be associated with a vascular ring (Fig. 15.17) and a complete tracheal ring.

Tracheal stenosis and pulmonary artery sling: A 6-year-old child with recurrent episodes of asthma and pulmonary infection underwent endoscopy after CT (Fig. 15.18). Severe tracheal stenosis was documented and a vascular pulse was present at the principal carina caused by a pulmonary artery sling.

Mediastinal mass: A 16-month-old child with recurrent airway infections, wheezing

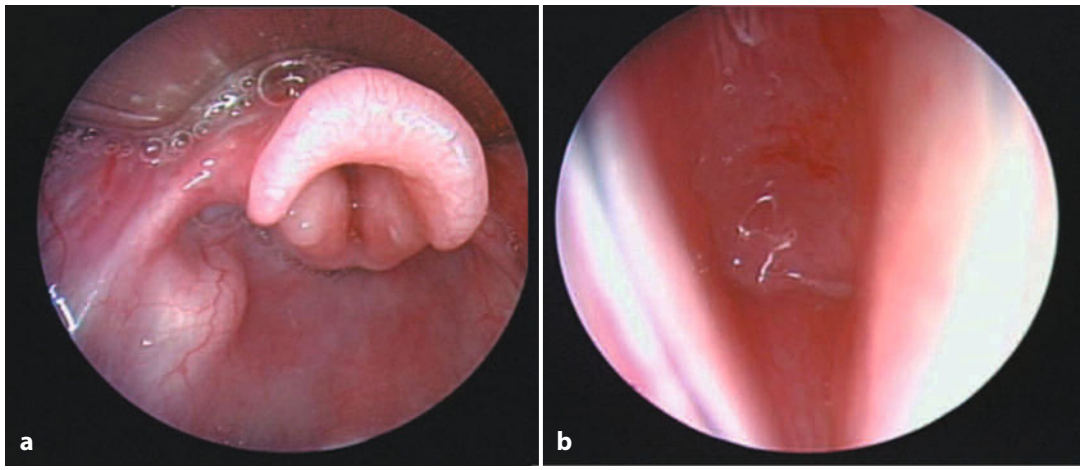

Fig. 15.14 Tracheal agenesis. View of the larynx (**a**). Subcordal stop (**b**)

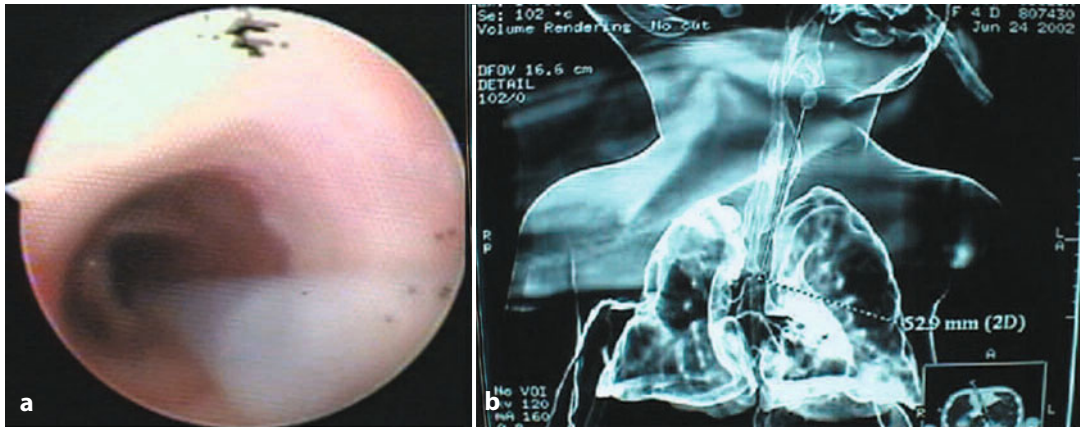

Fig. 15.15 Tracheal agenesis. A catheter inserted in the TEF in the distal tract of the trachea (**a**). CT (gap from upper stop and the TEF) (**b**)

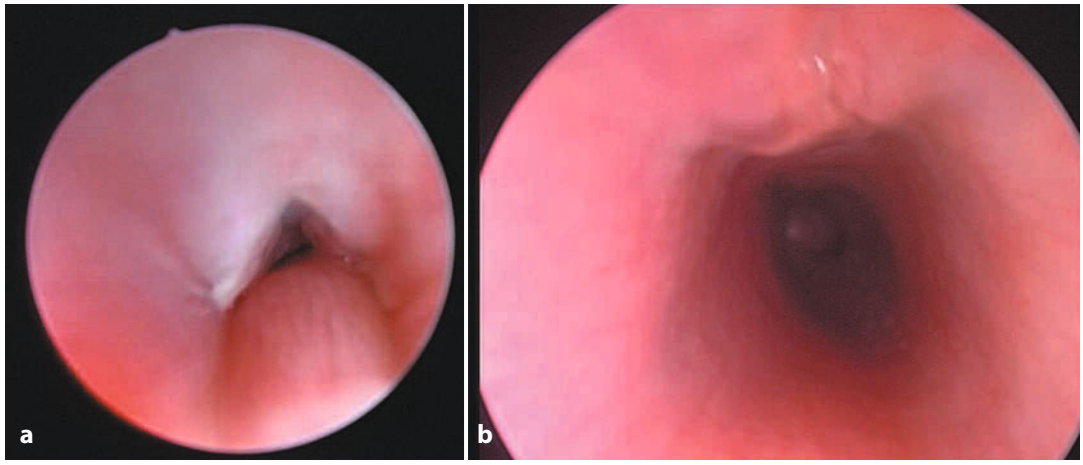

Fig. 15.16 Tracheomalacia. Severe tracheomalacia (**a**) and after aortopexy (**b**)

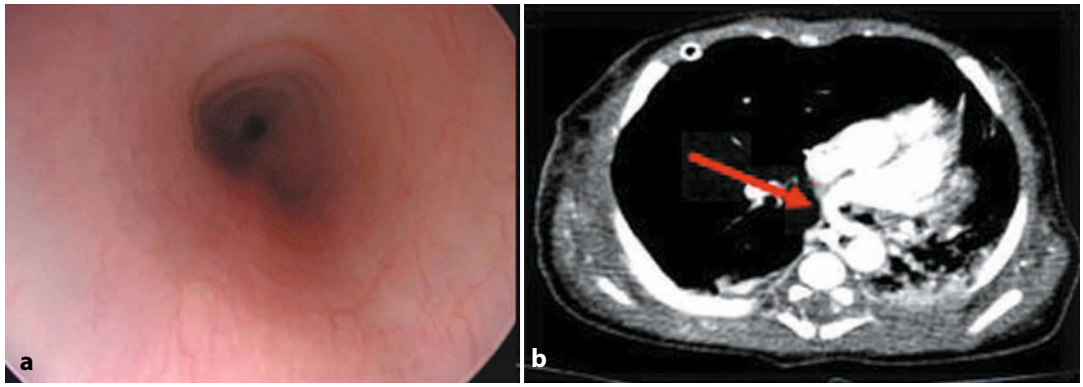

Fig. 15.17 Tracheal stenosis. Endoscopic view (**a**). CT showing pulmonary artery sling (**b**)

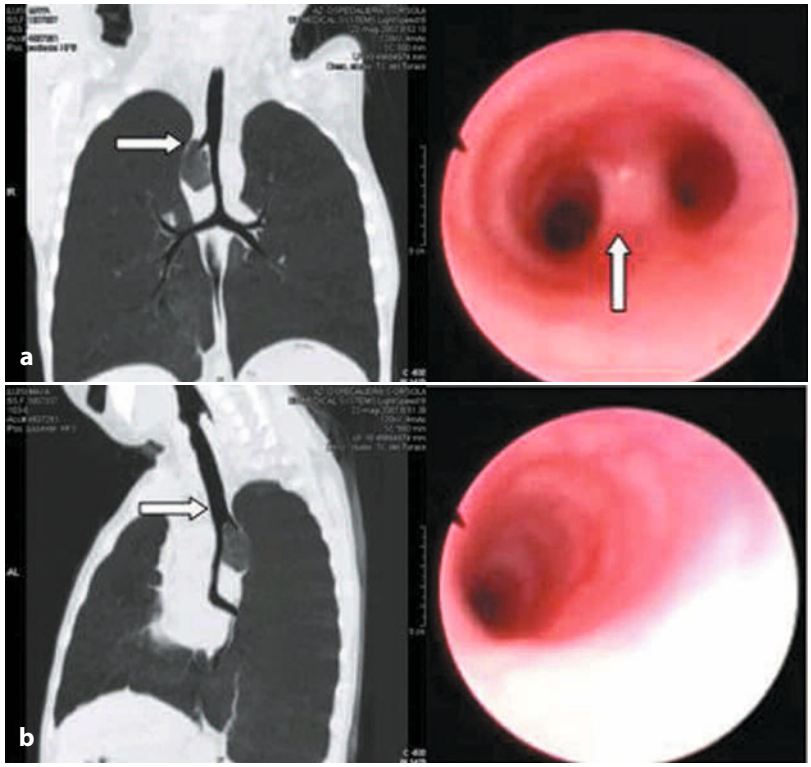

Fig. 15.18 Tracheal stenosis in accessory pulmonary lobe and pulmonary artery sling. Upper carina of the trachea (**a**). Tracheal stenosis (**b**)

and asthmatic status is shown in Figure 15.19. Endoscopy showed right bronchial closure. Radiological studies were needed to give a more precise definition of the pathology for the pediatric thoracic surgeons.

We have described only a few examples of laryngotracheal diseases to demonstrate that all endoscopic procedures (flexible and rigid) are useful in the evaluation of thoracic disease. Pediatric airway management is necessary in many situations with particular regard to subjects who may undergo surgery.

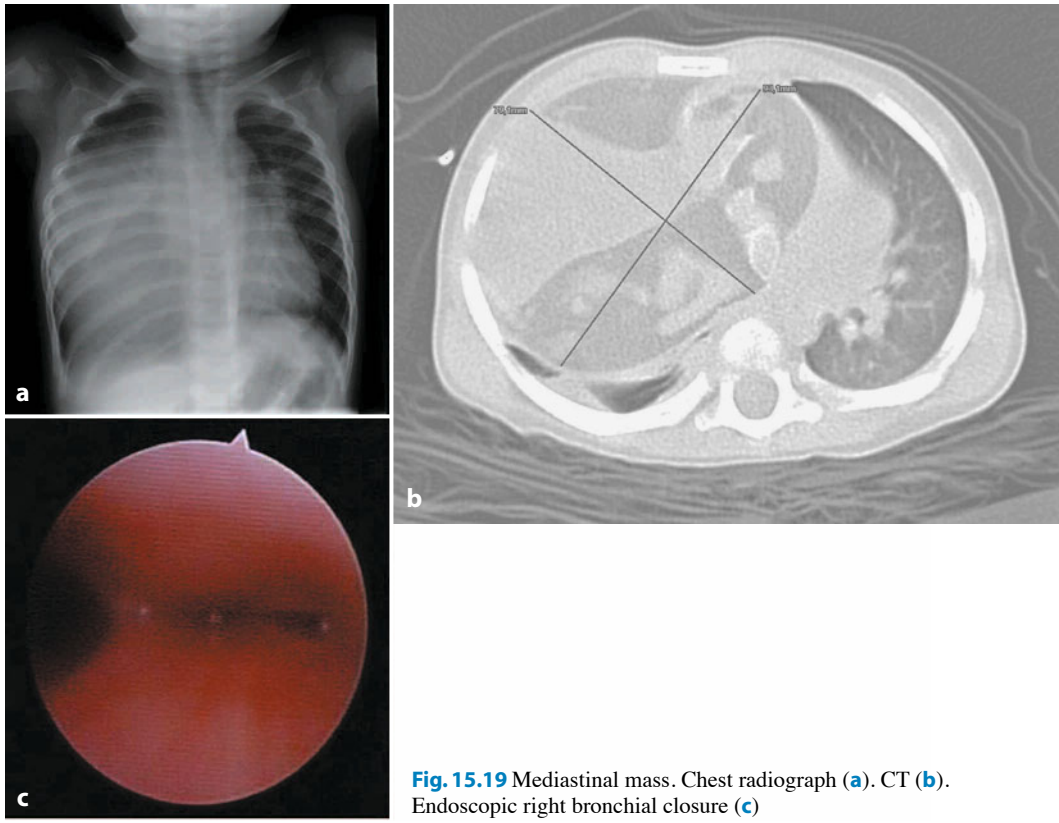

Fig. 15.19 Mediastinal mass. Chest radiograph (**a**). CT (**b**). Endoscopic right bronchial closure (**c**)

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Laryngeal Anomalies

16

Michele Torre, Marcello Carlucci
and Vincenzo Jasonni

16.1 Introduction

Laryngeal anomalies constitute a wide spectrum of conditions representing one of the most frequent causes of respiratory distress in infants. They can be congenital (due to malformations or prematurity) or acquired (usually related to a history of intubation). Some laryngeal anomalies can improve or resolve spontaneously with growth, but others can cause significant respiratory distress or even death. Laryngeal anomalies represent a challenge for the professionals involved in their management (which must be multidisciplinary). Also, the families of these patients have to face many challenges due to the: possible severity of the condition; difficult and sometimes long-lasting treatment; stress of tracheotomy-related complications.

The anatomy of the infant larynx is considerably different from that of the adult in terms of position (it is located at a higher level, at the third-to-fourth cervical vertebrae), shape (the thyroid cartilage is more rounded, the arytenoids are larger, and the cricoid more V-shaped) and consistency (the cartilages are softer and the mucosa more lax and prone to edema). The larynx is innervated by the superior and recurrent laryngeal nerves, which arise from the vagus nerve (both are of fundamental importance to the surgeon because surgical trauma to one of them can give rise to vocal cord palsy). The blood supply to the larynx is provided by the superior and inferior laryngeal arteries, which are branches of the superior and inferior thyroid arteries, respectively.

16.2 Epidemiology

The incidence of congenital laryngeal anomalies has been estimated to range between 1 in 10,000 to 1 in 50,000 live births [1]. The most common anomaly is laryngomalacia, which accounts for ≥60% of all congenital laryngeal anomalies. Less common conditions are vocal cord paralysis (VCP) and subglottic stenosis (both 15%). Uncommon anomalies are webs and atresia (5%), subglottic hemangiomas (2%), saccular cysts/laryngoceles (2%) and laryngeal clefts (1%).

Among acquired lesions, post-intubation subglottic stenosis is by far the most common. However, the prevalence of post-intubation subglottic stenosis has decreased dramatically in the last few years due to the availability of better types of endotracheal tubes. Nevertheless, it can occur in a selected population of extremely premature babies and infants under-

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going surgery for cardiac anomalies or requiring a long period of intubation. The prevalence of stenosis in all intubations is estimated to be 0.9–3% [1]. Among laryngotracheal stenoses, 90% are due to post-intubation sequelae.

16.3 Laryngomalacia

16.3.1 Etiology and Pathogenesis

Laryngomalacia is the most common congenital laryngeal anomaly and the most common cause of stridor in infancy. It occurs with a male-to-female ratio of 2:1. Laryngomalacia is due to collapse of the supraglottic structures during inspiration. Immaturity of the cartilage is thought to be a predisposing factor, but the pathogenesis has not been clarified. Laryngomalacia is not more common in premature than in full-term babies. Another theory gives importance to neurosensitive defects in laryngeal structures [2].

16.3.2 Clinical Features

The patient with laryngomalacia presents with crying and a high-pitched stridor upon inspiration. The supine position and feeding can worsen the stridor. Symptoms of gastroesophageal reflux can be associated and overlap with laryngomalacia symptoms. Sleep apnea or uncoordinated deglutition and aspiration can be present. Laryngomalacia is seldom associated with neurological conditions such as a Chiari malformation. Symptoms usually start a few days or weeks after birth and progress until 6–8 months. Laryngomalacia usually resolves by 2 years of life.

16.3.3 Diagnosis

In mild cases, a transnasal fiberoptic evaluation with the patient awake is the only investigation required. Laryngomalacia can be classified into three types at endoscopy:

- type I: inward collapse of the aryepiglottic folds (Fig. 16.1a);
- type II: omega-shaped epiglottis with short aryepiglottic folds that collapses circumferentially (Fig. 16.1b);
- type III: posterior collapse of the epiglottis onto the laryngeal inlet (Fig.16.1c).

Endoscopy under general anesthesia may be required in cases of worsening symptoms, growth retardation or severe respiratory distress. Flexible and rigid endoscopes can be used during the same anaesthesia because they provide different and complementary information. Flexible endoscopy under spontaneous breathing is necessary to assess inward collapse of the supraglottic structures, vocal-cord movements, and a possible associated tracheobronchomalacia. Rigid endoscopy can

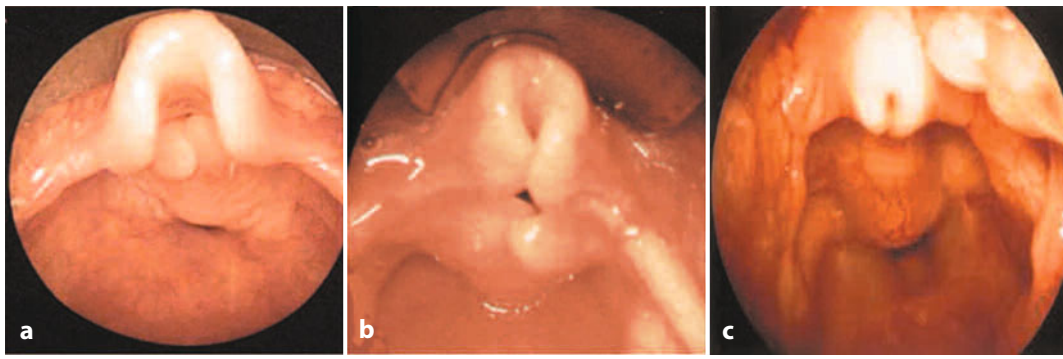

Fig. 16.1 Different types of laryngomalacia as assessed by endoscopy. Inward collapse of the aryepiglottic folds (**a**). An omega-shaped epiglottis with short aryepiglottic folds, collapsing circumferentially (**b**). Posterior collapse of the epiglottis onto the laryngeal inlet (**c**)

provide superior-quality views to exclude airway anomalies such as laryngeal clefts.

16.3.4 Management

Anti-reflux treatment with H_2 blockers or proton pump inhibitors is required in most cases. Respiratory distress, failure to thrive, and sleep apnea are the main indications for surgical treatment, which is usually required in only 10% of patients. Endoluminal supraglottoplasty is the surgical treatment for all three types of laryngomalacia (although the exact procedural details may differ). Tracheostomy should be avoided.

The principle of supraglottoplasty is to resect the tissue which is collapsing into the laryngeal lumen with micro-scissors or a laser. This is done through suspension microlaryngoscopy with the patient undergoing spontaneous breathing or in an anesthetized patient during interrupted apneic episodes. The CO_2 laser (in ultrapulse or superpulse mode) is the best option because it precisely resects the desired amount of tissue without causing bleeding and minimizes the burn effect on surrounding tissues.

The procedure adopted should be adapted to the type of laryngomalacia: in type I, the redundant mucosa of the aryepigottic folds is excised; in type II, the lateral aspects of the epiglottis are trimmed and the ayepiglottic folds resected; in type III, an area of wound is created on the anterior aspect of the epiglottis and on the tongue base to obtain the attachment of the epiglottis to the tongue after cicatricial retraction.

16.3.5 Outcome and Follow-up

In most cases, extubation can be attempted immediately after surgery. An overnight stay in the Intensive Care Unit (ICU) for monitoring purposes period is advisable. Antibiotics are usually not necessary (they are required only in supraglottoplasty for type-III laryngomalacia), whereas corticosteroids can help to prevent postoperative edema. Anti-reflux medications can be useful.

The results are good in most cases. Potential risks include infection and acquired supraglottic stenosis. The latter could be the result of improper use of the laser (or of the wrong type of laser) or of too-extensive mucosal resection. Some surgeons prefer to carry out a staged supraglottoplasty (e.g., monolateral) to minimize this risk.

16.4 VCP

16.4.1 Etiology and Pathogenesis

Bilateral VCP is the second most frequent congenital laryngeal anomaly. It is usually idiopathic but neurological disorders (e.g., Chiari malformation) can be associated. Traumatic delivery can also cause bilateral VCP. Unilateral VCP is most commonly due to previous surgery (in particular esophageal and cardiac surgery) or to trauma during delivery. In case of idiopathic VCP, delayed maturation of the vagal nuclei has been proposed as a possible cause.

16.4.2 Clinical Aspects

In bilateral VCP, the main issue is respiratory distress; the patient presents with a high-pitched stridor with a primarily normal voice. In monolateral VCP, the patient has a hoarse voice and can have feeding difficulties. The stridor in these infants is mild and can be position-dependent.

In bilateral VCP, breathing difficulties can be severe and cause apneic or cyanotic episodes. Associated neurological or gastroesophageal symptoms can be present. Other airway anomalies (laryngomalacia, subglottic stenosis) can be associated with VCP in more than 45% of cases, making the presentation different or misleading. Idiopathic bilateral VCP has a tendency to improve spontaneous-

ly in the first 1 or 2 years of age, but in unilateral cases the voice can improve naturally over time.

16.4.3 Diagnosis

Endoscopic evaluation under general anesthesia is the best way to diagnose VCP. A degree of sedation (but not too deep) must be reached to observe the movements of the cords and to make the correct diagnosis. Too-deep sedation may give the wrong impression of movement due to the passive approximation of the cords on the midline during inspiration. Therefore, it is important to observe if abduction occurs during inspiration (as in normal movements of the vocal cords) or whether adduction occurs (which is due to paradoxical movement). During endoscopy, one must differentiate between the diagnosis of VCP from that of posterior subglottic stenosis (which is an anatomical cause of impairment to movement of the vocal cords).

16.4.4 Management

VCP tends to improve spontaneously so it is better to avoid and delay treatment until the infant is 1–2 years of age. Tracheostomy, however, is necessary in about 50% of patients with bilateral VCP. Authors [3] have suggested that the infant should be kept intubated and to periodically reassess the movements of the vocal cords. Another useful therapeutic tool is non-invasive ventilation, i.e. continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) and/or the use of helium (a gas which is less dense than normal air and therefore makes lung ventilation easier). Different surgical options can be considered for the treatment of bilateral VCP, but none of these options is optimal. Classical open approaches (lateral [4] or through laryngofissure [5]) and arytenoidectomy, arytenoidopexy or posterior enlargement with interposition of an interarytenoid graft have been proposed [6, 7]. Nowadays, endoscopic treatment (CO_2 laser arytenoidectomy or posterior cordotomy, arytenoidopexy or posterior cricoid split with cartilage graft) is usually preferred [8–11].

Tracheostomy is seldom required for unilateral VCP. Medialization of the vocal cords is warranted in older children and adolescents only. The most used method is the injection of fat [12] and collagen [13] laterally and into the thyroarytenoid muscle, respectively. For bilateral and unilateral VCP, re-innervation through the hypoglossal and recurrent laryngeal nerves has been attempted and, in selected cases, proved to give good results [14].

16.4.5 Outcome and Follow-up

A patent airway can be achieved in most infants and children with VCP using all the above mentioned techniques. Open approaches are reported as more successful than endoscopic ones [5,15] but with the laser available nowadays the latter could give better results [1]. An important issue is the voice quality. After some of these procedures, as the posterior cordotomy, in most cases the voice cannot be restored satisfactorily.

16.5 Subglottic Stenosis

16.5.1 Etiology and Pathogenesis

Subglottic stenosis (defined as a subglottic diameter <4 mm in a neonate and 3 mm in a pre-term baby) may be congenital (10–15% of all congenital anomalies of the larynx) or acquired. Congenital stenosis is due to a failure of recanalization of the larynx during the tenth week of gestation. Acquired stenoses are usually the sequelae of intubation. Estimating the true relative prevalence is difficult because some cases of acquired subglottic stenosis could have a pre-existent congenital anomaly. In congenital stenosis, the cartilage is abnormal in size or shape (elliptical, cleft,

flattened or thick). In acquired cases, the stenosis involves soft tissues. Trauma is exerted on the internal cricoid wall by the endotracheal tube because the cricoid is the narrowest point and the only complete cartilaginous ring of the entire airway. At this level, the pressure creates necrosis, with the development of granulation tissue and then fibrosis. Multiple factors can predispose to acquired post-intubation subglottic stenosis: features of the tube; method employed; duration and the number of intubations; age; size of larynx; and systemic conditions.

16.5.2 Clinical Features

Biphasic stridor is the main symptom of congenital subglottic stenosis, but recurrent episodes of croup during infections can also occur. Acquired stenosis presents typically as extubation failure. In both cases, depending on symptom severity, assisted ventilation or tracheostomy (if the tube cannot be accommodated within the stenotic segment) may be required. Thorough evaluation of the infant with subglottic stenosis is crucial because comorbidities, previous surgery and associated deglutition problems are important factors in determining outcome.

16.5.3 Diagnosis

Investigation using a rigid endoscope with a 0° telescope is the "gold standard" Investigation using a fiberoptic flexible endoscope is usually employed to evaluate the vocal cords and possible associated malacia. A grading system devised by Myer and Cotton [16] (Fig. 16.2) can be used to classify stenosis into four grades according to the percentage of lumen occupied by the stenosis: grade I, 0–50%; grade II, 51–70%; grade III, 71–99%; and grade IV, 100% (no lumen). Recently, Monnier et al. proposed a modification to the Myer–Cotton classification, adding two parameters that have a crucial role in outcome: involvement of the vocal cords and comorbidities [17] (Table 16.1).

Using a rigid endoscope, besides the grade, the following features of the stenosis can be assessed: length and localization of the stenosis (posterior, anterior, circumferential); morphology of the cricoid (elliptical, flattened); and involvement of the soft tissues only or both soft tissue and cartilage. An important differential diagnosis is between posterior subglottic stenosis and bilateral VCP. Palpation with a Lindholm vocal cord retractor is very helpful in helping to distinguish between a VCP (in which the vocal cords can be spread out) and a posterior subglottic stenosis (in which the vocal cords do not open).

16.5.4 Management

Management is dependent upon the grade of stenosis, involvement of the vocal cords, comorbidities, and/or previous tracheostomy. Endoscopic treatment can be attempted for thin stenosis of soft tissue that extends craniocaudally for ≤3–4 mm in infants or 5–7 mm in children [18]. A CO_2 laser (ultrapulse or superpulse mode) must be used. Endoscopic dilation with angiographic balloons or bougies is undertaken after laser incision of the stenosis to open the lumen. Endoscopic treatment of cartilaginous stenosis must be avoided because the cartilage is left exposed to the lumen without a mucosal covering, thereby leading to fibrosis and recurrence [18].

Open surgery is indicated for all other cases and involves laryngotracheal reconstruction (LTR) with cartilage grafting (Fig. 16.3) or cricotracheal resection (CTR) (Fig. 16.4). LTR is indicated for mild-to-moderate stenoses (grade II or mild grade III), whereas CTR may be indicated for more severe stenoses (grade III and IV).

LTR with cartilage grafting was first described by Cotton [19]. It is carried out through a cervical incision and a laryngofissure extending from the thyroid cartilage (including the cricoid) to the first tracheal rings

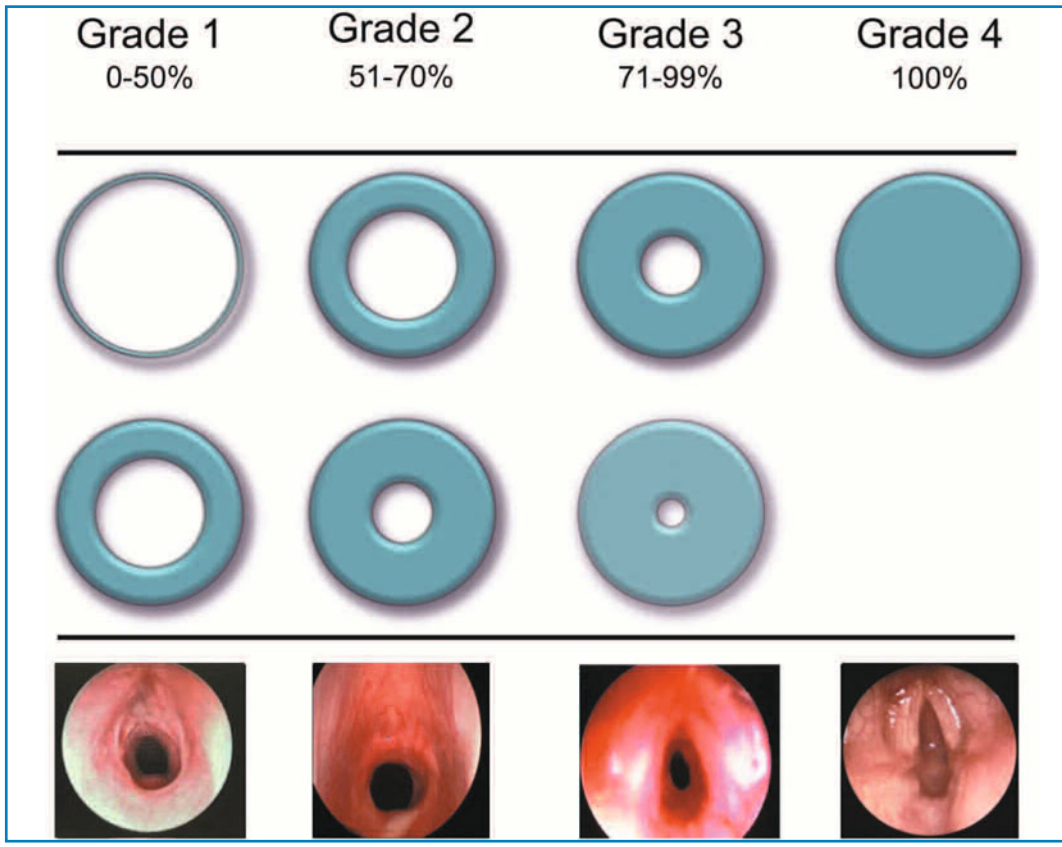

Fig. 16.2 Myer–Cotton classification of suglottic stenosis [16]

Table 16.1 New grading system of subglottic stenosis proposed by Monnier et al. [17]

Myer–Cotton grade	Isolated stenosis	+ Comorbidities	+ Glottic involvement	+ Comorbidities + glottic involvement
I	Ia	Ib	Ic	Id
II	IIa	IIb	IIc	IId
III	IIIa	IIIb	IIIc	IIId
IV	IVa	IVb	IVc	IVd

(Fig. 16.3a). The cartilage graft, obtained from one of the last cartilage ribs (Fig. 16.3b) and fashioned to fit into the airway wall, can be positioned according to the type and localization of the stenosis into the posterior and/or anterior wall, resulting in expansion of the lumen (Fig. 16.3c–d). The cartilage graft is sutured to the wall with absorbable stitches, with the pericondrium left inside the lumen. Usually, in a variable period of time, the mucosa can cover the pericondrium from each side. If a tracheostomy is done, it can be maintained or closed during the same procedure.

CTR was first described by Pearson et al. [20]. It is conducted through the same cervical incision but, unlike LTR, the stenosis is resected and not opened and enlarged. A transverse incision is made just below the thyroid cartilage, extended laterally (leaving the posterior cricoid plate and cricothyroid muscles

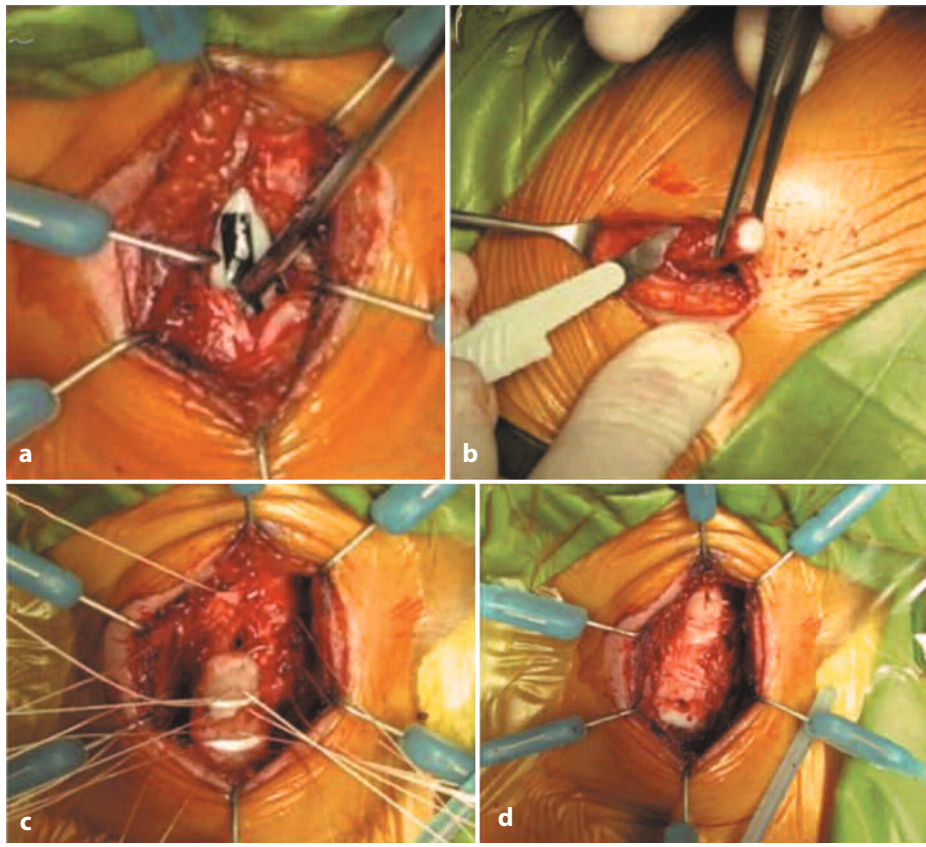

Fig. 16.3 Laryngotracheal reconstruction with cartilage grafting (see text for details of stages **a–d**)

to protect the recurrent laryngeal nerve) and prolonged inferiorly up to the first normal tracheal ring (or to include the tracheostomy if the procedure is done in a single stage) (Fig. 16.4a–b). A thyro-tracheal anastomosis in separate stitches re-establishes the airway continuity (Fig. 16.4c–d). Subsequently, Monnier et al. proposed the use of a pedicled flap of membranous trachea to resurface the denuded cricoid plate [21]. The necessity of postoperative stenting of the airway is controversial. The stent or endotracheal tube can protect the anastomosis but can lead to the development of granulation tissue or mucosal damage. In the case of transglottic stenosis, an extended CTR is indicated. This procedure is like CTR but also includes a complete laryngofissure (thyroid cartilage is opened completely in the midline), division of the vocal cords straight in the midline, and splitting of the posterior cricoid with interposition of a cartilage graft [22]. In such cases, a stent is required. Monnier et al. proposed an anatomic mold (LT-mold) [23] that seems to guarantee good stent function without causing excessive pressure on the airway wall.

16.5.5 Results and Follow-up

Antibiotics and anti-reflux treatment are initiated after surgery. The patient is kept in the ICU for a variable length of time. A nasotracheal tube can be tolerated by an awake patient. The stent (or endotracheal tube in the case of single-stage surgery) is usually left for 1–5 days after surgery. CPAP ventilation is sometimes necessary to "bridge" the patient to spontaneous ventilation after extubation. The neck is monitored daily to search for signs of

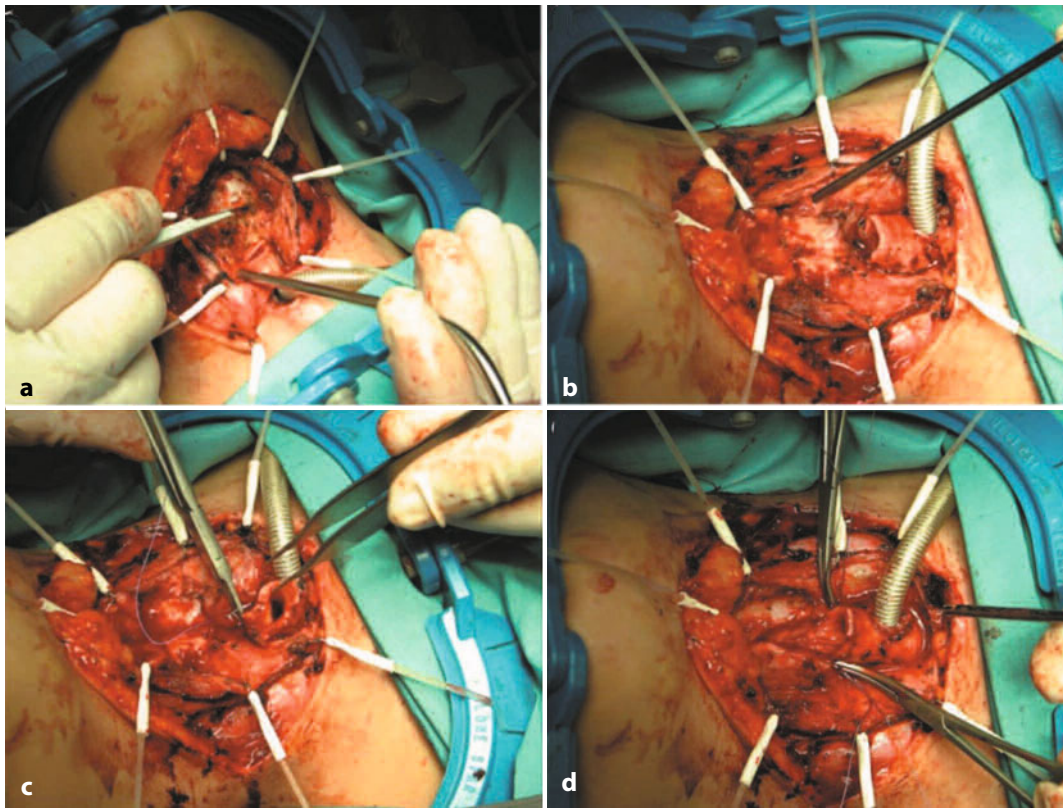

Fig. 16.4 Cricotracheal resection (see text for details of stages **a–d**)

complications (e.g. emphysema, infection, swelling, hematoma). The subcutaneous drain is usually removed after 48 h. VCP and anastomotic dehiscence are rare (<5% of cases) complications after CTR [24, 25].

The results of airway reconstructive surgery vary according to the: preoperative grade of stenosis; type of surgery; age and weight of the patient; expertise of the surgical team. Evaluation of outcome is difficult because only small series have been reported [26–28]. However, decannulation after LTR can usually be achieved in 65–70% of patients, with differences observed according to the degree of stenosis (>80% for grade I; 55–75% for grade II; 24–53% for grade IV). It has been reported that the prevalence of failure after first surgery is 33% and that 1–4 additional open procedures are necessary. The overall prevalence of decannulation after LTR was reported to increase to 89% with good results also for grade-IV stenoses (81%). The outcome for grade-IV or severe grade-III stenoses seems to be better after CTR (overall prevalence of decannulation = 92%) than after LTR, and the number of revision surgeries smaller (18% *versus* 46%) [29]. CTR is now accepted as first-line treatment for severe grade-III and -IV subglottic stenosis [30, 31].

16.6 Other Rare Anomalies

Rare anomalies include laryngeal clefts, hemangiomas, webs and cysts. Clefts are longitudinal defects of the wall between the airways and pharynx/esophagus. They can be classified according to length [32] as:

- grade I (extending to the arytenoid);
- grade II (extending to the cricoid);
- grade III (extending to the cervical trachea);

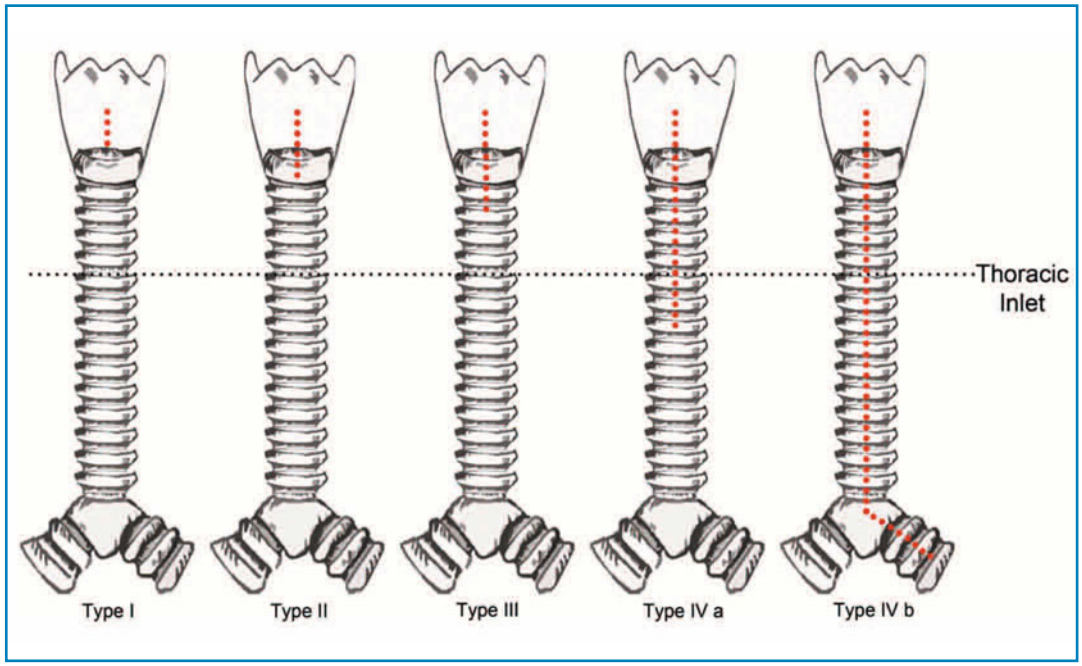

Fig. 16.5 Benjamin–Inglis classification for laryngeal clefts [32]

- grade IVa (extending to the thoracic trachea);
- grade IVb (extending to the main bronchus) (Fig. 16.5).

They can be isolated or associated with other airway or digestive anomalies (esophageal atresia, gastroesophageal reflux, malacia). The gold standard for the diagnosis (which can be difficult) is investigation using a rigid endoscope. Symptoms are correlated with the extension of the defect and are a combination of feeding and respiratory symptoms. Surgical treatment is required for symptomatic type-I clefts and for other types of cleft. Surgery can be endoscopic for grade-I and -II clefts (occasionally for grade III), whereas open surgery is the best treatment for grade-III and -IV clefts or for recurrences [33] (Fig. 16.6).

Subglottic hemangiomas (Fig. 16.7) typically present as a left posterolateral subglottic mass. In 50% of cases, the subglottic hemangioma is associated with other hemangiomas. Subglottic hemangiomas are more common in females. As with other hemangioma, they have a proliferative phase during the first 10

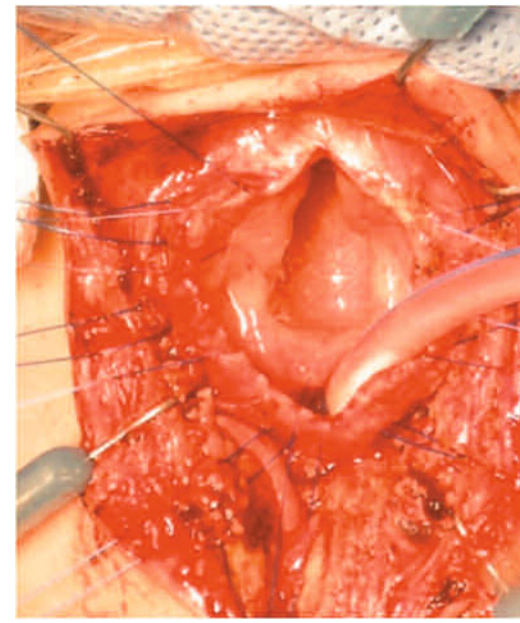

Fig. 16.6 Laryngeal cleft associated with esophageal atresia. The airway is opened and the upper esophageal pouch is shown (courtesy of Professor Patricio Varela, Clinica Las Condes and Calvo Mackenna Hospital, Santiago, Chile)

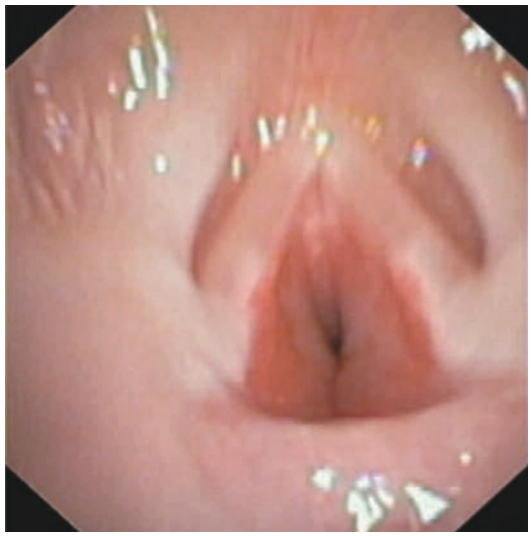

Fig. 16.7 A subglottic hemangioma that is extended bilaterally (without the typical aspect of a posterolateral left rounded mass). Image courtesy of Dr O. Sacco, Gaslini Children's Hospital, Genoa, Italy

months of life, they then tend to stabilize and to involute slowly in the next few years. Symptoms of respiratory distress start at 2–4 months of age. Investigation using a rigid endoscope is crucial for the diagnosis (though MRI is helpful to evaluate the extension of the malformation). Treatment options are conservative, medical (propanolol or other beta-blockers are now preferred to corticosteroids) or surgical (endoscopic approach with intralesional injection of corticosteroid, CO_2 laser resection, or open submucosal resection).

Laryngeal webs are derived from defects of the recanalization of the primitive larynx as laryngeal atresia; this occurs early in embryonic life and is usually incompatible with life. Laryngeal webs are classified according to a classification devised by Cohen [34] into four types:

- type I is a thin anterior web with <35% of glottic involvement;
- type II a thin-to-moderately thick web with a 35–50% of glottic involvement and minimal subglottic extension;
- type III is a thick web extending to 50–75% of the glottis and always with a subglottic extension;
- type IV is a thicker web involving 75–90% of the glottis with a cartilaginous subglottic extension.

Symptoms are a variable degree of voice anomalies (from a mild hoarseness in grade I to aphonia in grade IV) and respiratory distress (absent in grade I to severe distress with the necessity of tracheotomy in type IV). Treatment can be endoscopic (CO_2 laser) in mild cases, but cases with subglottic extension must be treated with an open approach (LTR or CTR).

Laryngeal cysts are more frequently ductal cysts resulting from obstruction of a mucus gland duct with mucus retention. Less frequently they are saccular cysts or congenital, characterized by a submucosal mass protruding between the false and true vocal cords. Laryngoceles are very similar to congenital laryngeal cysts except that they communicate with the lumen and are filled with air. Laryngeal cysts can be the cause of respiratory distress in newborns, but laryngoceles are usually diagnosed in children or adolescents playing wind instruments. All of these lesions can be treated *via* endoscopic means.

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Tracheal Lesions

17

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17.1 Introduction

Tracheal lesions are rare, with an estimated incidence of 1 per 60.000 live births [1]. Nevertheless, they represent a major challenge for pediatric surgeons and thoracic surgeons. Tracheal lesions can be subdivided into congenital and acquired anomalies.

17.2 Congenital Anomalies

17.2.1 Tracheomalacia (TM)

17.2.1.1 Etiology and Pathogenesis

TM is defined as a weakness or defect with collapsibility of the cartilaginous tracheal wall. It accounts for 50% of all congenital lesions. TM can be classified according to etiology in different groups.

Idiopathic TM is rare. It presents usually as diffuse TM in preterm babies. TM associated with esophageal atresia is the most common group where the posterior wall is typically more affected than the anterior wall. TM associated with cardiovascular or other external compression is a heterogeneous group. It includes: compression of the innominate artery; double or right aortic arch; compression by pulmonary vessels or other mediastinal masses as tumors; or pectus excavatum ("funnel chest"). TM associated with tracheostomy or other tracheal conditions can be a localized TM that is mainly due to the tracheostomy cannula or previous intubation, or diffuse (associated with laryngomalacia or bronchomalacia).

17.2.1.2 Clinical Features

Symptoms usually appear if the tracheal lumen is reduced by >50%. They can vary in intensity and include: barking cough; biphasic stridor; a prolonged expiratory phase; cyanotic and/or apneic spells; noisy or "washing machine" breathing; acute life-threatening events; chest retractions; and recurrent pulmonary infections. Symptoms are usually exacerbated by feeding and crying. Depending on the type of TM, other symptoms may be associated. Patients can have quiet and almost asymptomatic periods, sometimes during sleep.

17.2.1.3 Diagnosis

TM is diagnosed during fiberoptic endoscopy of the airways carried out under spontaneous breathing (Fig. 17.1). Respiratory dynamics should not be completely abolished by deep sedation. Variation in airway pressures by the anesthesiologist during endoscopy can also

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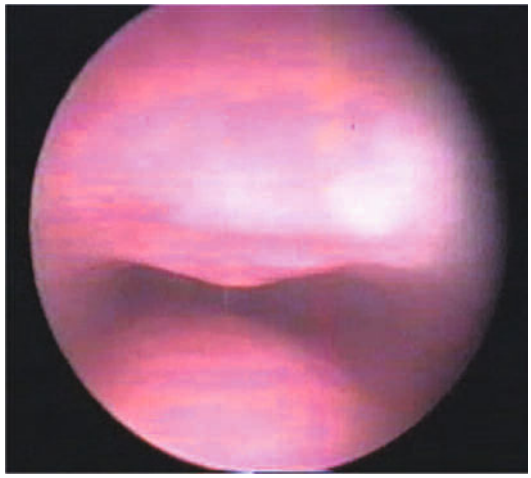

Fig. 17.1 Endoscopic image showing severe tracheomalacia

help in reproducing the respiratory dynamics, and better visualizing the collapsibility of the tracheal wall. During the endoscopic evaluation, associated conditions (e.g., tracheoesophageal fistula, diverticula, vascular compressions, other airway anomalies) must be excluded.

Another useful tool that can be used to diagnose TM is bronchography. Bronchogra-phy can help to define and show the morphology of the tracheobronchial tree and its modifications during the respiratory phases [2]. It can be done in association with bronchoscopy. Other relevant investigations include echocardiography, computed tomography (CT) and magnetic resonance imaging (MRI) to study mediastinal and cardiovascular anatomy.

17.2.1.4 Management

TM can improve spontaneously with the growth of the child. Lung physiotherapy, prevention of respiratory infections and anti-reflux treatment are useful tools for the conservative management of infants with TM. In the case of TM associated with external compression, surgical decompression can resolve airway symptoms. In the case of TM due to cardiovascular anomalies or complicated esophageal atresia, surgical treatment of the primary condition is the first step. A general consensus on surgical indications are lacking except one or more acute life-threatening events.

Therapeutic options for the surgical treatment of TM include: aortopexy; external reinforcement of the tracheal wall; resection and anastomosis of the trachea; or stent insertion. A recent Cochrane review focusing on the treatment modalities for TM in children showed a lack of randomized studies comparing different approaches, so the best treatment could not be demonstrated [3].

Aortopexy was first described in 1948 [4]. It is carried out in many centers to treat most cases of symptomatic TM. It is carried out through a left anterior thoracotomy (less frequently through a median sternotomy, right thoracotomy or thoracoscopy) and involves suturing the aortic wall to the posterior surface of the sternum. This maneuver results in opening of the tracheal lumen through elevation of the anterior tracheal wall. The aortic wall is tackled with non-absorbable stitches (avoiding entering the lumen) at the level of the origin of the innominate artery. Intraoperative tracheoscopy is useful to demonstrate improvement in the tracheal lumen.

External reinforcement of the tracheal wall was advocated by Hagl et al. [5]. They proposed the use of ring-reinforced polytetrafluoroethylene prostheses. However, this reinforcement can be achieved using many materials. Autologous materials (costal cartilage) are preferred by some authors [6] whereas resorbable (Vicryl plates) or non-resorbable materials (Gore-Tex™) are preferred by others.

Resection and anastomosis of the trachea is an option in the case of localized TM, as in tracheostomy-related TM as well as in a rare condition in which tracheal rings are absent. The use of a stent for the treatment of TM has been attempted by several authors [7]. Metallic balloon-expandable devices, silicone stents or biodegradable stents can be used for airway stenting.

17.2.1.5 Outcome and Follow-up

The results of aortopexy are usually good [8], with symptom resolution in the most patients.

The best results are for TM associated with esophageal atresia and vascular compression. In a recent review, the results of treatment of TM associated with other comorbidities or airway problems were suboptimal, but aortopexy should still be considered [9]. A study comparing tracheal stenting with aortopexy concluded that both were effective treatments for TM, but that tracheal stents were associated with a higher prevalence of failure, severe morbidity and mortality [10]. After tracheal stenting, granulation and in-stent stenosis are common complications which require endoscopic maneuvers such as dilation or granuloma resection. Metallic stents are usually permanent and attempts at removal can result in severe complications or death [10]. With growth of the child, metallic stents become progressively dilated but can break, causing the development of more granulation tissue. Stent erosion into a vessel with massive bleeding has also been reported [11]. Absorbable stents have been designed to overcome these problems. They have less radial strength than metallic stents, and these effects disappear when they are reabsorbed [12]. Silicone stents are retrievable but frequently dislocate and cause the development of granulation tissue [13]. Moreover, they prevent the clearance of mucus secretions in the tracheal segment in which the stent has been placed.

17.2.2 Congenital Tracheal Stenosis

17.2.2.1 Etiology and Pathogenesis

Congenital tracheal stenosis is a rare anomaly characterized by complete cartilaginous rings (Fig. 17.2). These circular "O" rings can be extended for a variable length of the trachea. Short-segment stenoses involve <50% of the length of the trachea; long-segment stenoses can be extended for the entire trachea (and sometimes beyond the carina). The etiology and pathogenesis are unknown, but they are the result of a developmental abnormality. Other tracheobronchial anomalies can be associated, such as tracheal bronchus, carina trifurcation, lung agenesis or hypoplasia [14]. A left pulmonary sling is associated in a significant percentage of cases. Other associated anomalies include cardiac anomalies, anorectal malformations, VACTERL association, Down syndrome and situs viscerum inversus [15, 16].

17.2.2.2 Clinical Features

Symptoms can start at birth with respiratory difficulty, need for intubation, and a disparity between respiratory demands and the possibilities of ventilation through a stenotic airway. A viral infection can unmask the condition and provoke severe symptoms. The condition can become evident during general anesthesia if intubation with an appropriate endotracheal tube is not possible.

The symptoms are: biphasic stridor or noisy breathing with a prolonged expiratory phase; chest retractions; cyanotic attacks; and respiratory infections. Endoscopic evaluation in a child with a certain degree of respiratory distress can precipitate symptoms because the edema caused by the endoscope can obstruct an already narrow airway. Respiratory symptoms in infants with congenital tracheal stenosis can be particularly severe; attempts at mechanical ventilation can be frustrating because the obstruction can be extended throughout the entire trachea or involve the bronchi. Tracheostomy in these cases is not useful. If mechanical ventilation cannot be carried out, the patient can be salvaged only with extracorporeal membrane oxygenation (ECMO) and surgical repair must be undertaken urgently. Conversely, some patients are not compromised in the activities of daily life and present symptoms only under exercise (e.g., stridor).

17.2.2.3 Diagnosis

Endoscopic evaluation under general anesthesia is the best way to diagnose congenital tracheal stenosis. The endoscopist must carry out the evaluation by avoiding touching the tracheal walls: the slightest trauma to the airway can decompensate the respiratory balance. Complete tracheal rings can be evaluated by

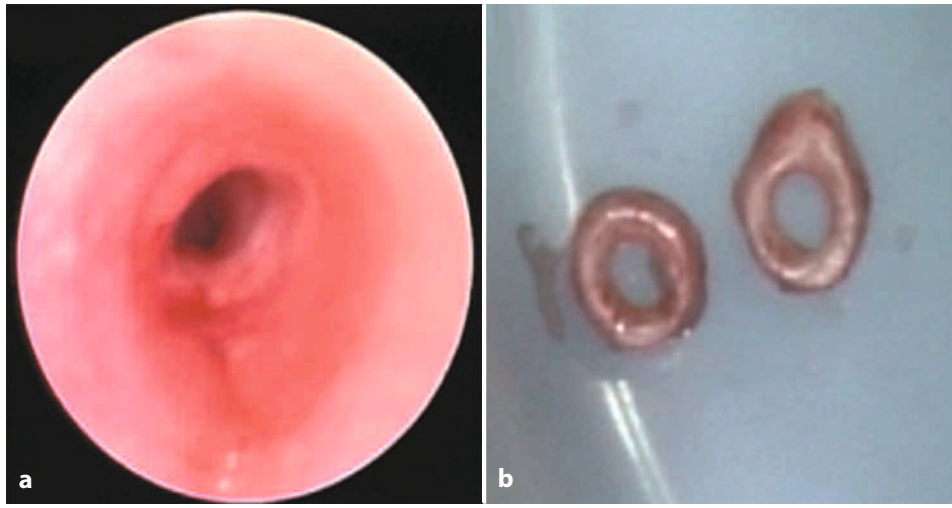

Fig. 17.2 Endoscopic image of congenital tracheal stenosis showing complete rings (**a**). Macroscopic samples of complete cartilage rings (**b**). Images courtesy of Professor Martin Elliott (University College London, London, UK)

flexible or rigid bronchoscopy (Fig. 17.2). In some cases, the rings are not so easily recognized (especially in neonates and in infected airways).

The "gold standard" modality for the evaluation of cartilaginous rings is optical coherence tomography (OCT) [17] (Fig. 17.3a). OCT is carried out during endoscopic evaluation by inserting a thin fiber conveying an infrared light. Reflection of the light by the tracheal wall (analyzed by the same fiber) details the composition of the tracheal wall. Cartilaginous components are seen clearly using this elegant investigation. OCT also gives useful information regarding the consistency of the trachea and bronchi, and can be used to detect tracheobronchomalacia.

CT using three-dimensional (3D) reconstructions can also accurately define the morphology of the tracheobronchial tree (Fig. 17.3b and c). The length and degree of the stenosis as well as study of associated cardiovascular anomalies is achieved using contrast agents.

Bronchography (Fig. 17.3d) is not used in most centers but still has an important role in: defining the morphology of the trachea, carina and bronchi; detailing the dynamics during inspiration and expiration; showing modifications in airway pressure [2]. Bronchography is also useful for evaluating the growth of the trachea as well as postoperative results.

Echocardiography is essential for the study of cardiovascular anomalies. Besides intracardiac anomalies, attention should be paid to the detection of a left pulmonary artery sling or other anomalies of pulmonary vessels.

Congenital tracheal stenoses can be classified into three types [18]: uniform stenosis extending to all (or almost all) of the trachea; funnel-shape stenosis; and localized stenosis. Another classification [19] divides the stenoses into three groups according to presentation, i.e., from asymptomatic to severely compromised.

Recently, the Great Ormond Street Classification has been proposed [20] in which the length of the stenosis and tracheobronchial anatomy are considered. In this new classification, airway stenosis is divided into tracheal stenosis (short- or long-segment if less or more than 50%, respectively) and tracheobronchial stenosis. Each group is then subdivided according to the morphology of the tracheobronchial tree (Fig. 17.4) into normal anatomy; tracheal bronchus; carina trifurcation; and single lung [20].

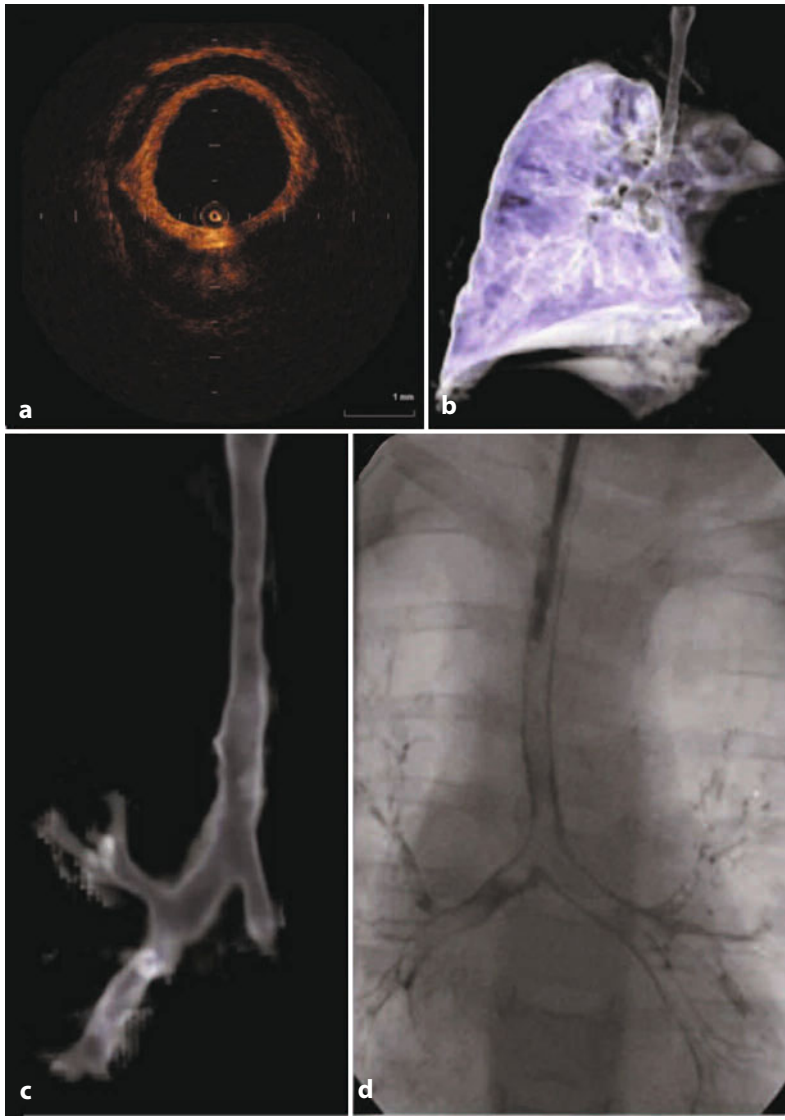

Fig. 17.3 Optical coherence tomography showing a complete tracheal ring (**a**). Computed tomography three-dimensional reconstruction of congenital tracheal stenosis (**b** and **c**). Bronchography showing tracheal stenosis (**d**). Images courtesy of Professor Martin Elliott (Great Ormond Street Hospital for Children, University College London, UK)

17.2.2.4 Management

Mechanical ventilation and ECMO are emergency measures employed to manage congenital tracheal stenosis. Complete tracheal rings are usually a surgical indication, even though in some patients congenital airway stenosis does not influence significantly with the activities of daily life and conservative treatment can be considered [19]. Most patients, however, require surgery to relieve respiratory symptoms during the first year of life. Treatment can differ according to the morphology and length of the anomaly. Short-segment stenoses can be treated successfully by resection and anastomosis of the trachea (Fig. 17.5). The length of trachea that can be resected is dependent upon the age of the patient. In infants, resection and anastomosis of ≥8–9 rings (corresponding to half of the length of the trachea) can usually be carried out safely [6].

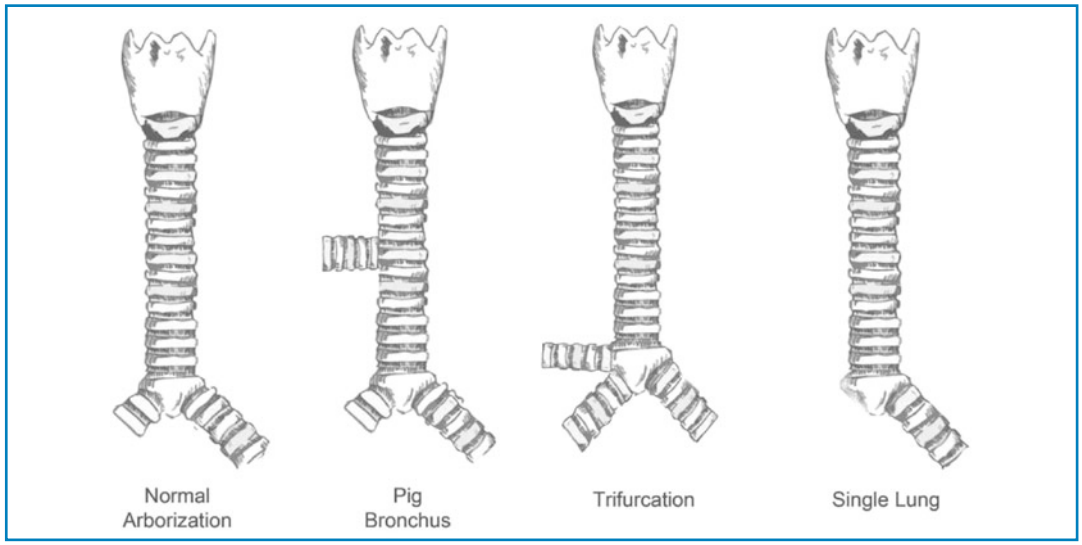

Fig. 17.4 Great Ormond Street Classification of congenital tracheal stenosis according to the morphology of the tracheobronchial tree [20] (schematic)

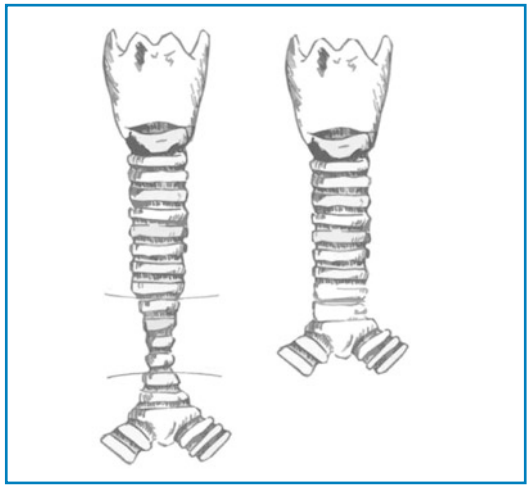

Fig. 17.5 Resection and anastomosis of the trachea (schematic)

Other surgical options are available for long-segment stenoses: enlargement patch tracheoplasty (Fig. 17.6); tracheoplasty with autografts or cadaveric homografts; and slide tracheoplasty.

Anterior patch tracheoplasty was the preferred choice before slide tracheoplasty was described. It was first undertaken using a costal cartilage [21], then with an anterior pericardial patch [22]. Anterior patch tracheoplasty is based on a median anterior approach, incision of the stenosis along its length on the anterior aspect, and insertion of the patch. This procedure results in enlargement of the lumen, and a postoperative stent is required after surgery.

Following the same principle of anterior enlargement, tracheoplasty with a cadaveric tracheal homograft has been proposed [23]. The homograft is sutured on the anterior tracheal wall opened in the midline. A silicone stent is placed in the lumen. The homograft is then revascularized from the native posterior tracheal wall.

Another approach that tried to reduce the postoperative problems typical of anterior patch tracheoplasty methods was introduced in 2001 [24]. Treatment using tracheal autografts involves mobilizing circumferentially the trachea and incising the stenosis on the midline. The mid-portion of the stenosis is then resected and its posterior wall used as free tracheal autograft. The two tracheal "stumps" are approximated and a posterior anastomosis completed. The autograft is sutured to the anterior aspect to cover the defect. If the graft is not sufficiently large to achieve this aim, 1–2 pericardial patches can be used to fill the defect.

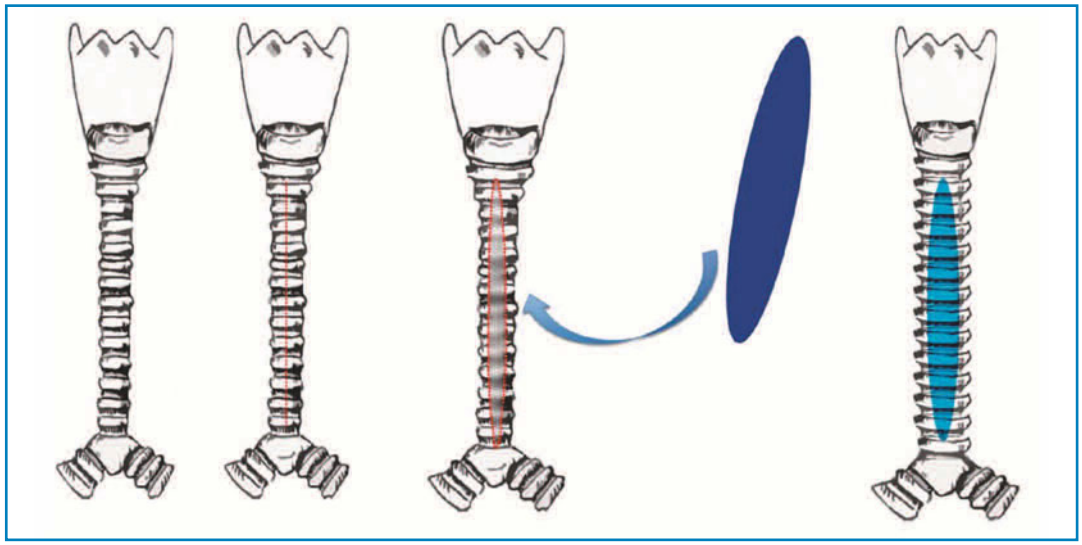

Fig. 17.6 Enlargement tracheoplasty (schematic)

Slide tracheoplasty was first described by Tsang et al. in 1989 [25]. It has become the preferred method for the repair of long-segment congenital tracheal stenoses in most centers. Slide tracheoplasty is carried out under cardiopulmonary bypass through a full sternotomy. If a cardiac anomaly is present, it is corrected during the same procedure. The stenosis is divided transversely in its midpoint. The two stumps are incised: one on the anterior and the other on the posterior wall. The two stumps "slide" along and an oblique anastomosis is created. The length of the trachea is reduced to one-half of the length of the stenosis but the caliber is doubled.

The advantage of slide tracheoplasty is that tracheal reconstruction can be achieved while avoiding appreciable tension and obtaining complete covering of the mucosa of the entire circumference of the lumen. This enables extubation within 24–48 h and avoids the development of granulation tissue in most cases (Fig. 17.7).

17.2.2.5 Outcome and Follow-up

Congenital tracheal stenosis is rare, so very few centers can report the surgical results on a large series of patients. The prevalence of granulation after patch tracheoplasty has been reported to be approximately 38%, and can require balloon dilations [26] or redo tracheoplasty [24]. After slide tracheoplasty, granulation has been observed in 0% to 23% of cases [27]. The prevalence of this complication is not clear, with one research team reporting that 28% of subjects underwent more than one balloon dilation or endoscopic resection of granulation tissue [28].

The prevalence of stenting after pericardial tracheoplasty has been reported to be 11.5% [24], whereas it has been reported to be 11.2% and 7.4% after slide tracheoplasty [27, 28]. Stenting was not reported by Fanous et al. [26] and Tsugawa et al. [28]. The stents implanted after slide tracheoplasty were retrieved in all patients but one [24], who eventually died. The stent implanted after pericardial tracheoplasty was the Palmaz stent [24].

The need for further surgery after pericardial tracheoplasty was shown to range from 9.5% [26] to 28% [24], whereas only 2.5% of subjects needed further surgery after slide tracheoplasty [28]. Tracheostomy after tracheoplasty was necessary in 11.5–28% of patients who underwent pericardial tracheoplasty [26, 24] compared with 2.5% who underwent slide tracheoplasty [28]. No tracheostomy was reported by Li et al. and Tsugawa et al. [27, 29].

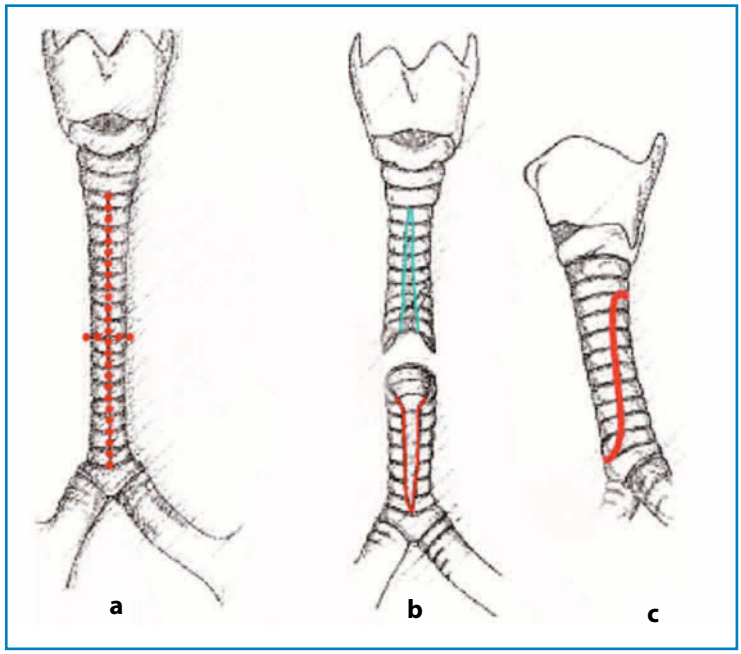

Fig. 17.7 Slide tracheoplasty (schematic). The blue color shows the incision in the posterior wall; the red color shows the incision in the anterior wall (modified from Grillo et al., Annals of Thoracic Surgery, 1994)

17.3 Traumatic Acquired Lesions

17.3.1 Etiology and Pathogenesis

Two major conditions belong to the group of acquired tracheal anomalies: cannula-related stenosis (chronic trauma) and acute traumatic lesions.

The cannula, due to its rigidity, can cause damage to the tracheal wall. Typically, suprastomal collapse develops as a result of the action of the curved cannula against the anterior wall of the trachea, which crushes down. At this level, a granuloma can be the consequence of the collapse. Another, less frequent cannula-related lesion, is a granuloma caused by the thrusting of the tip of the cannula against the tracheal wall due to inadequate placement or length of the cannula. Cuffed cannulae can also cause tracheal damage.

Tracheal lesions due to acute trauma are very rare. Trauma is more frequently blunt rather than penetrating. The most frequent causes are sporting activities, intubation, or endoscopic maneuvers. In blunt trauma, severe thoracic compression increases significantly intra-tracheal pressure; if this happens against a closed glottis, tracheal fracture can occur. The most commonly affected area is the posterior pars membranacea, whereas fractures of cartilaginous rings are extremely rare (Fig. 17.8).

17.3.2 Clinical Aspects

Patients with suprastomal collapse are usually asymptomatic because the cannula bypasses the problem. This condition is very commonly detected during routine endoscopy in a tracheostomized patient. Patients with a granuloma at the tip of the cannula are at risk of developing acute life-threatening respiratory distress. Subjects with a tracheal lesion due to acute trauma can be in severe respiratory distress and unconscious, whereas others can cope with a tracheal lesion relatively well. Neck emphyse-

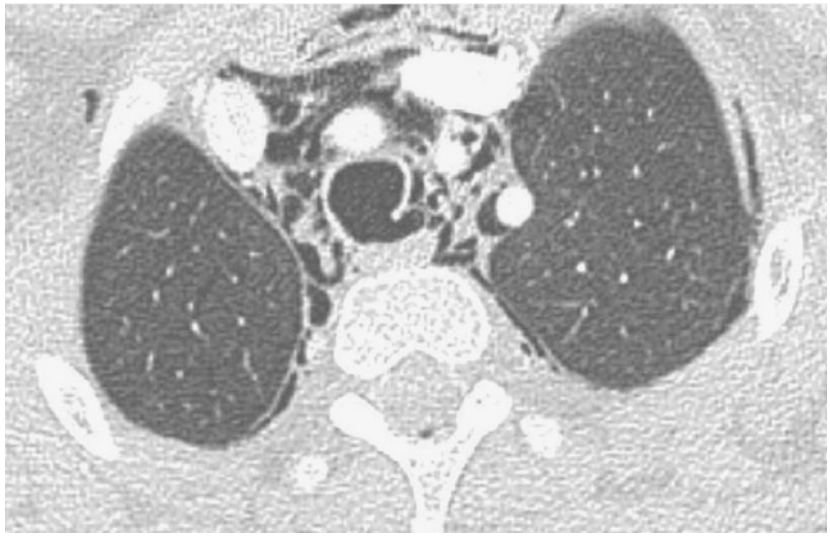

Fig. 17.8 Post-intubation lesion of the posterior tracheal wall

ma (with subcutaneous crepitus) or tenderness, pneumomediastinum, pneumothorax, dyspnea and hemoptysis are possible early signs of a tracheal lesion. Infection in the neck or mediastinum can occur subsequently.

17.3.3 Diagnosis

Endoscopy and/or radiological evaluation are helpful. Flexible fiberoptic tracheoscopy can be undertaken in severely traumatized patients through an endotracheal tube if it is withdrawn progressively and carefully. CT is the best investigation for the study of acute tracheal traumatic lesions.

17.3.4 Management

Suprastomal collapse can be corrected at the time of tracheostomy closure. Once diagnosed, granulomas on the tip of the cannula must be removed by forceps or laser resection. After acute trauma, surgery must be conducted in unstable cases or if cartilage is exposed, which can lead to significant post-traumatic stenosis. If the patient is well and the lesion is in the posterior wall of the trachea, conservative treatment is the best option because good spontaneous healing usually occurs.

17.3.5 Outcome

Cannula-related lesions can be treated successfully in most cases. However, the prognosis in traumatic lesions of the trachea is dependent upon the severity of the lesion, timing of the diagnosis, and adequacy of treatment.

17.4 Other Rare Anomalies

Tracheal neoplasms are very rare in children. Among the histotypes, multiple types of tumor (malignant and benign) have been described: carcinoid, carcinoma, chondroma, hamartoma, angioma, miofibroblastic inflammatory tumor (Fig. 17.9), granulosa cell tumor and lipoblastoma [29, 30]. All tracheal masses can present as ongoing respiratory distress; some have a history of repeated infections and others can mimic non-responding asthma. Endoluminal or open surgery (tumor resection or tracheal resection and anastomosis) is usually required. Medical treatment (beta blockers) is the best option for angiomas.

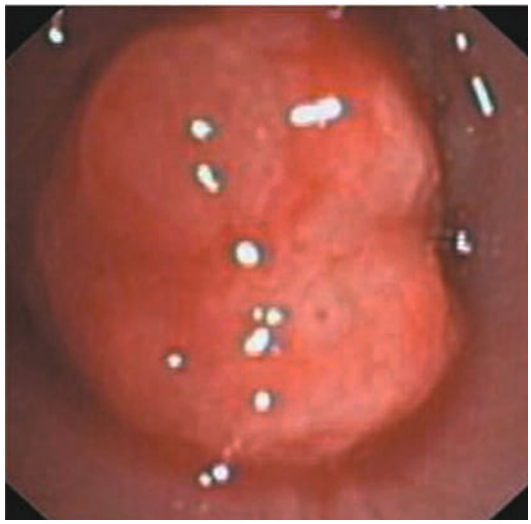

Fig. 17.9 Endoscopic image of miofibroblastic inflammatory tumor

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Vascular Rings and Pulmonary Slings

18

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and Gaetano Domenico Gargiulo

18.1 Introduction

Development of the mediastinal great vessels is the result of the growth and resorption of vessels derived from the two dorsal aortae and all the derived arches (Fig. 18.1). An alteration in the process that originates the great vessels can result in the development of a complete ring surrounding the trachea and esophagus. Depending on the type of alteration, several anatomical variants are possible, all causing an obstruction at respiratory and esophageal levels. The indication for corrective surgery to relieve the obstructive symptoms is a consequence of their tendency to constrict the trachea and/or esophagus [1]. Vascular rings comprise an estimated 1% of cardiovascular malformations that are managed surgically.

18.2 Vascular Ring

18.2.1 Etiology and Pathogenesis

Vascular development in the embryo starts from the connection of the ventral and dorsal aortae by the six pairs of aortic/branchial arches. Usually the first, second, and fifth arches as well as a segment of the right fourth arch regress, giving the normal left aortic arch. The residual third arch gives origin to the common carotid arteries, whereas from the residual portion of the right fourth arch and the seventh intersegmental artery develop the right subclavian artery. The proximal portion of the pulmonary arteries and the ductus arteriosus are formed by the sixth arch. Failure of this process causes erroneous persistence or reabsorption of segments of the primitive vascular system, thereby accounting for most of the congenital vascular rings and vascular slings [2].

18.2.2 Classification

Several anatomical variants can be present, and we report here the most frequently described. Most of these variants have a coexistent right aortic arch. A left dominant aortic arch is very rare but needs to be considered for a surgical approach through a right thoracotomy.

18.2.2.1 Double Aortic Arch

A double aortic arch is caused by persistence of the right dorsal aorta. In these patients, left and right aortic arches are present. The right arch gives rise to the right common carotid artery and the right subclavian artery, whereas

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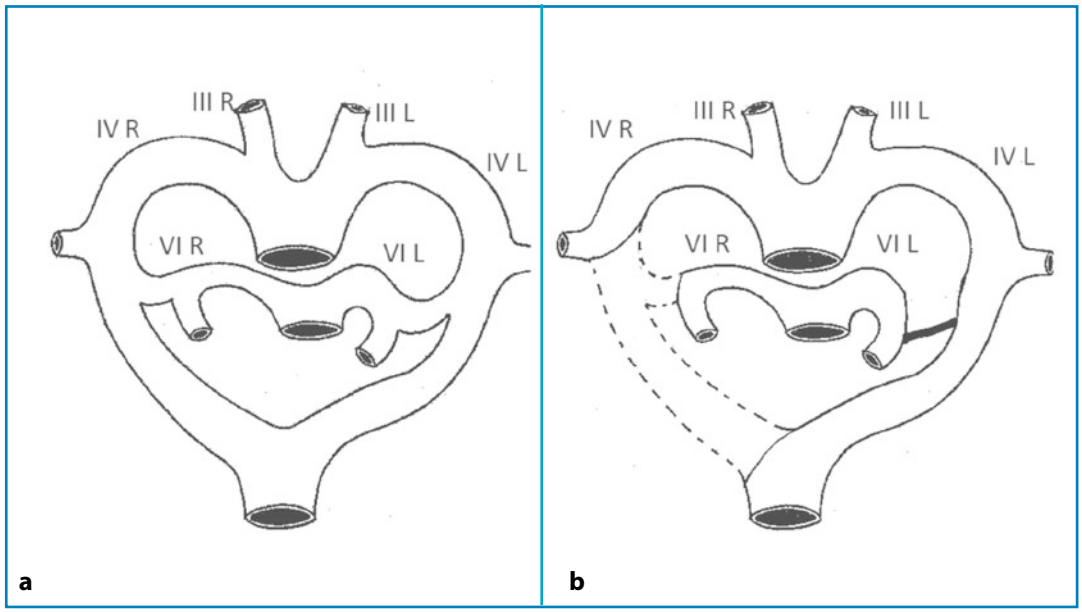

Fig. 18.1 The developing aortic arch (**a**) and the resulting normal left-sided aortic arch with all the vascular segments that disappear (*broken lines*; **b**) (schematic). Roman numbers refer to the embryological aortic arches

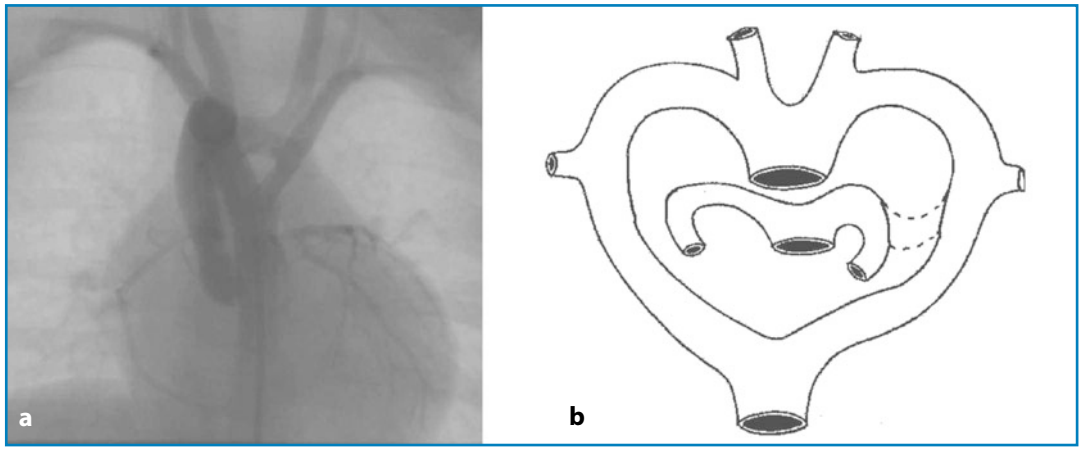

Fig. 18.2 Angiography in a double aortic arch (**a**) and schematic view showing the embryological origin (**b**)

the left arch gives rise to the left common carotid and left subclavian artery. In approximately 70% of cases, there is a dominant right arch and a hypoplastic (or even atretic) left arch that joins the descending aorta at its emergence from behind the esophagus near the insertion of the ligamentum arteriosus. The descending aorta is usually left-sided, but can be right-sided or in the midline (Fig. 18.2).

18.2.2.2 Right Aortic Arch, Aberrant Left Subclavian Artery and Left Ligamentum Arteriosus

This anomaly originates from persistence of the right fourth aortic arch with resorption of the left fourth aortic arch. The right aortic arch gives origin to the left common carotid artery, the right common carotid artery, the right subclavian artery and the left subclavian artery

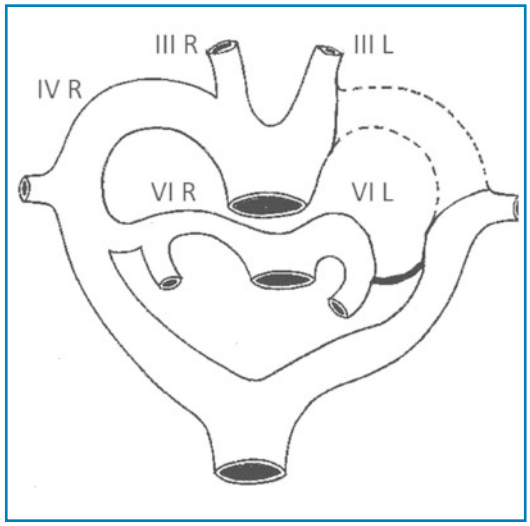

Fig. 18.3 Right aortic arch, aberrant left subclavian artery and left ligamentum arteriosus. The portion of the arch that is reabsorbed is represented by the broken lines. The *black bold line* is the ligamentum arteriosus. *Roman numbers* indicate the embryological aortic arches

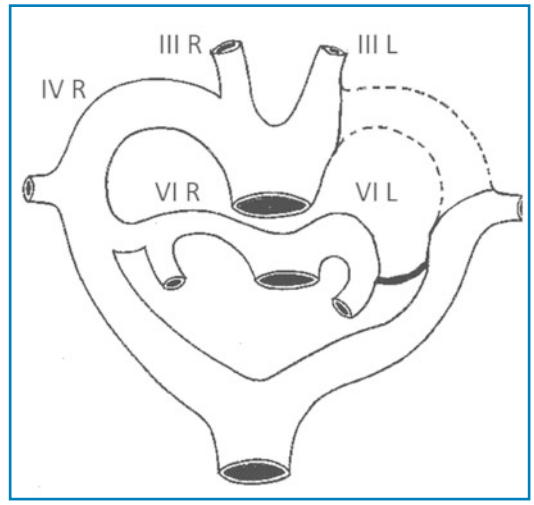

Fig. 18.4 Right aortic arch, mirror-image branching, and retro-esophageal ligamentum arteriosus. The portion of the arch that is reabsorbed is shown by broken lines. The *black bold line* refers to the retro-esophageal ligamentum arteriosus. *Roman numbers* refer to the embryological aortic arches

crossing the midline behind the esophagus. The ligamentum arteriosus, arising from the left subclavian artery, is connected to the left pulmonary artery originating a complete vascular ring that embraces the trachea and esophagus. Usually, the ligamentum arteriosus is on the same side as the aortic arch, but can develop on the contralateral side to the arch and is responsible for completing the vascular ring. A small diverticulum named "diverticulum of Kommerell" can occur at the site of the aberrant subclavian artery, and represents the aortic attachment of the ligamentum arteriosus (Fig. 18.3).

18.2.2.3 Right Aortic Arch, Mirror-image Branching and Retro-esophageal Ligament

This anomaly derives from persistence of the right fourth aortic arch and resorption of the fourth left aortic arch. A short portion of the distal end of the fourth left arch persists as the diverticulum of Kommerel. From the right aortic arch arise in sequence the left brachiocephalic trunk, the right common carotid artery and the left subclavian artery. A fibrous ligament originating from the prominent diverticulum passes leftward behind the esophagus and then anteriorly to connect to the left pulmonary artery, closing the ring around the trachea and esophagus (Fig. 18.4).

18.2.2.4 Left Aortic Arch, Mirror-image Branching, Right Descending Aorta and Atretic Right Aortic Arch

A normal left-sided aortic arch is present in this anomaly. After passing the midline in a retro-esophageal position, it joins the right descending thoracic aorta. An atretic right aortic arch, immediately superior to a right ligamentum arteriosum connecting to the right pulmonary artery, gives origin to the vascular ring.

18.2.2.5 Left Aortic Arch, Right Descending Aorta and Right-sided Ligamentum Arteriosum to the Right Pulmonary Artery

This anomaly is characterized by the mirror image of the right aortic arch that gives rise in sequence to the following arteries: right common carotid, left common, left subclavian and

right subclavian. The arch passes to the left of the trachea and then behind the esophagus to join the right descending thoracic aorta. At this level, an atretic right arch is found forming a diverticulum.

18.2.3 Clinical Features

Common symptoms include stridor, wheezing, respiratory distress, cough or evidence of dysphagia, or difficulty with feeding that can also worsen respiratory symptoms. In less serious cases, patients can remain asymptomatic throughout their life. In more severe cases, stridor is common as early as the neonatal period. Feeding can also be difficult, especially when progressing to solids. Reflux and respiratory infections are quite common [3, 4].

18.2.4 Associated Anomalies

A double aortic arch is usually an isolated lesion without other cardiovascular anomalies. In about 20% of cases, it is associated with a deletion in chromosome band 22q11. This deletion is responsible for DiGeorge, velocardiofacial, and conotruncal anomaly face syndromes. These syndromes are often referred to using the terms "catch-22 syndrome" or "chromosome band 22q11 deletion syndrome". For this reason, the most common associated defects are ventricular septal defect, tetralogy of Fallot and all the congenital cardiopathies referable to conotruncal anomalies.

18.2.5 Diagnosis

Chest radiography alone or barium esophagography can give strong clues to the definitive diagnosis by showing signs of compression in the airway or esophagus. However, more comprehensive imaging details are required, and magnetic resonance imaging (MRI) and computed tomography (CT) have sensitivities approaching 100% [5] (Fig. 18.5). In both cases, all the details necessary to plan corrective surgery can be provided [4, 6]. Bronchoscopy may be necessary to disclose pulsatile external airway compression.

18.2.6 Management

In a symptomatic child, surgery is indicated. Symptoms can be present in the neonatal period and prompt relief of obstruction may be indicated. Less serious symptoms may be diagnosed in the older infant (usually recurrent infection or other respiratory symptoms rather then stridor or dysphagia). In these cases, elective surgery is indicated.

18.2.6.1 Surgical Procedure

The first attempts at surgery for vascular rings were by Gross in 1945 [7]. Preoperative evaluation of imaging and clinical findings is crucial to plan the side of the thoracotomy [8]. In >95% of cases, a left thoracotomy is preferred. A right thoracotomy is necessary only if a left dominant aortic arch is present. In patients with a double aortic arch, the dominant one must be disclosed (which can be difficult). This evaluation is fundamental to choose the side of the thoracotomy, which will be on the right in case of dominant left arch and *vice versa*. Intraoperatively, arterial pressure in one of the arms and legs must be ascertained to check the effect of temporary closure of the smaller arch. This measurement ensures that a pressure gradient is not present at the level of the dominant aortic arch.

The patient is positioned in the lateral decubitus position. A conventional posterolateral thoracotomy (usually in the fourth intercostal space) is carried out. After retracting the lung anteriorly, descending aorta, distal arch, and all the vessels that can be reached are exposed and surrounded with a vessel loop (Fig. 18.6a). The vagus nerve (giving origin to the recurrent laryngeal nerve that passes around the ligamentum arteriosus) can be a useful landmark. In the case of a double aortic arch, the distal portion of the diminutive arch is clamped to check that

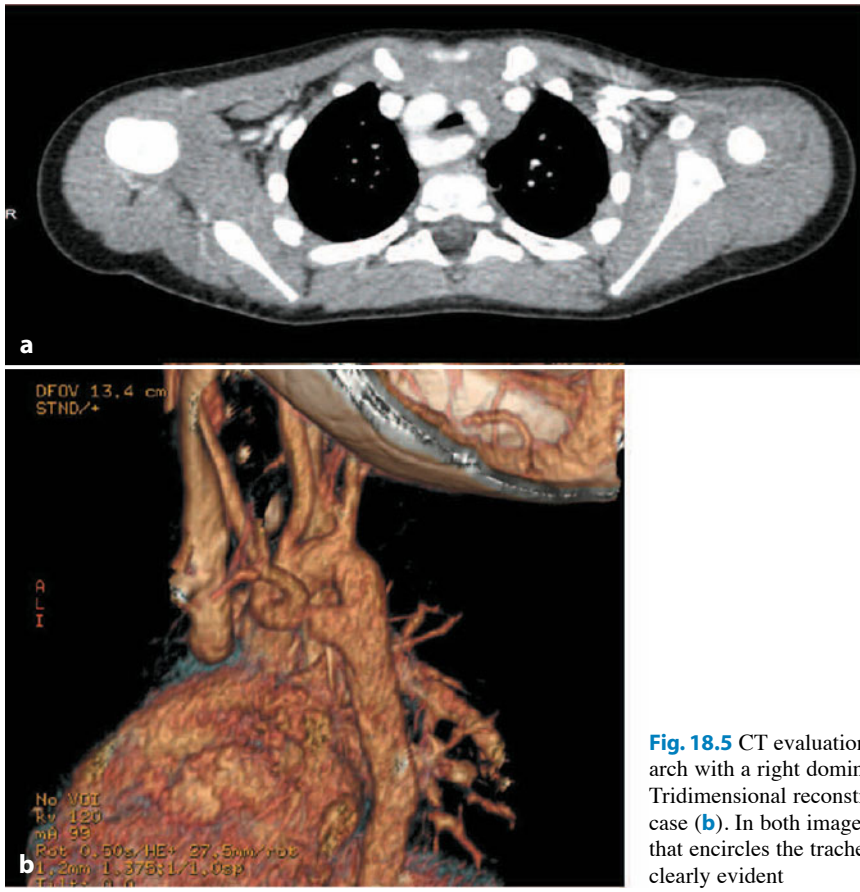

Fig. 18.5 CT evaluation in a double aortic arch with a right dominant arch (**a**). Tridimensional reconstruction of the same case (**b**). In both images, the vascular ring that encircles the trachea and esophagus is clearly evident

a pressure gradient between arms and legs is present. The arch is transected between the clamps and the two sides closed with a double running suture (Fig. 18.6b). This causes spontaneous retraction of the two stumps, indicating the tension with which the ring surrounds the trachea and esophagus. If a ligamentum is not present, this must be identified and transected. In both cases, careful dissection of the vessels from the surrounding tissue is important to provide space to the trachea and esophagus. Care must be taken not to dissect the esophagus, which can necrotize for the metameric vascularization that characterizes this organ. Moreover, checking for serous leakage and eventually solving the problem is very important because it can cause postoperative chylothorax.

18.2.7 Outcome and Follow-up

Mortality and morbidity have been reported to be very low [1, 4]. In infants, severe symptomatic tracheomalacia may be associated with long-standing compression. In these cases, relief of all respiratory symptoms can be progressive, and complete and rapid improvement in feeding is always obtained [3].

18.3 Pulmonary Artery Sling

A pulmonary artery sling is a rare anomaly in which the left pulmonary artery originates from the right pulmonary and, by surrounding the distal part of the trachea and right main-stem bronchus, runs between the trachea and esophagus [9] (Fig. 18.7).

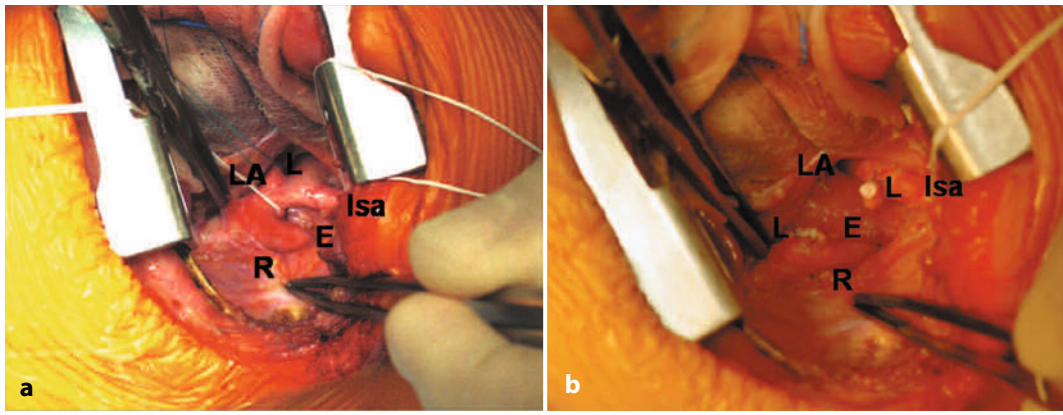

Fig. 18.6 Intraoperative view of a double aortic arch with a dominant right aortic arch. A left thoracotomy has been carried out and the two arches can be visualized (**a**). After division of the left arch, the two stumps move away, leaving more space for the esophagus (**b**). *L*, left arch; *R*, right arch; *LA*, ligamentum arteriosum; *lsa*, left subclavian artery; *E*, esophagus

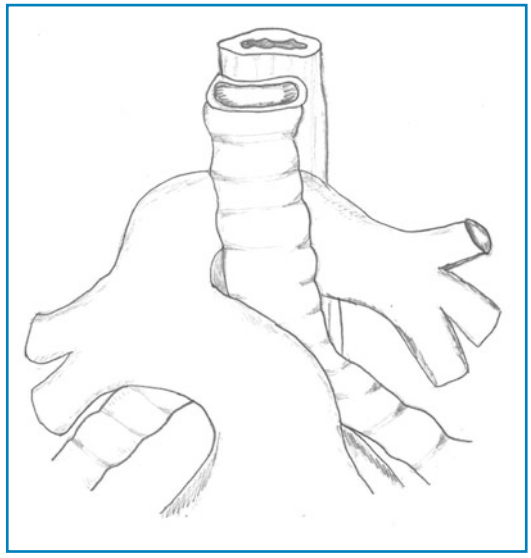

Fig. 18.7 Pulmonary artery sling (schematic). The left pulmonary artery arises from the right pulmonary artery and courses posteriorly to the trachea

18.3.1 Etiology and Pathogenesis

A pulmonary artery sling is a rare anomaly, accounting for <1% of all congenital heart defects. It is caused by abnormal progression of the aortic sac and/or development of the sixth arch. Such abnormal progression results in an extrapericardial origin of the left pulmonary artery from the posterior aspect of the right pulmonary artery. It then encircles the right main-stem bronchus and courses posteriorly between the trachea and esophagus. The ligamentum arteriosum or the ductus itself originates from the main pulmonary artery and passes anteriorly to the left main bronchus and anomalous left pulmonary artery to join the aorta and complete the vascular ring.

18.3.2 Clinical Features

The clinical features are secondary to the associated tracheal lesions and coexisting cardiac anomalies. In isolated cases (and different to vascular rings), symptoms are exclusively of a respiratory nature. In approximately 65% of cases, stenosis of the tracheobronchial tree is present. Tracheomalacia is not usually found in these patients.

18.3.3 Associated Anomalies

In approximately 50% of cases, other congenital cardiac defects are coexistent. The most common are atrial or ventricular septal defects, patent ductus arteriosus, and tetralogy of Fallot.

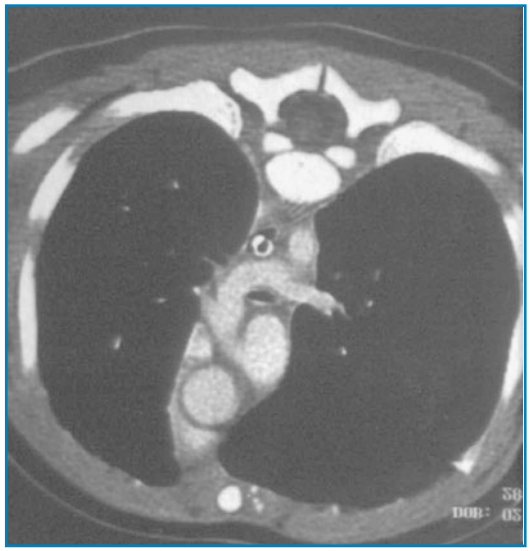

Fig. 18.8 MRI of a pulmonary artery sling

18.3.4 Diagnosis

The diagnosis is usually obtained by echocardiography (which can also disclose coexisting cardiac anomalies). Chest radiography can be useful if airway compression is suspected. Bronchoscopy is essential to exclude tracheal stenosis secondary to complete tracheal rings. CT or MRI can give the complete diagnostic picture and realistic reconstruction of the anatomy [10] (Fig. 18.8).

18.3.5 Management

The diagnosis of a pulmonary artery sling is an indication for surgery. In asymptomatic, isolated cases, a conservative attitude is preferable. Surgery alone can address the pulmonary artery sling or necessitate tracheal reconstruction if a stenosis or complete tracheal ring is present [11].

18.3.5.1 Correction of an Isolated Pulmonary Artery Sling

Surgery is usually *via* median sternotomy (Fig. 18.9). After extensive dissection of the left pulmonary artery, cardiopulmonary bypass (CPB) is established. The decision of undertaking the procedure on a beating heart or under cardioplegic arrest is left to the surgeon. The left pulmonary artery is divided at its origin and dissected free from the posterior aspect of the trachea and left bronchus. The proximal portion is closed with a running suture and, after relocating the artery in its usual position, it is implanted on the main pulmonary artery [12].

18.3.5.2 Correction of a Pulmonary Artery Sling and Tracheal Stenosis

Using a median sternotomy and CPB, extensive dissection of the left pulmonary artery is

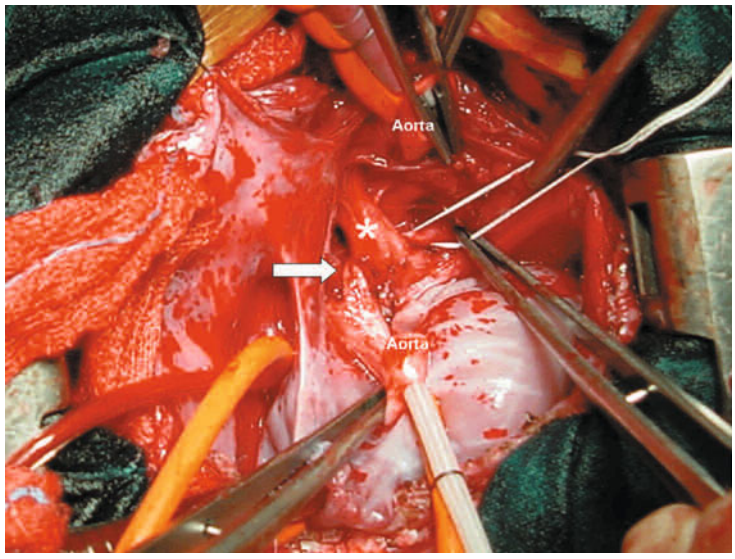

Fig. 19.9 Intraoperative view of a pulmonary artery sling. A median sternotomy has been carried out. The two stumps of the divided ascending aorta (*Aorta*) disclose the trachea (*asterisk*). The *white arrow* refers to the left pulmonary artery, which originates from the right pulmonary artery and courses behind the trachea. Its distal portion is surrounded by a white snare and is indicated by the forceps

achieved. The stenotic segment of the trachea is exposed and repaired, depending on the anatomy of the lesion, by: resection and end-to-end anastomosis; pericardial tracheoplasty; tracheal autograft; tracheal resection; cartilage tracheoplasty; slide tracheoplasty; or aortic homograft patch tracheoplasty [6]. In the case of transection of the trachea, the left pulmonary artery is moved anteriorly and can be left in this position unless a "kinking" at the origin is observed. In this case or if transection of the trachea is not carried out, the left pulmonary artery is re-implanted as described previously [13].

18.3.6 Outcome and Follow-up

Morbidity and mortality are consequences of the involvement of the respiratory tree. In these cases, the necessity to also undertake tracheal correction affects short- and long-term results. In isolated cases, results are very good and mortality has been reported to be <1%.

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Part IV

Diaphragm

Congenital Diaphragmatic Hernia

19

Francesco Molinaro, Rossella Angotti, Francesco Ferrara, Francesca Borruto, Mario Messina and François Becmeur

19.1 Introduction

Congenital diaphragmatic hernia (CDH) is a defect of development of the pericardioperitoneal canals. In general, it occurs at 6–7 weeks of gestation. It is responsible for herniation of the abdominal organs into the thoracic cavity. CDH is delimited anteriorly by the diaphragm, sideways by the diaphragmatic pillars and posteriorly by the costal margin. CDH causes lung compression on the side of the diaphragmatic defect, precluding normal development of the lung ("lung hypoplasia") [1, 2]. CDH has an incidence of 1 case per 3,000–5,000 in live births with a male predominance. CDH is not a hereditary disease. CDH is on the left side in 86% of cases (Figs 19.1 and 19.2).

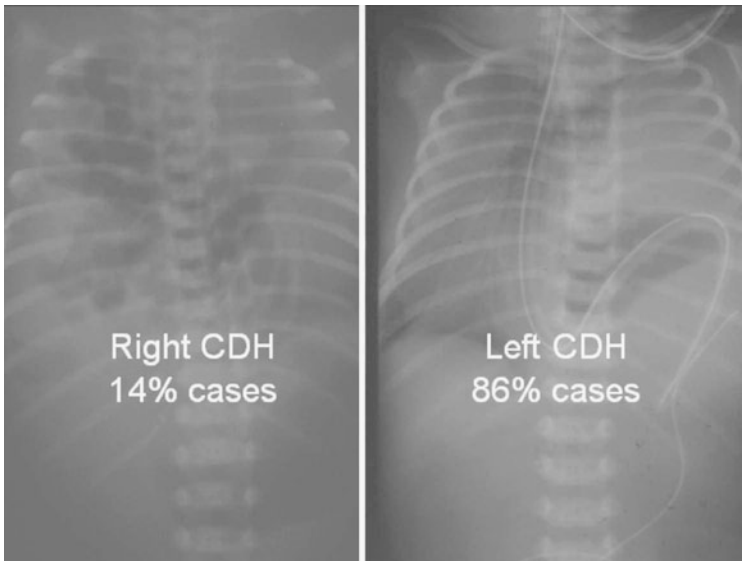

Fig. 19.1 Radiograph of the thorax showing right and left CDH

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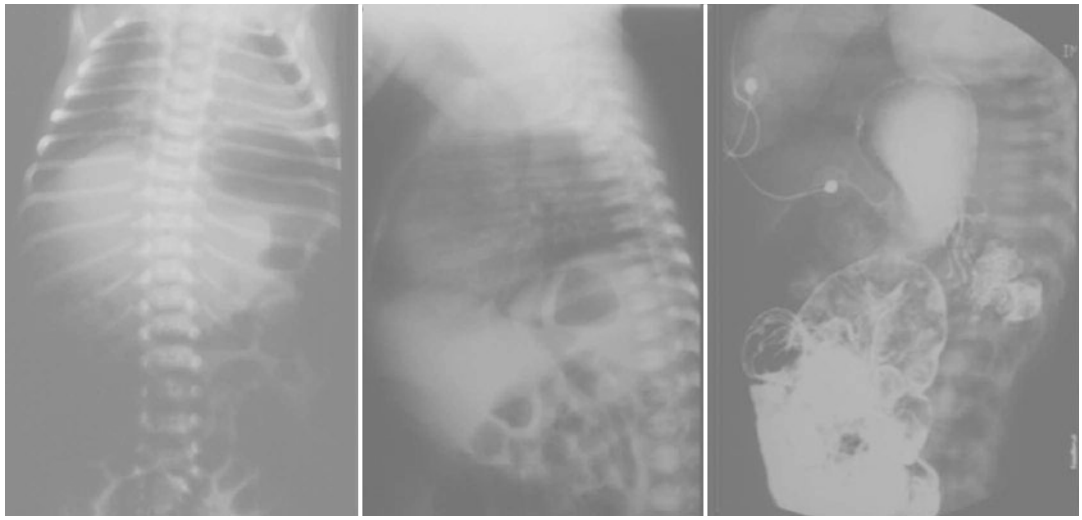

Fig. 19.2 Contrast studies showing left CDH

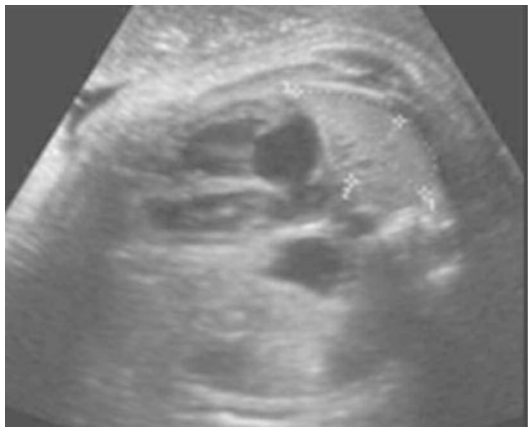

Fig. 19.3 Prenatal evaluation using ultrasound. Lung hypoplasia can be verified by calculating the lung-to-head ratio

Antenatal diagnosis is possible in the second trimester of gestation using ultrasonography, which reveals abdominal organs (gut, spleen, stomach, liver) in the thorax; evaluation of lung hypoplasia is also possible (Fig. 19.3). The thorax and heart are shifted to the right because the left side is more affected [1, 2]. At birth, due to lung hypoplasia, babies can show acute respiratory distress. Sometimes CDH is in the first months or years of life. In these patients, CDH can present with incarceration or strangulation of the herniated organs [3].

The first reports regarding the thoracoscopic approach for the treatment of CDH were in patients with late-onset CDH. Recently, several reports focusing on neonatal video-assisted surgery have been published, but the benefits and risks of thoracoscopic and laparoscopic approaches are controversial. In selected patients, the thorascopic approach allows easy reduction of herniated viscera by low-pressure insufflation of carbon dioxide (CO_2) and a complete view of the diaphragmatic defect. Surgeons based at the Pediatric Surgery Department of Strasbourg University (Strasbourg, France) have used a thoracoscopic approach for CDH treatment since 1999, initially in patients with a late diagnosis of CDH and subsequently in neonates.

In this chapter we describe the surgical procedure and the potential advantages and disadvantages of this approach.

19.2 A Thoracoscopic Approach for the Video-assisted Treatment of CDH

19.2.1 Instrumentation

The thoracoscopic approach requires the placement of two 3-mm trocars and one 5-mm

trocar in a triangular fashion. The 5-mm trocar is used to introduce a 5-mm 0° telescope; the two 3-mm trocars are used for surgical repair. In general, 3-mm trocars are adequate for this procedure. Good positioning of the trocars is essential because the operative field is very small. Monopolar cautery can be used in most cases. Closure of the defect is made using interrupted non-absorbable sutures: Ethibond 2/0 or 3/0 is preferred depending on the age of the child. Most pediatric endosurgery sets should include instruments if conversion to open thoracotomy is required as well as a patch (Gore-Tex™ or Mersilene™) [4].

19.2.2 Preoperative Management

In general, extensive preoperative preparation is not necessary, but video-assisted repair should be undertaken only in selected patients [4–7]. Each surgeon must ascertain if thoracoscopy can be undertaken. The patient may have no signs of pulmonary hypertension and may be hemodynamically stable. Absolute contraindications to a thoracoscopic approach are:

- cardiopulmonary instability;
  - severe hemodynamic instability requiring multiple pressors;
  - persistent pulmonary hypertension;
  - severe lung hypoplasia with a high partial pressure of carbon dioxide (PCO_2);
- abnormalities associated with the cardiovascular or central nervous systems;
- large defect with herniation of the stomach and liver.

Candidates for video-assisted diaphragmatic repair are:

- newborns requiring oxygen administered through the nasal route;
- newborns with minimal or decreasing parameters of mechanical ventilation;
- infants with late-onset CDH;
- delayed/recurrent CDH;
- incarcerated diaphragmatic hernia.

General anesthesia is used. Unlike in adults in whom single-lung ventilation is achieved relatively easily, the induction of general anesthesia is more difficult in infants or small children. Infiltration of port sites with a local anesthetic, epidural analgesia and intercostal nerve block can be useful in the postoperative period to control pain [8].

19.2.3 Procedure

19.2.3.1 Patient Positioning

The patient is placed in the lateral decubitus position (slightly semi-prone) just as in a thoracotomy carried out in an adult (Fig. 19.4). The surgical team comprises one surgeon and one surgical assistant in front of the patient. The surgeons are positioned at the head of the patient. The scrub nurse is at the foot of patient, at the side of the surgeons. The monitor is in front of the surgeons, near to the legs of the patient. The screen is slightly oblique towards the patient so that the surgeon, di-

Fig. 19.4 Patient positioning and placement of trocars

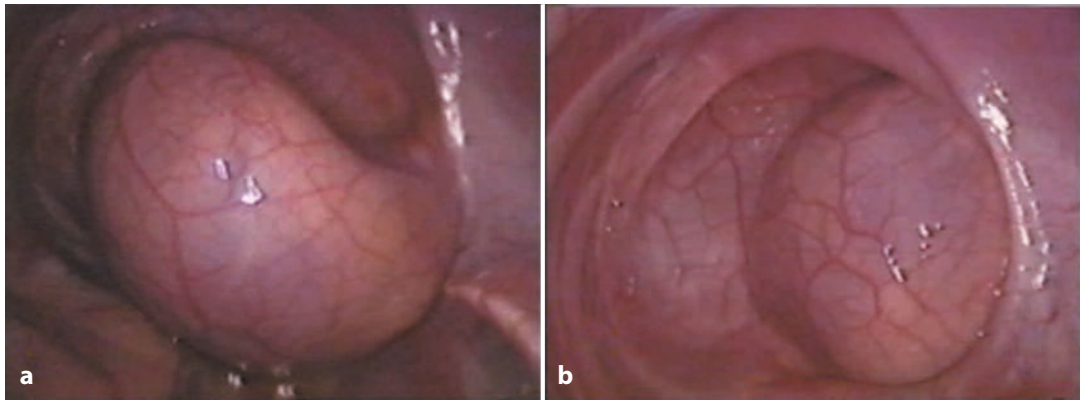

Fig. 19.5 CDH with hernial sac. Intrathoracic images show CDH with a sac before (**a**) and after (**b**) reduction by the induction of pneumothorax

aphragmatic defect and monitor are in the same direction.

19.2.3.2 Port Placement

The optic port is positioned below the tip of the scapula. The anterior working port is in the fifth intercostal space on the anterior axillary line. The posterior working port is in the fourth intercostal space between the optic port and spinal column. This last trocar must be positioned precisely because good mobility of trocars must be ensured [9–11].

19.2.3.3 Surgery

After introduction of the first trocar, intrathoracic insufflation with CO_2 is started to promote lung collapse. The intensity and duration of insufflation must be reduced in time to avoid the complications associated with abnormal intrathoracic insufflation of CO_2. Hence, low pressure (4–8 mmHg) and intermittent insufflation is usually appropriate. The first step is reduction of herniated viscera. Right-sided defects are, in general, are more difficult to repair.

If a hernial sac is present (found in approximately 20% of patients), intrathoracic insufflation (after waiting a few minutes) is sufficient to reduce the organs in the abdomen (Fig. 19.5). The sac can be excised using monopolar cautery without damaging the blood vessels and nerves of the diaphragm. Instead, the peritoneum can be entered to avoid leaving a loculated space-occupying lesion in the chest.

If a hernial sac is not present, the stomach and abdominal viscera must be reduced first. The spleen is the last organ to be repositioned. In this case, releasing posteriorly the pleuroperitoneal canal can be useful. Usually, the anterior rim of the diaphragm is evident. However, the posterior rim may not be immediately apparent and may require dissection for delineation. The defect is closed by interrupted non-absorbable sutures: Ethibond 2/0 or 3/0 is preferred depending on the age of the child (Fig. 19.6). If the defect cannot be repaired directly using sutures, prosthetic patches can be fixed by interrupted non-absorbable sutures and incorporated into adjacent tissue (Fig. 19.7). A chest drain (aspiration, 5–10 mmHg) can help lung expansion [9–11].

19.2.3.4 Limitations of the Thoracoscopic Approach

Thoracoscopy in newborns can be difficult: conversion to open thoracotomy may be indicated. There are some limitations of this approach that the surgeon must consider before surgery. These include: a restricted operative field; an unstable respiratory condition; early presentation; and inability to recognize malrotation of the abdominal viscera [9–11].

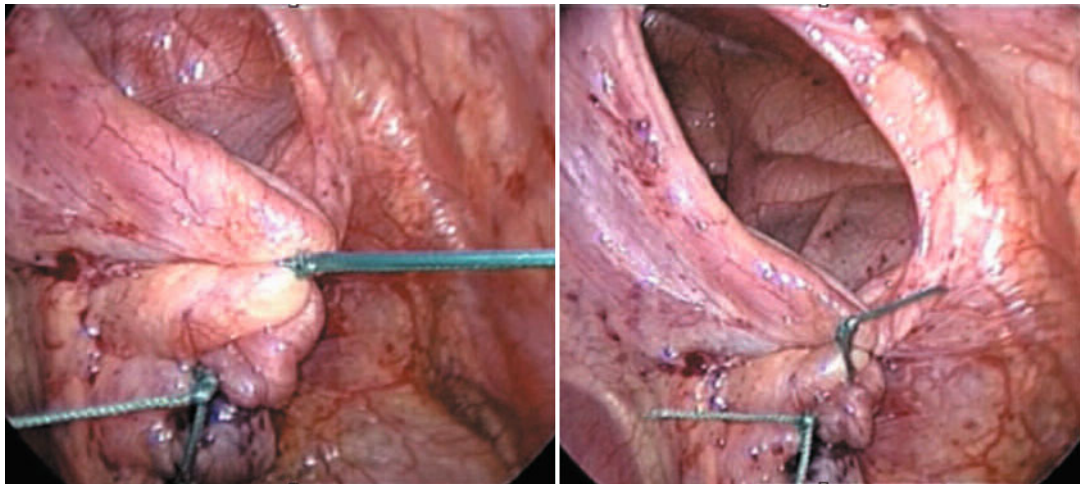

Fig. 19.6 Closure of the defect by suturing with a non-absorbable suture

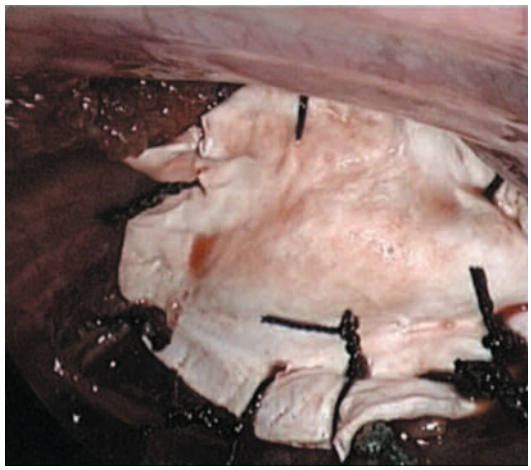

Fig. 19.7 Position of a prostethic plaque for a large CDH

19.2.4 Postoperative Management

The infant is transferred to the Intensive Care Unit. Vital signs are monitored and fluids given *via* the intravenous route. The postoperative course is dependent upon pulmonary hypoplasia and persistent pulmonary hypertension. These factors determine the ventilatory and hemodynamic situation. An epidural catheter is used to administer morphine and is removed on the second postoperative day. The chest drain is removed 24 h after surgery. Enteral nutrition is usually started on the first postoperative day.

19.2.5 Complications

Intraoperative complications related to thoracoscopic repair of a diaphragmatic hernia are usually rare. However, apart from the comments made above about the surgical procedure, the spleen must be handled very carefully, and CO_2 insufflation should be monitored very carefully because excess CO_2 can worsen respiratory status. Postoperative complications include recurrent herniation, obstruction of the small bowel, pleural effusion, chylothorax, and patch-associated problems such as infection [1, 2]. Scoliosis, asymmetry of the chest wall, and weakness in the shoulder girdle are linked with the position of non-absorbable plaques for CDH with a large defect (Fig. 19.8).

19.3 Conclusions

Video-assisted thoracoscopic surgery is a type of surgical approach for the correction of congenital CDH. During the past decade, employment of this type of surgery has increased dramatically. It is usually a simple procedure because CO_2 insufflation of the thorax allows good visualization of the defect and contributes to reduction of the viscera in the abdomen. The advantages of thoracoscopy for CDH include:

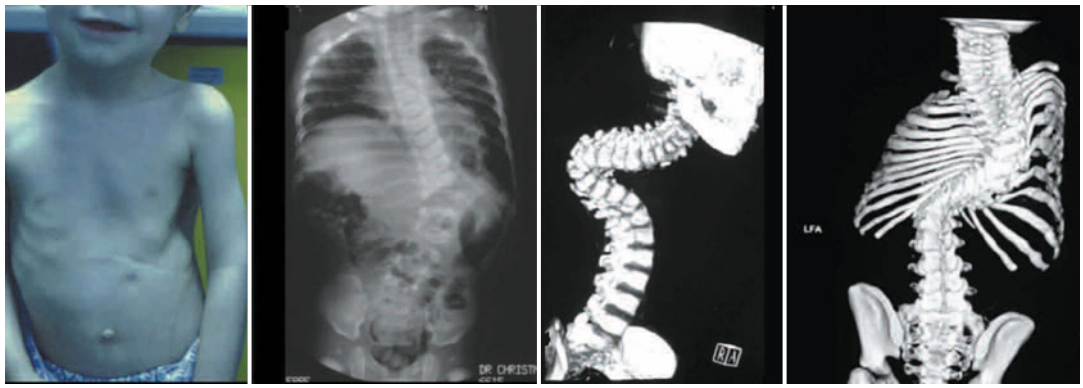

Fig. 19.8 Various images showing a patient with scoliosis after placement of a plaque for CDH

- smaller incisions in the chest that provide much better visualization and access to the anterior and posterior mediastinum;
- reduction of postoperative pain;
- more rapid postoperative recovery.

However, there are also some disadvantages:

- a relatively long learning curve for the surgeon;
- accurate selection of patients because CO_2 insufflation can worsen respiratory status, which is already unstable.

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Diaphragmatic Eventration

20

Francesco Molinaro, Anna Lavinia Bulotta, Elisa Cerchia, Francesca Borruto, Mario Messina and François Becmeur

20.1 Introduction

In general, diaphragmatic eventration (DE) is defined as abnormal elevation of all (or a portion of) an attenuated (but otherwise intact) diaphragmatic leaf [1]. The term "eventration" was used first by Becklard in 1829 (through Petit probably described the condition in 1970). Bingham described plication of the diaphragm in 1954 [2, 3]. Based on etiopathogenesis, DE may be classified as "congenital" or "acquired" even though the clinical features and principles of management are similar for both forms.

20.2 Pathogenesis

Congenital DE is a developmental abnormality characterized by muscular hypoplasia of the diaphragm. It is often confused with congenital diaphragmatic hernia (CDH) with a hernial sac. However, unlike the uniform contour in an eventration, the margins of the normal diaphragm should be apparent in a CDH with a hernial sac. In addition, unlike CDH, pulmonary hypoplasia is uncommon. Congenital DE shows a male predominance and involves usually affects the left side of the diaphragm. It has been reported as a single entity and in association with other malformations.

Acquired DE is caused by injury to the phrenic nerve with resultant paralysis and elevation of the entire diaphragm. Hence, acquired DE is often termed "paralytic". The phrenic nerve may be damaged at birth, by trauma, or during intrathoracic surgery [4, 5]. Involvement of the phrenic nerve at birth is associated with obstetric brachial plexus injury (OBPI). The incidence of OBPI is about 1.51 per 1,000 live births in the USA [6], and reports vary from 0.38 [7] to 5.8 [8] per 1,000 live births worldwide.

Risk factors for injury include shoulder dystocia, macrosomia (defined as birth weight >4,500 g), instrument-assisted delivery, and downward traction of the fetal head [9]. The most common cause of diaphragmatic paralysis (DP) in children is injury to the phrenic nerve during thoracic surgery. Cardiac surgery involves procedures in which DP can be a complication: DP occurs in 0.3–13% of cardiac operations. The superficial course of the left phrenic nerve renders it prone to injury during cardiac surgery, although the right phrenic nerve is also occasionally damaged (possibly as a result of traction). High incidences of DP have been noted after procedures

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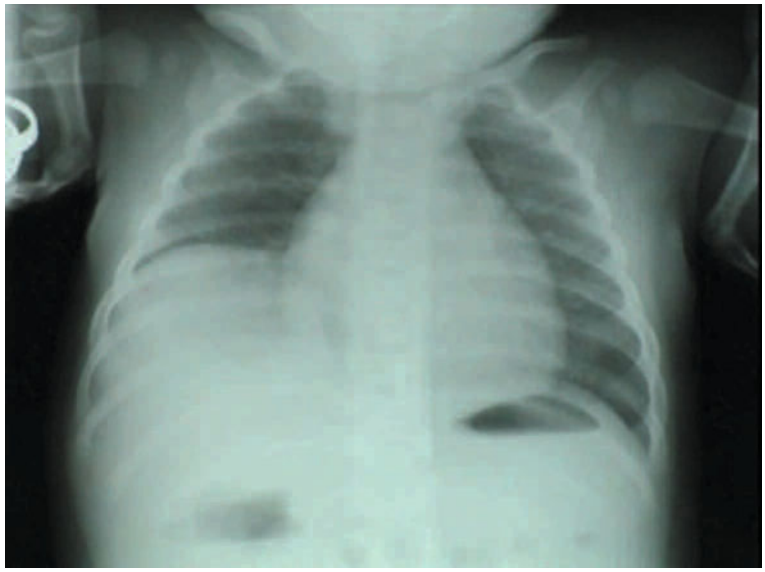

Fig. 20.1 Chest radiograph showing right diaphragmatic eventration

such as the arterial switch, Fontan procedure, and Blalock–Taussig shunt. Phrenic-nerve injuries are more likely to occur during revision procedures [10-12]. Diaphragmatic palsy may be a feature of injury to the spinal cord [13]. This may be traumatic, as a result of compression from tumors, or after infarction or transverse myelitis. Spinal-cord injury at or above the C3–C5 level is likely to involve the phrenic nerves and cause total or partial paralysis of the diaphragm. Spinal-cord injuries are caused by motor vehicle accidents (47% of cases), accidental falls (24%), firearm injuries (14%) and sports injuries (9%) [9].

20.3 Clinical Features

Clinical features range from asymptomatic to severe respiratory distress. Patients may present with pneumonia, bronchitis, bronchiectasis, atelectasis, tachypnea, dyspnea, or cyanosis. Severe hypoxia may require intubation and ventilatory support. Occasionally, patients present later in childhood with vomiting or epigastric discomfort: these symptoms are due to the change of the esophagogastric angle [14].

20.4 Diagnosis

The diagnosis is usually made on frontal and lateral radiographs of the chest, which show an elevated diaphragm with a smooth, unbroken outline (Fig. 20.1). This is a simple and non-invasive investigation, but is not sufficient for the diagnosis of DE or for differentiating DE from a hernia because it does not provide information about diaphragmatic function.

Fluoroscopy is the main dynamic investigation which can assess the motion of the diaphragm dome, yielding real-time information. The lateral projection is often employed because it allows simultaneous views of both hemidiaphragms. A paralyzed hemidiaphragm will move paradoxically cephalad during inspiration. Assessment of diaphragmatic excursion during quiet respiration may be inconclusive. The investigation is best undertaken by asking the child to inhale as fully as possible and then to exhale as fully as possible or, alternatively, asking the child to sniff [15]. This requires considerable compliance and is applicable only for older children. False-negative results are common in ventilated children be-

cause positive end-expiratory pressure tends to flatten the diaphragm. If the investigation is conclusive under these conditions, the ventilator must be disconnected temporarily.

The limited use of ultrasonography for the diagnosis of DE is because the magnitude of movement of the dome of the diaphragm cannot be determined accurately. However, ultrasound has several advantages: avoidance of ionizing radiation; portability; non-invasive nature; and minimal requirement of cooperation from the patient. Hence, several authors have investigated its use in DE. The thickness of the diaphragm at the end of expiration has been measured along with changes in thickness during inspiration using ultrasound. Changes in thickness during inspiration are proportional to diaphragm shortening in adults and infants, whereas the thickness of the diaphragm measured at the end of expiration is proportional to diaphragm strength. With diaphragmatic paralysis, the diaphragm does not thicken during inspiration [16, 17].

Other modalities include: pneumo-peritoneography; contrast peritoneography: transcutaneous electrical stimulation of the phrenic nerve: intragastric and intraesophageal manometric catheters for measuring transdiaphragmatic pressure changes; radioisotope imaging; and computed tomography. However, these are used mainly in adults because of the difficulty in compliance with infants [14, 18].

20.5 Management

Treatment of DE is dependent upon the presence or absence of symptoms. Children (and slightly older subjects) with asymptomatic DE in children may be amenable to conservative treatment. Symptomatic DE in children (congenital or acquired), especially patients in respiratory distress, requires prompt surgery but only once physical status has stabilized. Stabilization can be through: endotracheal intubation and ventilation with humidified oxygen to minimize diaphragmatic movement; a nasogastric tube to decompress the stomach; and intravenous fluids. The "gold standard" surgery is plication of the diaphragm, for which several methods have been described. This type of surgery can be undertaken by open or minimally invasive methods [10, 19].

One particular scenario is the child with phrenic-nerve palsy after cardiac surgery. The indications for plication in this case are controversial. Phrenic-nerve palsy after cardiac surgery causes significant morbidity. These children require prolonged mechanical ventilation and are more likely to develop respiratory infections. These sequelae are considerably more common in the presence of bilateral palsies. Historically, several authors argued that most phrenic palsies resolve within a few weeks of surgery (presumably because of neuropraxia). Hence, waiting 2–3 weeks after surgery before considering placation was not uncommon [20, 21-33]. However, it is now widely accepted that there is little merit in delaying plication for these children because plication avoids lengthy periods of mechanical ventilation [10].

20.5.1 Surgical Management

Plication of the diaphragm is carried out under general anesthesia. The subject is positioned supine on a warm blanket. Several approaches have been described. Open surgery allows an approach to the diaphragm through the abdomen or thorax. Several authors have argued that the right diaphragm should be approached by thoracic access through a posterolateral incision *via* the sixth space to avoid the liver [19]. An abdominal approach through a subcostal incision is the favored approach for the left diaphragm. Open bilateral plication should be done through the abdomen because this approach allows good visualization of the entire diaphragm from front to back as well as easier mobilization of abdominal contents [10]. The aim of the procedure should be to flatten the diaphragm to a physiological position. Plication of the diaphragm is carried out using non-absorbable sutures and avoiding injury to the

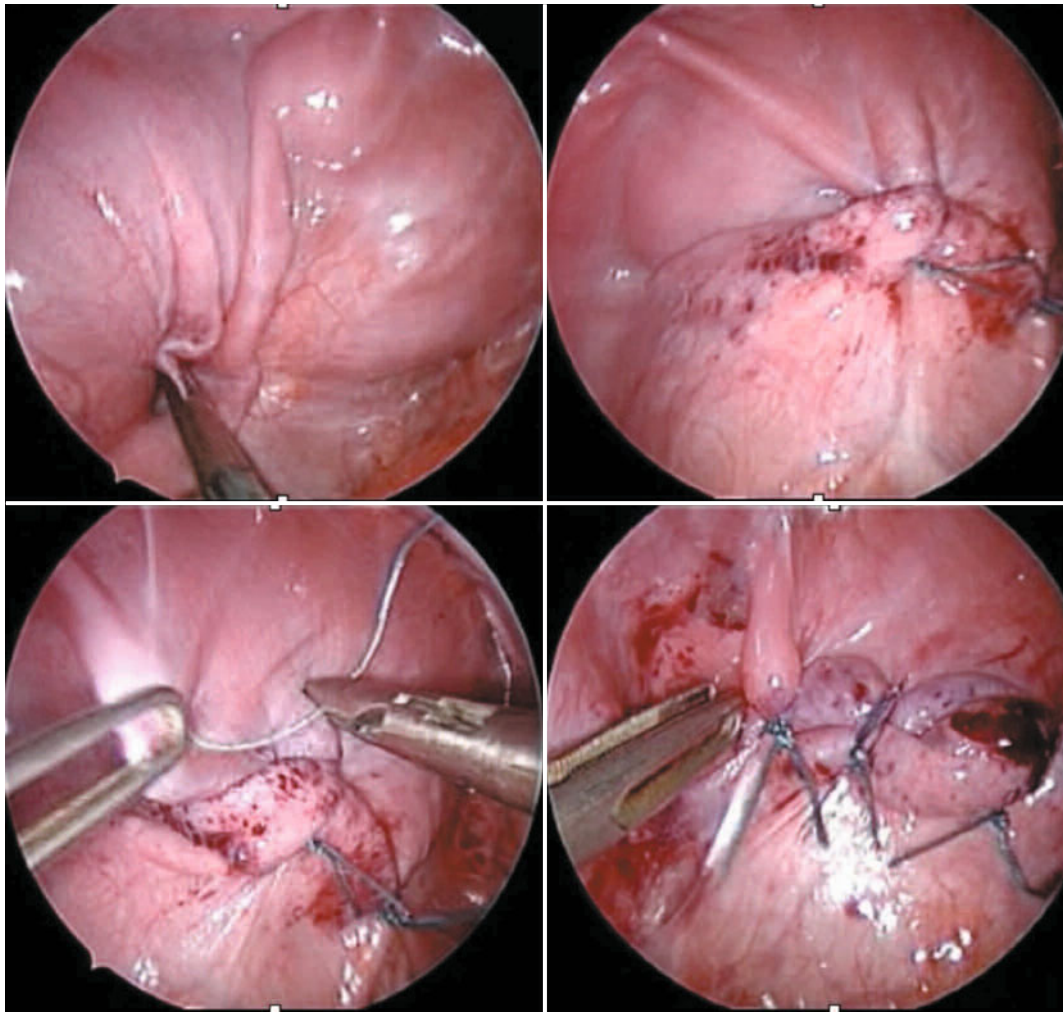

Fig. 20.2 Plication of a diaphragmatic eventration using a non-absorbable suture

phrenic nerve and structures on the blind side of the diaphragm. In cases of complete eventration, the diaphragm may be strengthened by a muscle flap or prosthetic patch [19].

In the last few years, minimally invasive methods of plication have become increasingly popular. The transthoracic approach allows plication of the diaphragm to be carried out readily. The procedure can be done in an identical fashion to open plication and the view is excellent, with magnification helping to avoid branches of the phrenic nerve. Infusion of CO_2 is used for enhancement of intrathoracic visualization. There is also the added benefit of the diaphragm being pushed down due to the infused pressure used for pneumothorax. This pressure enlarges the involved pleural space and aids the plication of the hemidiaphragm. Plicating sutures are placed and tied thoracoscopically (Fig. 20.2). Thoracoscopic plication using a knifeless Endo-GIA™ stapler has been described in adults [19, 34-36].

20.5.2 Postoperative Care

After transfer to the Intensive Care Unit, the infant is kept warm, and given maintenance of

intravenous fluids. Vital signs are monitored closely with regular analyses of blood gases and measurement of pre-ductal and post-ductal oxygenation. Ventilatory support is continued with the aim of maintaining pre-ductal partial pressure of oxygen (PO_2) at approximately 80–100 mmHg. The intrathoracic air pocket usually reabsorbs, but evidence of increasing air and fluid with mediastinal shift necessitates insertion of a chest drain. However, if intraoperative complications and pulmonary hypoplasia are absent, the patient can be extubated 24 h after surgery [19].

20.5.3 Complications

There are three main potential complications of diaphragmatic plication:

- recurrent eventration is rare except in children with neuromuscular disorders (for whom the procedure is of no benefit anyway);
- persistent respiratory failure after plication is the result of parenchymal lung disease, and results in death;
- gastrointestinal morbidity is largely due to gastroesophageal reflux (which is common), but there is a small incidence of adhesional obstruction. Failure to thrive may require nutritional support *via* gastrostomy, and many patients require fundoplication for intractable reflux [10].

20.6 Conclusions

Rapid identification and treatment of patients with symptomatic DE can improve outcome and reduce or avoid lengthy periods of mechanical ventilation. The treatment for symptomatic patients is surgery. Plication can be carried out equally well through the chest or abdomen, and the results of endoscopic surgery are equivalent to those of open surgery. The prognosis of patients in the absence of pulmonary hypoplasia is usually excellent.

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Part V

Lungs

Congenital Cystic Adenomatoid Malformations

21

Juan A. Tovar

21.1 Introduction

Congenital cystic adenomatoid malformations (CCAMs) are relatively rare disturbances of lung development in which part of the parenchyme is replaced by hamartomatous cysts of different sizes lined by a respiratory epithelium that may communicate indirectly with the airway. It occurs in about 1 in 30,000 gestations and is slightly more frequent in males [1]. CCAMs account for infectious complications later in life and can: interfere with the lung development and physiology of the fetus; cause neonatal respiratory distress; be associated with some tumors. The origin of CCAMs is not well known, their behavior is unpredictable, and their treatment controversial. These aspects will be addressed in this chapter.

21.2 Pathology and Classification

The terms "cystic" and "adenomatoid" (gland-like) summarize the main pathological features of CCAMs: a part of the lung (generally one single lobe, rarely two and very rarely both sides) is replaced by cysts lined by a respiratory epithelium with polypoid projections into the lumen and mucus-secreting cells. Strands of smooth muscle, sacculi or alveoli (and sometimes embedded bronchi) can also be visualized. These structures may contain air as a result of some type of connection with the airway. However, this is peripheral and without frank openings into the major bronchi. The large cysts are generally lined by pseudo-stratified ciliated bronchial epithelium with mucogenic cells, whereas small cysts are covered by cuboidal cells resembling type-II pneumocytes.

On the basis of the gross pathological patterns, CCAMs were divided by Stocker et al. [2] into three types:

- type 1 (in which large cysts, 3–10 cm in diameter, predominate);
- type 2 (in which the cysts are smaller, <2 cm in diameter);
- type 3 (characterized by minute cysts, <0.3 cm in diameter) that constitute a nearly solid structure.

Type-1 CCAMs correspond to hamartomatous proliferation of bronchiolar structures whereas type-3 CCAMs seem to be due to a subsequent disorder and involve sacculo-alveolar structures. Type-1 CCAMs represent >50%, type 2 represent around 40% and type 3 represent ≤10% of neonatal cases. Associated anomalies are not uncommon in type-2 CCAMs [3, 4].

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More recently, two more types were added to the original classification by Stocker et al. [5–7]:

- type 0, a solid malformation constituted by acini, which is incompatible with life;
- type 4, in which only a few peripheral (generally apical) cysts are lined by an alveolar epithelium.

Neither this new classification nor an alternative denomination (congenital pulmonary adenomatoid malformations, CPAMs) coined by Stocker to point out that type 3 is hardly cystic and that only type 3 is adenomatoid, have had wide use in the pediatric surgical community. A simplified classification into microcystic (diameter <5 mm) and macrocystic (diameter >5 mm) malformations (8) seems quite practical but has not gained widespread use. Therefore, we shall maintain the accronym CCAM and the classical type-3 classification in this chapter.

Bronchial atresia (BA) is a related condition consisting of prenatal obstruction of large or peripheral bronchi. This causes microcystic areas surrounded by emphysematous areas and, sometimes, centered by a dilated, mucus-filled mucocele or bronchocele. The nature of the lesion was characterized by microdissection of resected specimens, and it has been shown that BA can be associated with CCAMs, sequestration and lobar emphysema. Although BA is considered to be an independent condition by some authors [9] it is probably better classified (along with CCAMs) as lobar emphysema and sequestration among foregut malformations [10, 11].

21.3 Pathogenesis

The tracheobronchial tree is derived from the ventral surface of the foregut and therefore shares an endodermal origin with the gastrointestinal (GI) tract. On the fourth week of embryonal life, the respiratory anlage arises from the foregut and bifurcates to form the stem bronchi. These subsequently undergo several branchings and generate the lobar and segmental bronchi and bronchioli. The terminal buds of the peripheral sacs ultimately become the alveoli. This process can be divided into the embryonal (fourth to seventh week), pseudoglandular (until the seventeenth week), canalicular (until the twenty-sixth week), saccular (until the thirty-sixth week) and alveolar (until full postnatal development) stages. During these embryo–fetal periods, the epithelium makes contact with the surrounding mesenchyme and interacts with it, sending and receiving various molecular signals that contribute to shape the gas-exchange surface, the surrounding capillary network, bronchial cartilage and muscle, and a large variety of cells (bronchiolar lining, mucus-secreting cells, Clara cells, type-I and -II pneumocytes) that constitute the structure of the mature lung. In parallel, nerve fibers and neuroblasts from the vagal neural crest shape the innervation and neuroepithelial bodies.

Respiratory organogenesis and differentiation are controlled by many genes, transcription factors and growth factors [12, 13]. Hox genes (particularly *Hoxa-3* and *Hoxb-5*) determine the moment and topography of the emergence of the respiratory anlage and direct organogenesis thereafter. Several other factors act at different moments. These include bone morphogenic protein 4 (bmp4) [14], thyroid transcription factor 1 (NKX2.1 or ttf1) [15], hepatocyte nuclear factor 3-β (hnf3-β, the retinoic acid receptor (RAR) [16], fibroblast growth factors (fgf4, fgf7, fgf8) (17), and GATA. The main regulators of branching are sonic hedgehog (shh) and its downstream factors (patched, smooth and the Gli proteins) on the epithelial side [18] and fibroblast growth factor 10 (fgf10) on the mesenchymal side [13]. Vascular development is regulated mainly by vascular endothelial growth factor (VEGF) [19]. Abnormal expression of these and other genes and transcription factors can transmit incorrect signalling that leads to the production of disbalanced amounts of the lung tissue components that shape hamartomatous areas. There is some evidence of this abnormal signalling in human CCAM material.

Hoxb-5, whose expression is located in the mesenchyme surrounding the canalicula and which is supposed to participate in the regulation of airway branching, was found to be overexpressed in human specimens of CCAMs [20, 21]. GDNF was abnormally expressed [22] and fatty acid binding protein-7 (FABP-7) was underexpressed in these tissues (23) in CCAMs. Platelet-derived growth factor-B (PDGF-B) was overexpressed in the mesenchyme surrounding the cysts of CCAMs [24], as was fibroblast growth factor 9 (fgf9) in the respiratory epithelium whereas mesenchymal fgf7 was underexpressed [25]. Microinjection of fgf10 into developing mouse lung caused large cysts lined with a bronchiolar epithelium when the injection was made in the proximal tracheobronchial tree, whereas it caused small cysts lined with type-II pneumocytes when the microinjection was made in the periphery of the organ [26, 27]. A disbalance between proliferation (notably increased in CCAM tissue) and apoptosis (which is decreased) plays a crucial part in the pathogenesis of this lung malformation [28].

21.4 Clinical Features

Fetal disease: Most diagnoses of CCAMs are made before birth. This has led to a considerably increase in the overall number of affected fetuses. In rare cases, particularly in type-3 (microcystic or semi-solid) malformations, polihydramnios and eventually fetal hydrops (ascites, pericardial and/or pleural effusion, trunk edema) with placentomegaly demonstrate the extent of fetal circulatory disturbance (particularly caval obstruction). The surrounding lung is compressed and the risk of lung hypoplasia is considerable. In these cases, fetal death is possible and neonatal compromise may be severe. A "mirror" syndrome with edema, hypertension and pre-eclampsia requiring immediate Caesarean section may appear in the mother due to release of unknown factors by the CCAM. In most other cases, however, this does not happen and the diagnosis is made solely on the basis of observation of lung cysts surrounded by more or less normal parenchyme during routine ultrasonographic fetal screening. In general, CCAMs grow (sometimes rapidly) between the fifth and the seventh months of gestation, but at least one-third of CCAMs subsequently regress (and may even practically disappear). The mechanism by which progression or resolution occurs are not known but certainly the non-proportional growths of the lung and of the malformation have a role during late gestation [29].

Neonatal disease: Depending on the size of the affected part of the lung, CCAMs can produce more or less severe respiratory distress at birth, ranging from mild embarrassment to neonatal death by asphyxia. In some cases, hyperinflation of large lung cysts interferes severely with breathing and, because the corresponding hemithorax is distended, a tension pneumothorax can be diagnosed. The mediastinum and heart sounds can be displaced to the contralateral side. In some cases, air bubbles in the hemithorax and mediastinal displacement with respiratory distress suggest a diagnosis of diaphragmatic hernia. Close inspection of the gastric and colonic air in the chest radiograph allows the correct diagnosis.

"Asymptomatic" cases: A considerable number of babies with prenatally diagnosed CCAMs have no symptoms at birth and even purposefully radiological search may reveal normal or near-normal images. This occurs because cyst size tends to decrease at the end of gestation. The choice between a purely expectant attitude and active observation of the affected lung with elective resection is controversial (see below).

21.5 Diagnosis

Fetal diagnosis is based on ultrasonography and, in most countries in which fetal screening is routine, CCAMs are detected during the second trimester of gestation and their nature ascertained (Fig. 21.1). Differental diagnoses

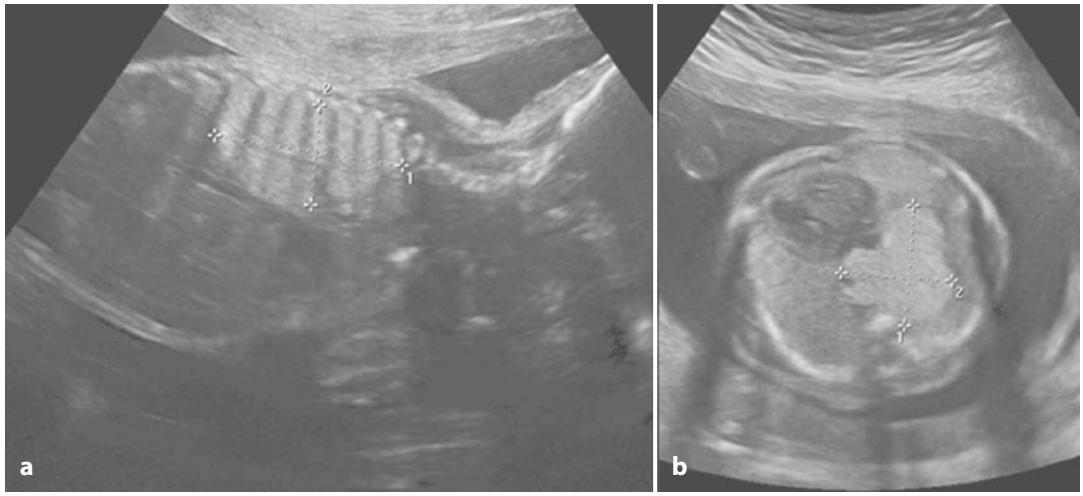

Fig. 21.1 Fetal ultrasonography showing a type-3 CCAM with polihydramnios. The malformed tissue occupies most of the hemithorax (**a**), is denser than the surrounding lung and displaces the heart (**b**)

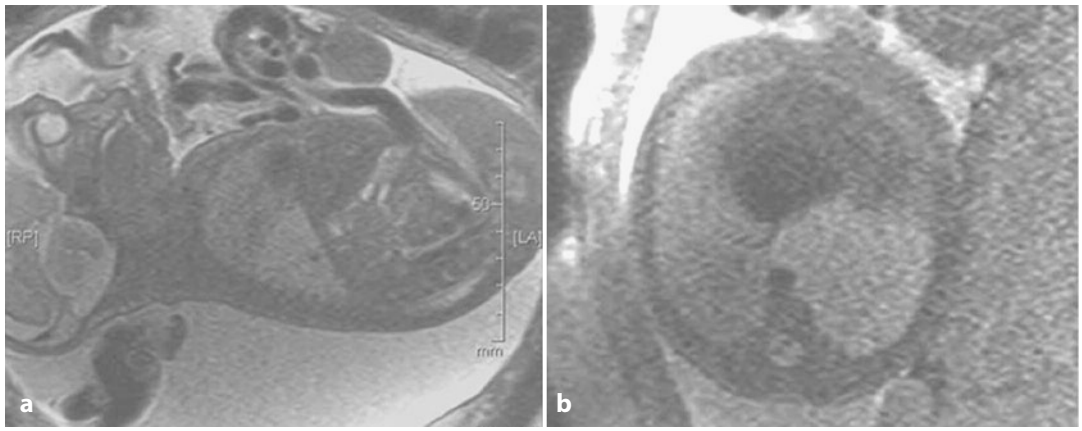

Fig. 21.2 a, **b** Fetal MRI showing a type-3 CCAM with polihydramnios. Definition is better than that obtained with ultrasonography but, in this case, both procedures yielded similar results

with bronchogenic cysts, pulmonary sequestration and lobar emphysema are often possible at this time on the basis of the size, location and number of cysts as well as the origin of arterial supply as imaged by Doppler ultrasonography. Bronchial atresia can also be suspected prenatally. Polihydramnios, hydrops and placentomegaly are clearly depicted upon ultrasonography. In fetuses with type-3 CCAMs and hydrops, it is convenient to measure the volume-to-head circumference ratio (CVR) of CCAMs as introduced by Crombleholme et al. [30]. This index is calculated by estimating the volume of the CCAM ellipsoid (length × width × height × 0.52) and dividing it by the head circumference as a corrector for gestational age. Values ≥1.6 are indicative of a bad fetal and neonatal prognosis (>80% have hydrops and a survival expectancy near 0% if left undisturbed [31]). Fetal magnetic resonance imaging (MRI) may be useful in CCAMs, particularly for refining the diagnosis in some cases (Fig. 21.2). Doppler ultrasonography can be very useful

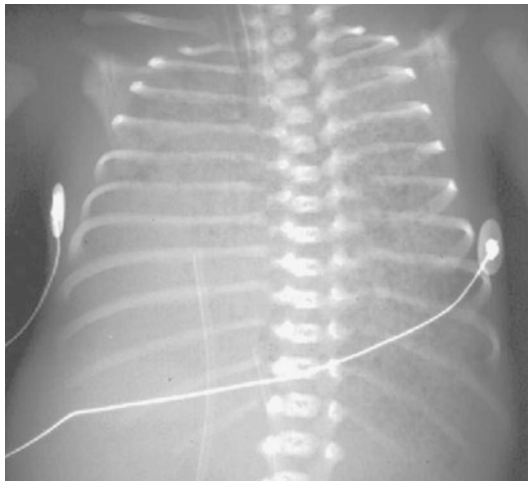

Fig. 21.3 Chest radiographs after birth of a type-3 CCAM in a fetus with polihydramnios and hydrops. The left lung has a honeycomb pattern of density, and the mediastinum is shifted to the right. The patient died of respiratory insufficiency shortly after birth

for ascertaining the nature of the arterial supply and for depicting details of the heart structure or detecting other associated anomalies.

Radiographs and ultrasonography are the best diagnostic tools during the neonatal period. A pattern of condensation and/or honeycomb aeration is typical of type-3 CCAMs (Fig. 21.3). Lobar emphysema is usually ruled out by the absence of cystic images, the upper-lobe location, and a typical pattern of air distribution. Pulmonary sequestration cannot be distinguished from CCAMs by plain radiographs of the chest, but Doppler ultrasonography readily depicts the abnormal vascularization. Upper GI series (if necessary) and observation of gut motility by ultrasonography may help to differentiate between diaphragmatic hernia and CCAMs.

Computed tomography (CT) carried out during the first year of life helps in the delineation of the nature and extent of the disease, less conspicuous upon X-ray films of the chest (Fig. 21.4a) CT shows cysts of variable size (sometimes filled with mucus) embedded into more or less normally ventilated parenchyma (Fig. 21.4b, c).

21.6 Treatment

During fetal life: Large CCAMs that compress healthy surrounding lung may cause life-threatening hypoplasia and prompt some form of fetal treatment. If large cysts are visible, puncture and emptying of the leading cysts may allow decompression provided that the cysts communicate [32]. This relatively non-invasive procedure can be repeated but, in case of new recurrence, thoraco–amniotic shunts inserted percutaneously under ultrasonographic control are an alternative aimed at decompressing the lesion for longer priods of time [33–35]. Percutaneous sclerotherapy of the cysts by injection of ethanolamine oleate has also been proposed for cases with

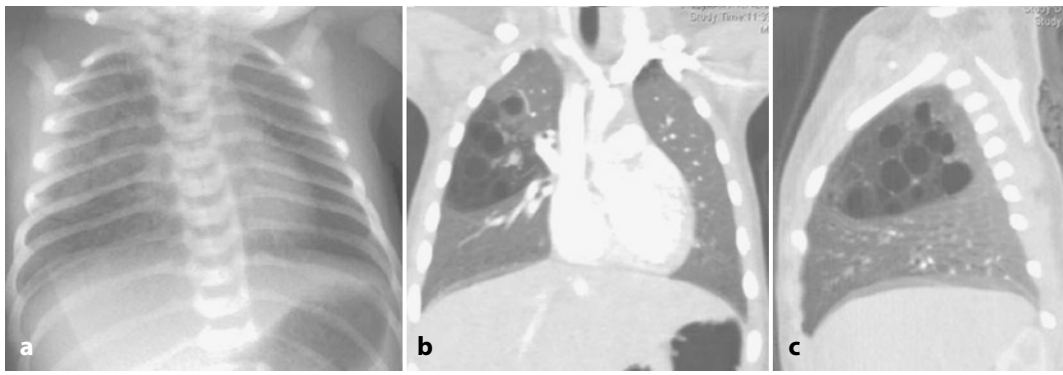

Fig. 21.4 Chest radiograph after birth of a type-1 CCAM (**a**). Density with small cysts is seen in the upper right lobe. (**b-c**) correspond to a CT done a few months later showing the cystic nature and topography of the malformation

large cysts, mediastinal shift and polihydramnios [36, 37].

Babies with CCAMs accompanied by hydrops during fetal life have a grim prognosis [1, 8, 38]. Most of these have semi-solid microcystic masses and a CVR ≥1.6, but some bearing macrocystic CCAMs may also have hydrops [35]. Prenatal active treatment is necessary for survival, and this requires refined techniques and raises serious ethical problems. Open fetal resection of the mass involves maternal hysterotomy, fetal thoracotomy and lobectomy followed by closure and subsequent Cesarean section as close to term as possible [39–41]. In the largest series, such procedures achieve survivals close to 60% [42], although gestation may be shortened with some undesirable consequences.

The use of transplacental corticosteroids to prevent lung immaturity in these cases led to the observation of regression of the mass and hydrops with this medication, and opened a new non-invasive method of treatment [43–45]. Two doses of betamethasone or dexamethasone given to the mother may avoid the vast majority of invasive intrauterine treatments and achieve variable degrees of regression of the CCAM [46]. The mechanisms of action of the corticosteroids on the abnormally developing lung tissue are incompletely understood but this therapy has replaced open surgery in most cases in the last few years.

In cases without fetal hydrops but with severe compression of the surrounding lung, an *ex utero* intrapartum treatment (EXIT)-to-resection procedure may safe life. This consists of carrying out a Cesarean section while maintaining the umbilical circulation intact for some time to operate promptly before spontaneous ventilation starts. The fetus is oxygenated *via* the placenta and the surgeons have several minutes for carrying out the thoracotomy and resection [47, 48]. Immediate post-natal extracorporeal membrane oxygenation (ECMO) cannot replace this procedure because the distended CCAM distorts the vessels of the thorax and neck and may preclude adequate cannulation. Conversely, postoperative ECMO may be required after EXIT-to-resection if there is severe lung hypoplasia.

After birth: CCAMs may become symptomatic at birth due to the space-occupying nature of the lesion. However, it is rare for an urgent procedure to be necessary, and removal of the cystic tissue can be done electively. In fact, in most cases, there are no symptoms at birth, and the issue of whether or not to resect the malformed part of the lung should be considered. An expectant attitude is tempting in a totally asymptomatic, healthy baby with a small CCAM [49, 50]. This wait-and-see attitude is controversial [51] and should be advised only after detailed discussion with the parents and keeping the patient under close surveillance [52].

Routine resection should be probably recommended in all CCAMs [53, 54] mainly because of the mucus-secreting nature of the epithelium that lines the cysts. This fact and the absence of frank communication with the airway make progressive growth in the lung likely along with the additional risks of infection, repeated pneumonia, pneumothorax or hemorrhage. These complications rarely occur during the first 6 months of life and, therefore, it has been recommended to undertake elective resection immediately after the newborn period [55, 56], at 3–6 months [57, 58] or in the first year of life [59]. Lobar resection is usually necessary [60, 61], although occasionally more extensive or only segmental resections may be indicated [62].

Thoracoscopic resection has been shown to be possible and safe into the hands of experienced pediatric surgeons [63–67] probably with longer operative times but with similar results and less visible scars [64, 68]. Thoracoscopy can also be used for decompression of the cysts in selected cases [69].

Regardless of the approach selected, lung resection for this indication has minimal morbidity and excelent results. Earlier surgery might permit better parenchymal regeneration because alveologenesis persists for some months after birth.

The other reason for advising resection

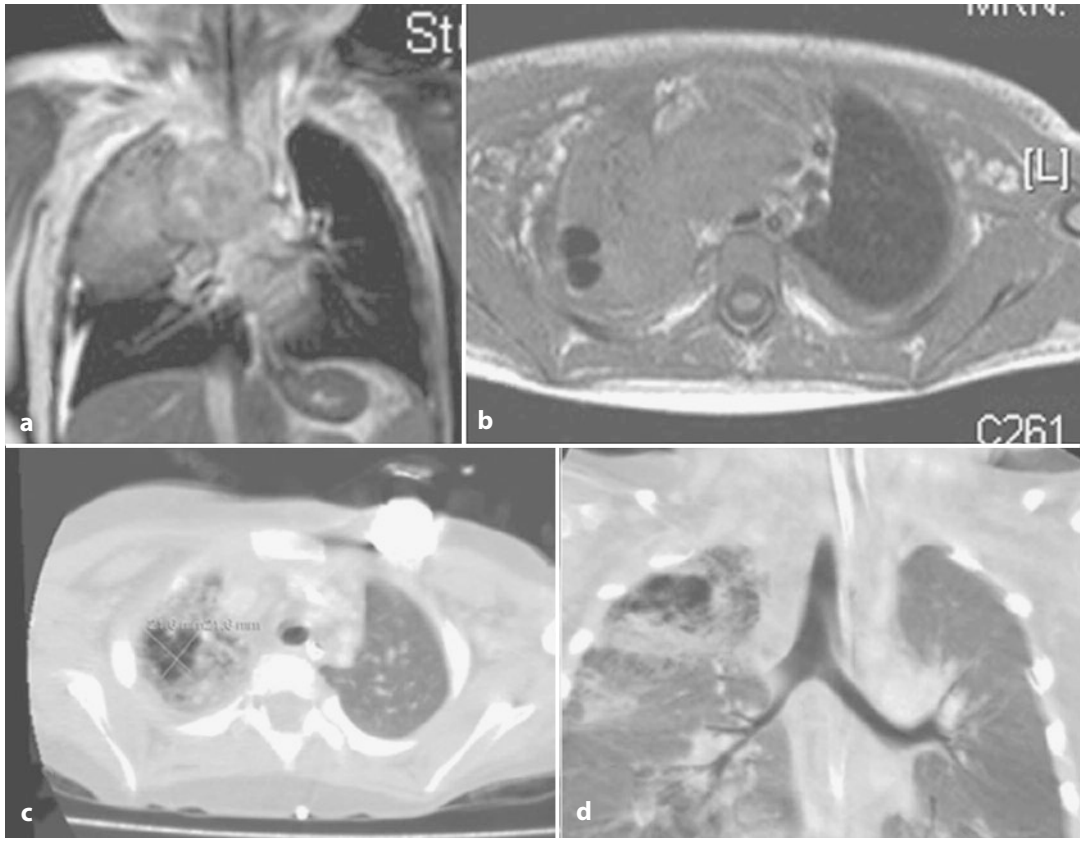

Fig. 21.5a, b Chest MRI of a 3-year-old female with a large mediastinal tumor that compressed the trachea and extended to the left side. Biopsy was consistent with rhabdomiosarcoma. After chemotherapy, CT demonstrated the decrease in size and the partially cystic nature of the lesion (**c-d**). Upon resection (upper and middle right lobectomy), a PPB on a CCAM was found

even in asymptomatic CCAMs is the certain (but rare) association of this malformation with some types of lung cancer. This risk should not be overemphasized, but cannot be ignored.

21.7 CCAMs and Cancer

In some rare instances, tumors develop on the malformed, hamartomatous tissue that constitutes the CCAM. The most common is pleuropulmonary blastoma (PPB), a malignant tumor that has been described as sarcoma or rhabdomyosarcoma [70, 71] and which may contain other tissue elements due to its blastematous nature [72]. Half of the cases of PPB develop in areas with macrocystic or microcystic structures [73] and the diagnosis of the tumor may be difficult (Figs 21.5 and 21.6). A recent study revealed that, out of the 74 CCAMs and 5 PPBs treated surgically between 1999 and 2008, 3 PPBs were diagnosed by imaging as being CCAMs [74]. More recent series further demonstrated the difficulties for the diagnosis of cystic PPBs and CCAMs. Syndromic and older children are more likely to have PPB [75]. However, although the association between CCAM and PPB is well established, the biological features of both tissues seem to be different [76].

Only very rarely does PPB develop during infancy, and this (as well as the limited number of cases reported) discourages the use of this argument as a justification for routine re-

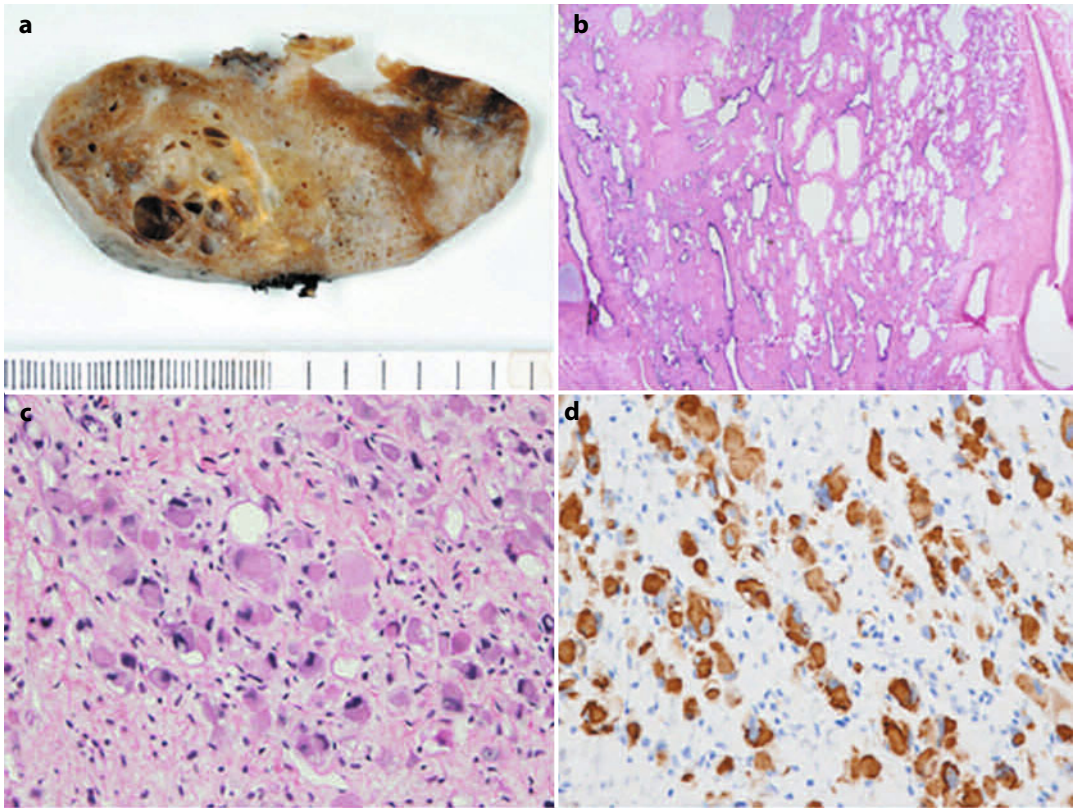

Fig. 21.6 Formalin-fixed specimen from the patient shown in Figure 21.5 in which the tumor and cysts are visible (**a**). H&E staining showing CCAM features with cysts of variable size and several types of respiratory epithelium, including mucus-secreting cells (**b**). Malignant rhabdomyoblasts embedded in the CCAM that stained positively for actin (**c- d**). Courtesy of Professor M. Nistal (Hospital Universitario La Paz, Madrid)

moval of asymptomatic CCAMs [77]. However, for understandable reasons, physicians confronted with this particular association tend not to recommend expectant attitudes.

Bronchoalveolar carcinoma (BAC) has also been observed in association with CCAMs [78–82]. This can be explained (at least in part) by the fact that both tissues share the nature of the mucinous cells [83].

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Bronchopulmonary Sequestration

22

Juan A. Tovar

22.1 Introduction

Bronchopulmonary sequestration (BPS) is a rare developmental disorder in which part of the lung is disconnected from the main airway and receives aberrant arterial inflow from the aorta instead of from the pulmonary arteries. BPS belongs to the group of foregut malformations and is often accompanied by other defects. The incidence of BPS has increased considerably in the last few years due to the widespread routine use of fetal ultrasound screening. Several patterns of clinical expression are possible and therapeutic attitudes ranging from expectant observation to early surgical removal or embolization remain controversial.

22.2 Pathology and Classification

The sequestered lung tissue has bronchial and bronchiolar ducts, areas of collapsed airspaces and occasionally cysts lined by pseudostratified cilliary epithelium with mucus-secreting components similar to those found in congenital cystic adenomatoid malformations (CCAMs). The coexistence of BPS with CCAMs was highlighted after observation of a relatively large number of cases diagnosed prenatally as CCAMs that had both features. Such "hybrid" tissues [1] were also described by other authors [2–4] and confirmed by pathological microdissections of surgical specimens [5]. These studies showed also that bronchial atresia is a relatively common finding in BPS along with other foregut malformations such as CCAMs and lobar emphysema [6]. The aberrant arteries of the sequestered tissue are rich in elastic fibers that are consistent with their systemic origin (Fig. 22.1). Atherosclerosis, even in young individuals, can be occasionally observed in the wall [7].

The recent finding of abnormal expression of mucinogenic factors such as MUC5AC, cytokeratin 20 and human v-erb-b2 erithroblastic leukemia viral oncogene homologue 2 (HER)2 as well as of K-RAS mutations within secretory areas of CCAMs and BPS called particular attention to the risk of cancer in these tissues [8].

Pryce et al. [9, 10] distinguished two types of BPS:

- intralobar bronchopulmonary sequestration (IBPS), in which the malformed tissue is a part on one lobe of the lung surrounded by lobar pleura;
- extralobar bronchopulmonary sequestration (EBPS), in which there is a clear sepa-

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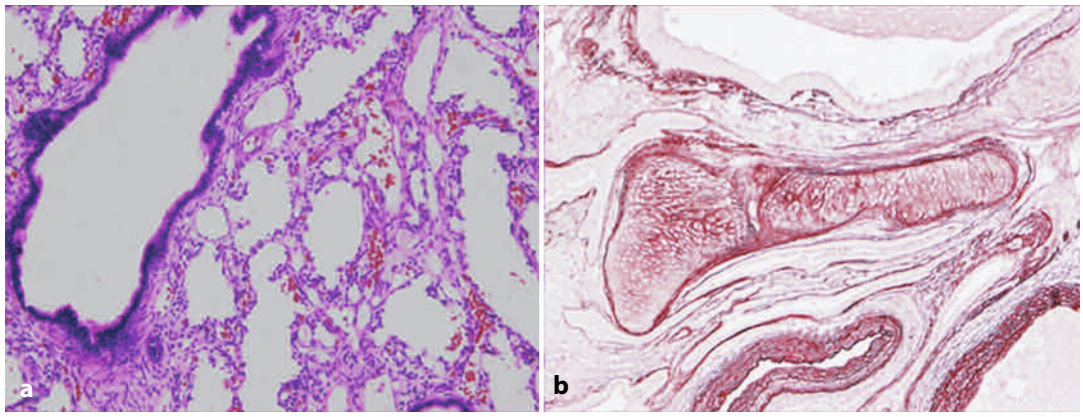

Fig. 22.1 a H&E staining of a section of an IBPS specimen shows disorganized airspaces with secretory bronchial-like cysts lined by a ciliated mucus-secreting epithelium. In **b**, stained for elastic fibres, systemic arteries with abundant elastic elements are seen below a cartilaginous island

ration between the normal lung and the sequestered tissue, including often a complete fissure and individual pleural covering.

Very seldom, as proof of its foregut origin, the malformed lung parenchyme (intralobar or extralobar) is connected with the esophagus or the stomach through a more or less well-formed bronchus.

BPSs are more often located in the lower lobes or below them. In these cases, arterial inflow originates from the thoracic or abdominal aorta and reaches the malformed tissue directly or by traversing the diaphragm. The pattern of venous return may be normal into the left atrium (as in most cases of IBPS) or into a systemic vein, the inferior vena cava or the azygos in EBPS. When venous return is anomalous and runs through the diaphragm to reach the inferior vena cava or portal vein, the malformation is known as the "Scimitar syndrome" because of the particular vascular silhouette delineated by the venous collector upon imaging [11]. Lung hypoplasia, bronchial malformations and dextrocardia are common in these cases and, although arterial inflow from the aorta occurs occasionally, the nosologic and therapeutic problems of the Scimitar syndrome are different from those of BPS, and are out of the scope of the present review.

EBPSs are more often located underneath the lower lobes of the lung, particularly in the left side. They can be incorporated into the sac of a congenital diaphragmatic hernia and can even be infradiaphragmatic, a location in which they can be misdiagnosed as adrenal masses. EBPSs have no connection with the airway and are therefore often compact. However, upon detailed histological study, a number of them [4, 5] that may amount to one-half [12] or more [13] have areas of CCAMs. EBPSs are relatively often associated with other malformations, particularly of the lung, heart, great vessels and gastrointestinal (GI) tract [14].

IBPSs are 3–4-times more frequent than EBPSs. They are also located predominantly in the lower lobes of the lungs, and the proportion of patients with associated malformations is much lower than in EBPS. Bilateral or whole-lung involvement is rare, but may occur [14]. IBPSs often have areas of associated CCAMs [15, 16].

22.3 Pathogenesis

Although in the past an acquired post-inflamatory origin was attributed to BPSs [17] and particularly to IBPSs [18], frequent prenatal diagnosis, pathology close to that of CCAMs,

and an association with other defects point to an embryonic, maldevelopmental origin that is further supported by some anomalies of molecular signalling. A few familial observations further reinforce this interpretation [2]. In cases with connection with the foregut, the simplest topographic explanation is the late and ectopic emergence of an abnormal lung bud from the distal foregut that becomes vascularized by systemic arteries. This would explain why EBPSs (but not IBPSs) seem to derive rather from "orthotopic" lung buds. Nevertheless, they probably share similar mechanisms because they occasionally have connections with the foregut.

Molecular and genetic actors leading to BPSs are not well known, but there is evidence of a wide degree of overlap with those of CCAMs and other foregut malformations [19]. Hox gene Hoxb5 protein is abnormally increased in BPS and CCAM tissues. This gene is normally expressed in the subepithelial mesenchyme of the airway branching points during the pseudoglandular stage of lung development and should not be so active at term [20]. Conversely, the cell adhesion molecules alpha (2)-integrin and E-cadherin, which are related to Hoxb5, are also overexpressed in them, attesting their likely participation in the pathogenesis of such conditions [21].

22.4 Clinical Features

Fetal disease: A large proportion of BPSs are diagnosed before birth when a solid or cystic portion of the lung receiving systemic arterial inflow is detected upon fetal ultrasonography. The vast majority of fetuses with BPS do well and only occasionally does the mass cause massive pleural effusion and life-threatening hydrops. In a series of 14 BPSs selected from 192 fetuses with lung lesions, only 2 BPSs required some form of prenatal intervention for drainage of ipsilateral hydrothorax, whereas in 4 BPSs, the mass regressed during gestation, and in the remaining 8 post-natal surgery was successful [22]. Some cases with BPS, pleural effusion and hydrops have abnormal venous anatomy and obstructed venous outflow that explain these disturbances [23]. Regression of BPS during fetal life is not uncommon [24], particularly in hybrid cases with adenomatoid components [1]. Some intraabdominal BPSs detected during pregnancy progressively involute and disappear [25].

Neonatal disease: Except in cases in which the malformation is huge and accompanied by pulmonary hypoplasia, neonatal symptoms are often absent in BPS. These infants, particularly those with EBPS and therefore without airway connection with the mass, have mild or no symptoms [26] and are often diagnosed by serendipity. Patients with massive hydrothorax or pulmonary hypoplasia have severe respiratory insufficiency (eventually pulmonary hypertension) and may require refined neonatal intensive care, including extracorporeal membrane oxygenation (ECMO) [27] prior to surgery (28). Infradiaphragmatic or intra-abdominal BPS, often hybrid in nature, tend to remain silent and are also diagnosed during imaging for other purposes [29–33].

Late symptoms: BPSs without CCAM components have no secretory tissue. Therefore, they do not tend to increase in size after birth. However, their marginal connection with the airway may insuflate the sequestered part of the lung. Infection is possible (particularly in IBPS) and "repeated pneumonia" in the same area of the lung (particularly in the lower lobes) should be investigated looking for BPS. Recurrent respiratory infection is the leading picture of BPS, but occurs predominantly in IBPS in which there are communications with the airway [13, 26]. Increased pulmonary blood flow from the systemic arterial supply can result in hemorrhage, hemoptysis, or high-output cardiac failure, although these are rare events [34]. Most BPSs remain asymptomatic during infancy and childhood, and repeated infection, shortness of breath and hemoptysis may manifest later or even in adult life [35].

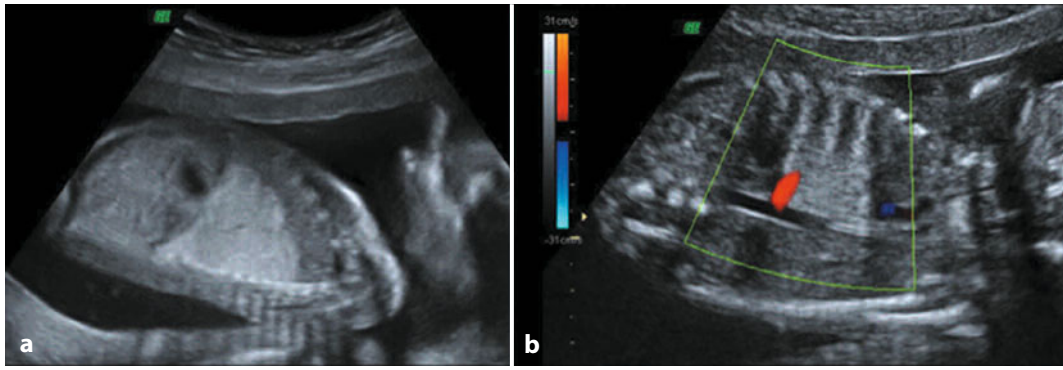

Fig. 22.2 Fetal ultrasound in which a condensation is visible in the lung (**a**). Upon color-Doppler ultrasonography, arterial inflow from the aorta is obvious (**b**)

22.5 Diagnosis

Routine prenatal ultrasound screening allows the diagnosis of most cases of fetal BPS from the twentieth week onwards. Areas of the lung with solid or complex ecogenicity and systemic arterial inflow upon color Doppler ultrasonography are indicative of BPS [36], especially if they are located in the lower lobes (Fig. 22.2). Pleural effusion and hydrops are rare but, in these particular cases, assessment of pulmonary development is necessary. Infradiaphragmatic BPSs located in the adrenal areas require diagnosis from congenital neuroblastoma (although these are more often cystic). Fast fetal magnetic resonance imaging (MRI) may occasionally help to define prenatally the nature and features of the sequestration and its vascular supply [37, 38].

Later in life, the diagnosis of BPS is based on the same methods used for imaging CCAMs plus the demonstration of the aberrant systemic arterial supply. Plain radiographs of the chest may show areas of condensation (eventually with cysts) in the lower lobes of the lung (Fig. 22.3). These may often be so discrete that they are easily missed. MRI [39] and computed tomography (CT) [40] can show the features of the sequestered tissue, but CT fares better for this purpose. In prenatally diagnosed, clinically silent cases, it is better to undertake an elective CT between the first and sixth months of life in order to define the features of the malformed tissue. Color Doppler ultrasonography is the preferred method for demonstrating the aberrant arterial supply at any stage of the diagnosis. However, detailed imaging is necessary whenever treatment is contemplated. Arteriograpy used to be the method for this purpose, but it has been progressively replaced by multidetector three-dimensional (3D) angio-CT [41-44], which allows complete mapping of the arterial inflow and venous outflow in amazing detail (Fig. 22.4).

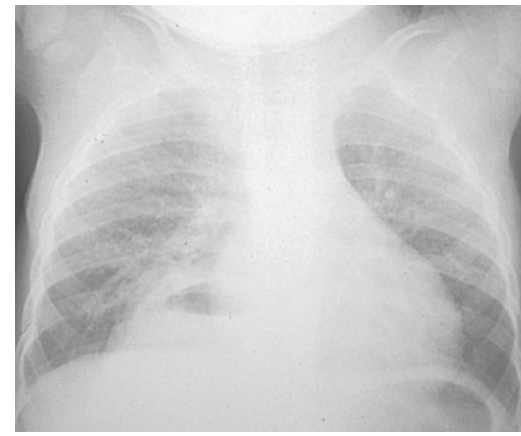

Fig. 22.3 Plain radiograph of the chest in a 18-month-old female with repeated lung infections. A right basal condensation with a cystic image is visible. She had an IBPS that was resected successfully

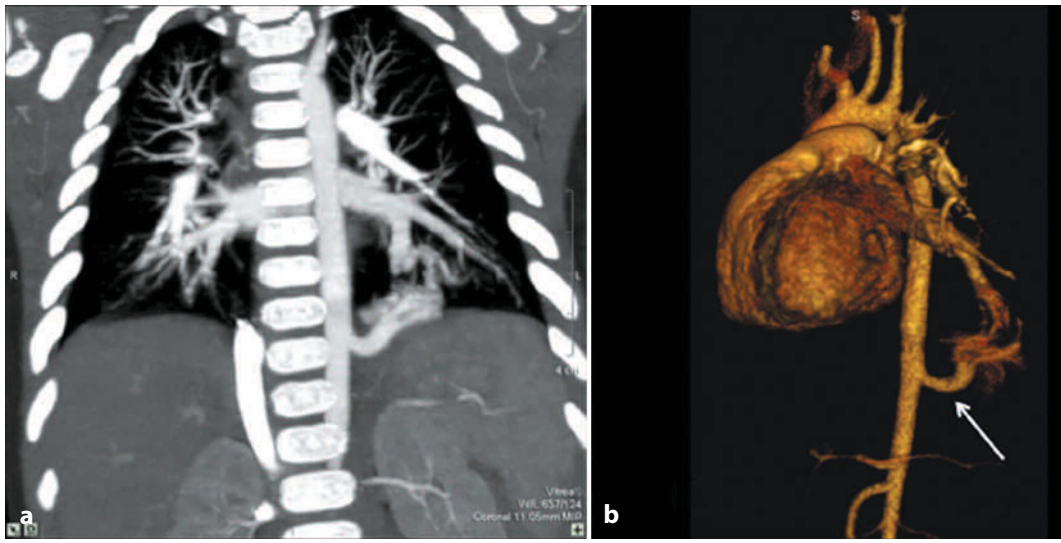

Fig. 22.4 Angio CT in a patient with a left basal IBPS. An ectopic arterial supply from the aorta and venous drainage to the pulmonary veins is readily visible (**a**). Reconstruction of the arterial supply (*arrow*) greatly facilitates the surgical strategy (**b**)

Other diagnostic procedures such as bronchoscopy are probably unnecessary. If communication with the foregut is suspected, esophagoscopy and barium meals are indicated.

22.6 Treatment

During fetal life: BPSs do not require prenatal treatment except in cases with massive pleural effusion and hydrops. Fetal thoracentesis and thoraco–amniotic shunts may be indicated if this life-threatening condition is detected, and have been applied successfully in several cases [22, 45-47]. Very seldom, large BPSs causing pulmonary hypoplasia have been treated by open surgery on the fetus [48]. Most BPSs detected before birth remain stable or undergo variable degrees of regression.

After birth: Symptomatic cases, those with neonatal respiratory distress, repeated pneumonia during infancy or childhood, or rarer events such as hemoptisis or high-output cardiac failure require active treatment. However, most BPSs are asymptomatic and whether they require treatment is debatable, particularly because of their well-known potential for regression. Some authors advise observation only for BPS, particularly for small, asymptomatic EBPSs [46, 49, 50]. Conversely, removal of the aberrant tissue is advised by other authors [35, 51, 52] on the basis of two arguments. The firstly is the presence of mucus-producing, cystic elements in one-half to two-thirds of cases. The tendency to accumulate mucus and the risks of infection that constitute the indications for removal of CCAMs also apply for BPSs. Secondly, the risk of cancer in the aberrant tissue later in life is rare but real (see below).

After elective imaging during the first semester of life, active treatment should be planned. There are two possible approaches: embolization or surgical removal.

Embolization was introduced in the stream of the rapid progress of percutaneous interventional radiology and cardiology. It was originally applied in the Scimitar syndrome to re-route the venous outflow by plugging the infradiaphragmatic collector while occluding the systemic arterial inflow with coils [53].

Coils [54, 55], plugs [53, 56] or ethylene vinyl alcohol copolymer [57] introduced through arterial catheters in the lumen of the feeding vessel can selectively destroy the sequestered tissue, and it is certainly tempting to rely on these methods as an alternative to major surgery. In cases with high-output cardiac failure, this procedure can save life and may be followed by surgical removal if necessary [34]. Preoperative embolization has also been recommended [58]. However, embolization for the primary treatment of BPS had only limited development in pediatric surgery [59] because it has its own complications (e.g., pleural effusions, limb ischemia) [54, 60] and because the sequestered tissues are not fully destroyed [61] and require further embolization or surgery [54, 60, 62, 63] in a sizeable proportion of cases. Most publications on the embolization of BPS involve case reports or small series that rarely contribute information to the long-term results of the procedure.

Surgical removal after ligation of the vascular pedicles is the preferred alternative in EBPS in which the sequestered tissue is separated from the lung and has its own pleural covering [26, 35, 46, 64]. The same applies to infradiaphragmatic EBPSs and to those associated with diaphragmatic hernia, which can be removed with the hernial sac during repair.

When dealing with IBPS, lobectomy is the first-line treatment [26, 27, 64, 65]. Parts of the affected lobe may be healthy and have normal arterial inflow, but complete resection is the only way to achieve destruction of the entire sequestered tissue. It has been shown for CCAMs (and most BPSs contain such tissue) that macroscopic appreciation of the extent of the diseased tissue is rarely precise, and that lobectomy remains the best way of staying on the safe side [66]. The procedure should be started by carefully mobilizing the affected lower lobe upwards to identify first the aberrant systemic artery (Fig. 22.5). This may be very large, but with thin elastic walls, and careful ligation and division should be done taking into account that retraction of the artery underneath the diaphragm could be cat-

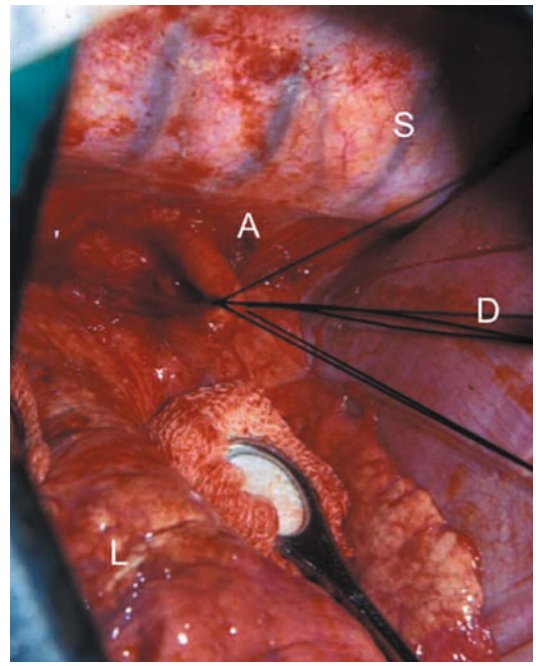

Fig. 22.5 First step for a right basal lobectomy for IBPS. The ectopic artery (*A*) is being ligated. The spine (*S*), lung (*L*) and diaphragm (*D*) are visible

astrophic. Once the artery is secured, lobectomy proceeds in the usual way (although dense adhesions due to previous repeated infections may make this part of the procedure difficult). In expert hands, lobectomy in an infant has few complications and minimal functional consequences provided that most of the resected lung is isolated from the airway.

Thoracoscopic lobectomy for BPSs has developed rapidly. This trend will probably continue because the proportions of conversions and complications are low [67–73].

22.7 BPS and Cancer

The risk of cancer in BPS is probably related to the hybrid nature of many of these lesions [74] and to the presence of CCAM elements and mucus-secreting structures prone to becoming malignant [8]. This practically never happens during childhood, but several cases that developed in adults with undiag-

nosed sequestrations were reported. The nature of these tumors was variable: sclerosing hemangiomas [75], pleuropulmonary blastomas (PPBs) [76, 77], adenocarcinomas or bronchoalveolar carcinomas [78, 79], carcinoid tumors [80], multiple neuroendocrine tumorlets [81, 82], fibrous mesothelioma [83] or lymphoepithelioma-like carcinoma [84]. It is obvious that the risk of malignancy (even if very remote) is an argument for the removal of the sequestered tissue.

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Congenital Lobar Emphysema

23

Giovanni Ruggeri, Michela Maffi, Francesca Destro and Mario Lima

23.1 Introduction

Congenital lobar emphysema (CLE) is a pulmonary congenital malformation characterized by hyperinflation. After birth, a dysfunctional valve mechanism (air enters the alveoli thanks to negative pressure but cannot be released because the tracheobronchial tree has collapsed) leads to air trapping. CLE has all the features of obstructive emphysema: compression of lung parenchyma; mediastinal shift, herniation of the emphysematous lobe across the anterior mediastinum; and reduced respiratory reserve due to lowering of the diaphragm [1–2].

CLE is a relatively common congenital malformation of the lung (1 in 20,000 to 1 in 30,000 deliveries). However, it is not always detected during prenatal ultrasonographic evaluation [3]. There does not appear to be a significant predominance for a particular sex [4], but some authors have shown that males are affected three times more often than females, and that it occurs predominantly in Caucasians [5]. Bilateral localization of CLE is not common [2]. The frequency of distribution is [6]:

- superior left lobe (40–50%);
- middle right lobe (30–40%);
- superior right lobe (20%);
- inferior lobes (<5%).

CLE often presents with alveolar destruction, but sometimes alveoli are intact but over-distended. Over-distension of alveoli is associated with polyalveolosis (or "polyalveolar lobe", described for the first time by Hislop and Reid) [7]. The term "polyalveolosis" describes a lobe in which, compared with normal airways and arteries, the total number of alveoli is increased, along with impairment of gas exchange. Clinical and radiological findings cannot be used to differentiate between CLE and polyalveolar lobes. Congenital lobar over-inflation is used to define both entities [2, 6, 8]. Cardiac malformations (12–14% of cases) [9], renal or bones anomalies, pectus excavatum ("funnel chest") and hiatal hernia are possible associated anomalies [3].

23.2 Etiopathogenesis

The origin of CLE is air trapping. The affected lung allows the passage of air during inspiration but not its complete emission during expiration, resulting in pulmonary hyperexpansion. Several theories have been postulated to explain air trapping but the precise etiology is unknown in 50% of cases [3, 9, 10]. The most reliable include [6]:

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- Dysplastic bronchial cartilage or complete bronchial atresia allow the valve effect [11];
- endobronchial obstruction (accumulation of thick mucus [12], excessive mucosal proliferation and subsequent refolding [1]);
- extrinsic bronchial compression by aberrant vascular structures, enlarged heart chambers or thoracic masses [13];
- widespread and atypical bronchial abnormalities that may or may not be related to infections [14, 15].

We could say that CLE is due to intrinsic (bronchomalacia, stenosis) or extrinsic (bronchogenic cyst, vascular structures) bronchial obstruction that led to progressive air trapping and hyperinflation.

23.3 Clinical Features

The spectrum of clinical presentation is broad and is dependent upon: the age of the patient; size and location of the malformation; and associated anomalies. Symptoms can arise at birth (25% of cases), within the first month of life (50% of cases) or sporadically after 6 months of age [6]. Symptoms in the newborn are often associated with rapid progression that requires early resection of the malformation. In general, lesions associated with poorly defined symptoms remain stable or regress and they do not damage the surrounding parenchyma [2, 6, 16].

In the neonatal period, CLE can lead to mild-to-moderate respiratory distress and only occasionally to severe respiratory failure [17]. In the latter, there is severe mediastinal shift, lobar distension, reduced respiratory excursion and pulmonary compression in the affected and controlateral lung. Reduction of breath sounds and hypophonia can be observed at clinical examination. In early childhood, the cardinal symptom is tachypnea that worsens with crying or feeding. Children may also have wheezing, dry cough, stridor, failure to thrive and cyanosis that necessitates urgent treatment. Thoracic infections are typical at older ages [1, 18].

23.4 Diagnosis

The routine use of ultrasonography during pregnancy has changed the natural history of many congenital anomalies and has permitted better comprehension of their pathophysiology [15]. Prenatal diagnosis is fundamental for the planning of birth and the management of congenital malformations as well as for the psychological support of parents. Congenital malformations of the lung are not usually identified before the second trimester. A precise prenatal diagnosis of CLE is difficult [3]. Sometimes the malformation is suspected only by indirect signs (mediastinal shift, polyhydramnios, fetal hydrops). CLE appears as a luminescent unilateral lesion with no systemic vascularization and is sometimes associated with cysts [3, 6, 15-19]. Recently, prenatal diagnosis has become more accurate thanks to the use of magnetic resonance imaging (MRI) of the fetus that allows precise anatomical representation of the thoracic cage and of its contents [6, 20]. Prenatally, a lung-to-thorax transverse area ratio (L/T) of <0.25), polyhydramnios, and hydrops are important prognostic factors [21].

In the first 24 h of life, CLE has the radiological appearance of a radiopaque mass due to fluid accumulation in the affected lobe that is dependent upon delayed clearance [2]. Progressive over-inflation occurs together with fluid absorption that leads to acinar shadowing, a reticular interstitial pattern and, finally, lobe hyperlucency [1, 2, 9, 22] (Fig. 23.1).

The emphysematous lobe herniates and crosses the mediastinum, compressing the normal parenchyma and causing mediastinal shift. Intercostal spaces are expanded and the diaphragm is flattened [1, 9]. The lesion does not change during breathing but has a reduced blood supply. Computed tomography (CT) is useful for the diagnosis and scintigraphy can be undertaken the diagnosis is unclear. CT

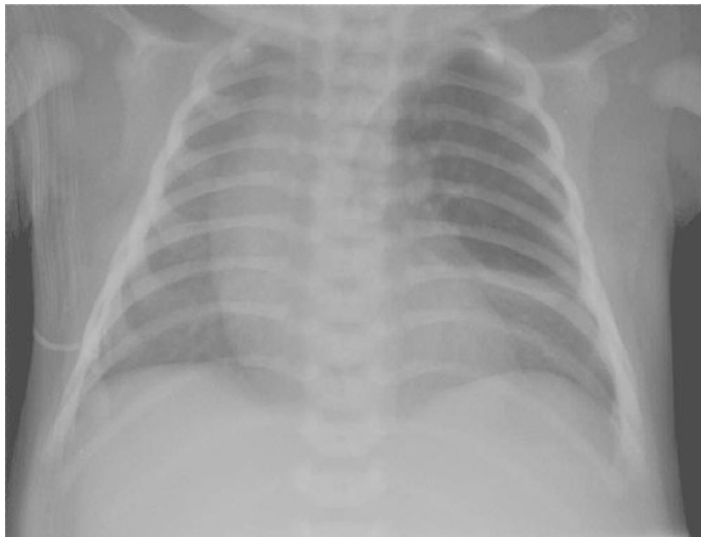

Fig. 23.1 Chest radiograph showing hyperluciency of the affected left lobe and mediastinal shift

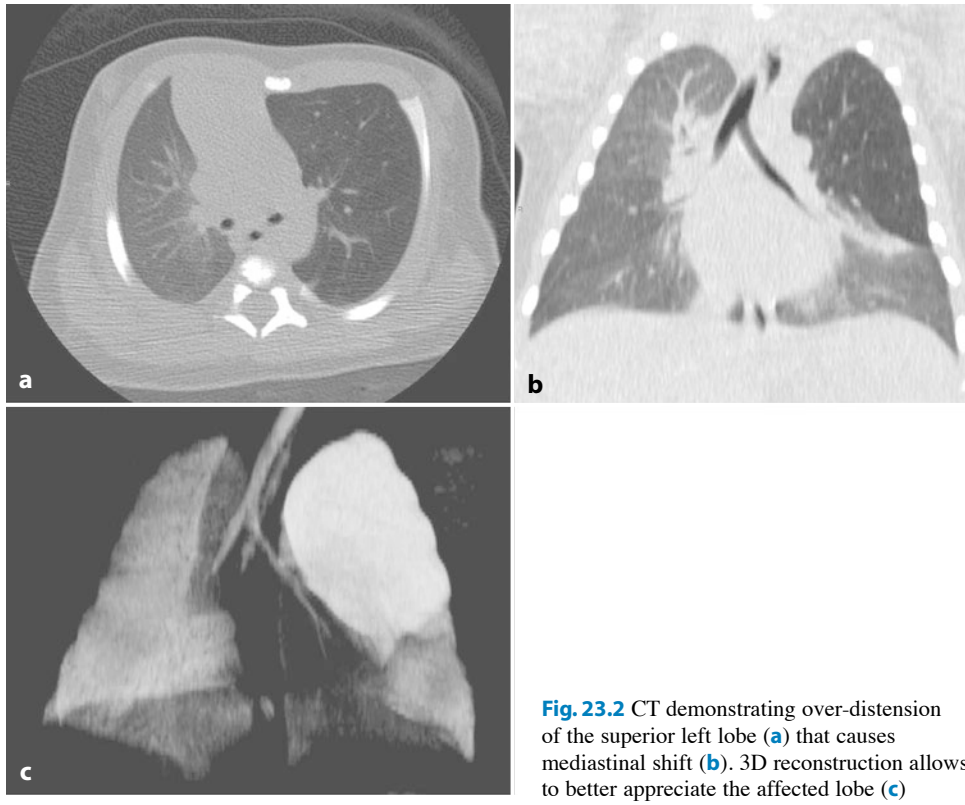

Fig. 23.2 CT demonstrating over-distension of the superior left lobe (**a**) that causes mediastinal shift (**b**). 3D reconstruction allows to better appreciate the affected lobe (**c**)

shows an enlarged affected lobe that is hypodense with atelectasis of the surrounding parenchyma. Contrast-enhanced CT along with magnetic resonance angiography is particularly useful for the diagnosis of congenital lobar over-inflation due to extrinsic compression (vascular rings, cystic lesions) (Fig. 23.2). Scintigraphic perfusion/ventilation

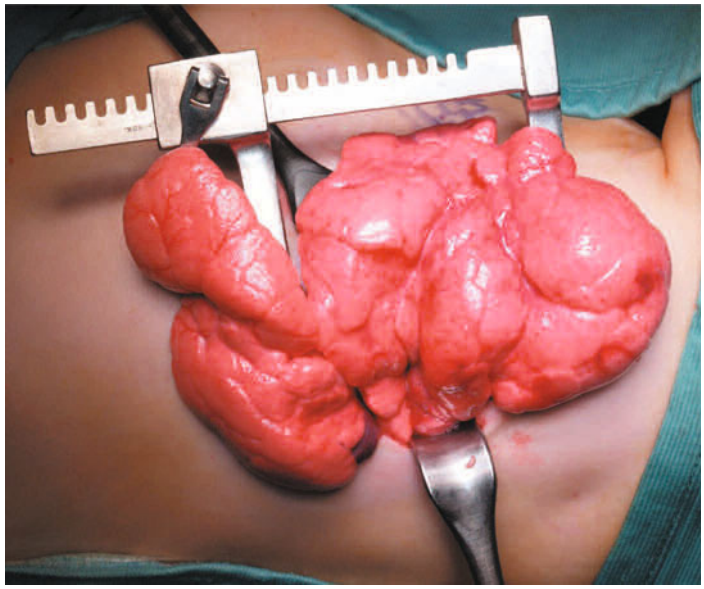

Fig. 23.3 After thoracotomy, the affected lobes "pop out" from the wound

scans demonstrate delayed uptake and washout of the radioisotope and little blood flow [6]. Bronchoscopy may show intrinsic or extrinsic obstructions but is not so widespread because it may exaggerate the distress [1, 23].

The differential diagnosis includes acquired emphysema (usually associated with high-pressure ventilation), pneumothorax, aspiration of foreign bodies, cystic congenital lesions, diaphragmatic hernia, and bronchogenic cysts. The position of the collapsed lung (which is not around the hilum in CLE) and lung markings (that are not present in pneumothorax and only attenuated in CLE) help the differentiation from pneumothorax [2].

23.5 Management

The treatment of congenital malformations of the lung is planned using a multidisciplinary approach. A limited number of cases with severe fetal hydrops profit from prenatal intervention, otherwise most cases are treated only after birth [17]. Symptomatic lesions should be resected by lobectomy [24-26] to allow compensatory pulmonary growth and to improve respiratory function. Acute postnatal respiratory distress requires emergency surgery. Respiratory function should be supported with high-frequency ventilation, administration of nitric oxide or extracorporeal membrane oxygenation to stabilize the patient. Positive-pressure ventilation may increase the amount of air trapped, thereby worsening the emphysema. Likewise, placement of a drain tube for presumed pneumothorax impairs clinical status [24]. The management of asymptomatic lesions is controversial, especially with regard to the need and timing of surgery. Stable CLE can reduce over time and have a good prognosis, justifying a "wait and see" approach [3, 4, 17, 18, 24]. These patients should undergo CT at around 6 months of age. If necessary, elective surgery can be arranged after radiological evaluation.

Lobectomy with traditional thoracotomic access is undertaken. The affected lobe characteristically "pop outs" through the wound [6] (Fig. 23.3). Thoracoscopy has been advocated by some authors as an alternative method [27] but has some limitations. That is, the expanded lobe prevents the creation of a work space and the procedure should be carried out only in stable patients by expert surgeons. A minimally invasive approach can be used if the over-inflation is mild or after effective endoscopic decompression of the affected lobe.

23.6 Outcome

CLE carries a good prognosis. A high percentage of cases are treated successful with conservative management, but symptomatic patients require surgery. The prevalence of long-term pulmonary growth after lobectomy is excellent [6].

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Foregut Duplications

24

Giovanni Ruggeri, Francesca Destro, Giulio Gregori and Mario Lima

24.1 Introduction and Epidemiology

Foregut duplications are rare cystic (by far the most frequent) or tubular masses, representing 20% of mediastinal masses [1]. These duplications include a wide spectrum of anomalies, usually enteric cysts or bronchogenic malformations.

Enteric cysts arise from the upper gastrointestinal (GI) tract (esophagus, stomach or first portion of the duodenum) and may communicate with the esophagus. Rarely, enteric cysts extend to the abdomen, where they are connected with the stomach, jejunum, ileum or pancreatic duct through fistulae or end blindly. Bronchogenic cysts are the most common (50–60% of cases) and can be found in many locations (paraesophageal, paratracheal, perihilar, intraparenchymal; rarely in the tongue, neck, back) although they are usually found in the upper airways [1]. There is a third group of cystic lesions that involve the spine and have a neurological component: neuroenteric cysts. Recently, rare and complex associations have been described, such as hybrid pulmonary lesions, in which congenital cystic adenomatoid malformations, pulmonary sequestration and bronchogenic cysts can be found in the same lesion, or the simultaneous presence of cystic duplications and esophageal atresia [2]. Multiple cysts (with an abdominal component) are described in 20–30% of cases [2, 3].

Over the years, several classifications have been proposed but none adequately explain the embryology, location and symptoms of foregut duplications. In 1674, Blasius was the first to use the term "duplication" to define an esophageal cyst. In 1968, Gerle coined the term "bronchopulmonary foregut malformations". Before Gerle, Ladd had tried to simplify the nomenclature by using the term "duplication of the alimentary canal" to indicate those malformations that had three characteristics [1–4]:

- a well developed coat of smooth muscle (now defined as a "double layer");
- an epithelial lining representing some portion of the mucosa of the intestinal tract;
- intimate anatomical connection with any part of the GI tract.

24.2 Etiology and Pathogenesis

All foregut malformations share a similar embryologic origin. The gastrointestinal and respiratory tracts derive from the same primitive foregut. The differentiation starts in the

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fourth week of gestation, when a diverticulum arises cranially from the ventral foregut. The diverticulum is connected with the dorsal foregut by two laryngotracheal ridges that later become the laryngotracheal septum that separates the esophagus (dorsal) and the airways (ventral). The esophagus, stomach, duodenum, liver, gall bladder and pancreas originate from the dorsal tube. The tracheobronchial tree originates from buds that arise in the distal part of the ventral tube and differentiate during pregnancy. The neurological system derives from the notochord, which has close relationships with the endoderm early in development and then separates from it at approximately 3 weeks of gestational age. Most of foregut malformations arise between the fourth and eighth week of gestation. Multiple theories have been proposed to explain their origin, but none explain all the variants.

It is believed that bronchogenic cysts result from an alteration of the budding process which occurs at the level of the ventral side of the primitive intestine. For this reason, bronchogenic cysts are lined by a ciliated pseudostratified columnar epithelium, and they contain elements of the tracheobronchial tree (sometimes mucus- or air-fluid levels are inside them). Otherwise, abnormal budding of the dorsal primitive intestine leads to the formation of enteric cysts that are covered by a gastrointestinal epithelium (esophageal or gastric epithelium covered by smooth muscle) [1]. The origin of neuroenteric cysts is even more complex because they often present as a spectrum of anomalies and not as a single entity. Neuroenteric cysts are made of heterotopic rests of gastrointestinal and respiratory tissue (columnar or cuboid epithelium, with or without cilia and mucus glands, coated by muscle wall and no serosa), connected to the nervous system or associated with vertebral anomalies. There are four reliable theories relating to the formation of foregut duplication cysts [1, 3].

The partial or abortive twinning theory is based upon the concept that the duplications are the result of a function of partial or abortive twinning. This theory also explains cases with doubling of the mouth, genitourinary tract and lower intestine. The extent of the twinning is dependent upon the moment the process starts.

The split notochord theory was proposed by Bentley and Smith in 1960 [5]. The theory is based on the possibility that a gap appears during the separation between the notochord and endoderm. Once the gap is formed, a foregut diverticulum (endoderm) can bind to the ectoderm, thereby generating a cyst. Alternatively, endodermic tissue can remain attached to the notochord, acting as a barrier to the anterior fusion of the mesoderm (anterior spina bifida) [6]. This theory can explain the high incidence of associated spinal abnormalities and dorsal location of most enteric cysts. Nevertheless, it does not explain the entire spectrum of abnormalities (such as heterotrophic gastric mucosa). There is evidence that a central part in the origin of foregut malformations is played by development of the notochord. An alteration in the Shh-Gli signalling pathway may contribute to a spectrum of bronchopulmonary anomalies [4].

Canalization defects: According to this theory, enteric cysts are the result of an alteration in the primary intestine channelling phase. The fetal intestinal tract arises as a solid tube, and subsequently a lumen is formed through its progressive cranio–caudal growth. This theory does not explain the possibility of etherotopic mucosa in the cysts.

Environmental factors: The fetus can be stressed at different times, which alters the developmental process. Trauma, hypoxia and infections are examples of environmental stresses [7].

24.3 Clinical Features

The presentation can vary depending on the anatomical position of the cysts, their size (and therefore the possibility of exercising a "mass effect" on adjacent structures) and the presence of heterotopias. These factors result in a wide spectrum of possible symptoms [1,

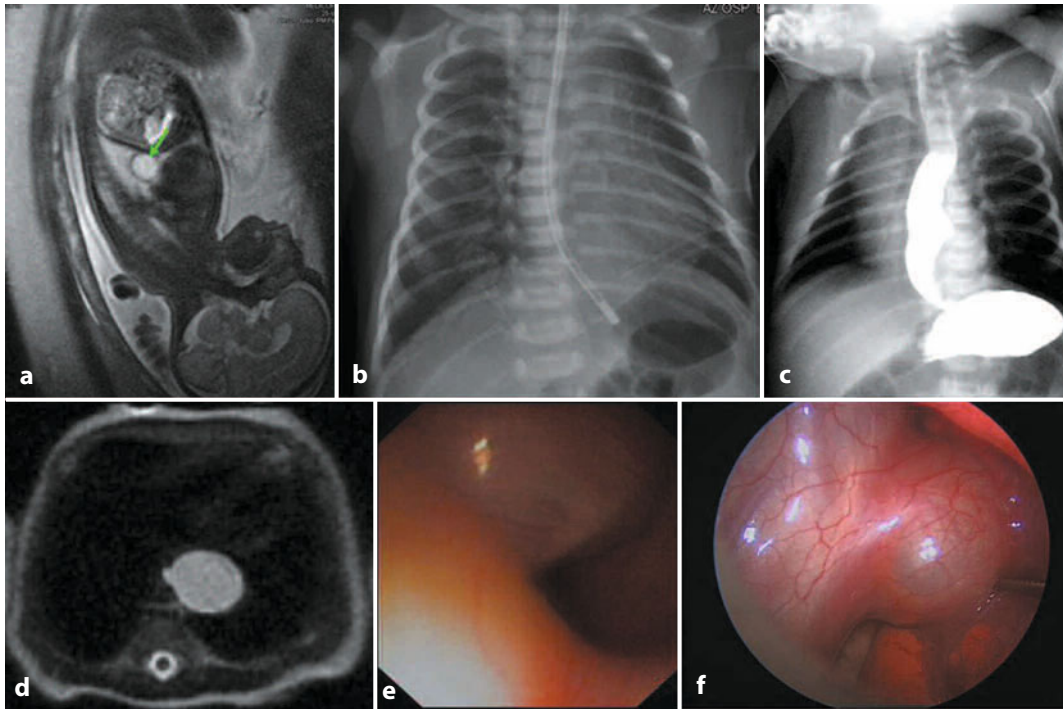

Fig. 24.1 Male patient born at a gestational age (g.a.) of 38 weeks with scheduled Cesarean section for suspected esophageal duplication. Fetal ultrasonography suggested a cystic thoracic mass. The lesion was identified also by fetal MRI as a round cystic mass in the lower part of the left thorax (*green arrow* in **a**). Post-natal evaluation was completed with radiography of the thorax (**b**), contrast esophagogastric study (**c**) and MRI (**d**): the left paraesophageal cyst (diameter: 2 cm). The mass compressed and displaced the esophagus to the right. The lumen of the proximal esophagus was dilated (**c**). Prior to surgery, an esophagogastroscopy was undertaken which showed no evidence of communication between the mass and esophageal lumen (**e**). The cyst was identified clearly during thoracoscopic removal (**f**)

3, 4]. Patients are asymptomatic in 20–35% of cases (Fig. 24.1) [8]. Most foregut cysts present with respiratory symptoms, often under the age of 2 years [9]. Respiratory symptoms (around 55% of cases) are due to compression of the tracheobronchial tree or infection (Fig. 24.2). The mass effect can led to dyspnea, persistent cough, stridor or respiratory distress that is frequent in small infants with large masses compressing the airways (Fig. 24.3). Dysphagia can be the expression of masses that reduce the esophageal lumen (Fig. 24.4). Mediastinal dislocation may be responsible for electrical cardiac abnormalities (cardiac arrhythmias) [10]. A rare symptom, found in older children, is pain in the chest or epigastrium.

There are also specific complications. Bleeding, peptic ulceration and stenosis of the wall is dependent upon the presence of ectopic gastric mucosa within the duplication (an anomaly found in one-third of cases) [4]. Neurological symptoms (caused by compression or infections), pain, limitation of movements and scoliosis are suggestive of neuroenteric cysts. Rare cases of enteric cysts connected with abdominal organs through transdiaphragmatic fistulae have been documented and are associated with bilious vomiting.

24.4 Diagnosis

Foregut duplications often present a diagnostic dilemma. In 30% of cases they are found incidentally during imaging (prenatal ultra-

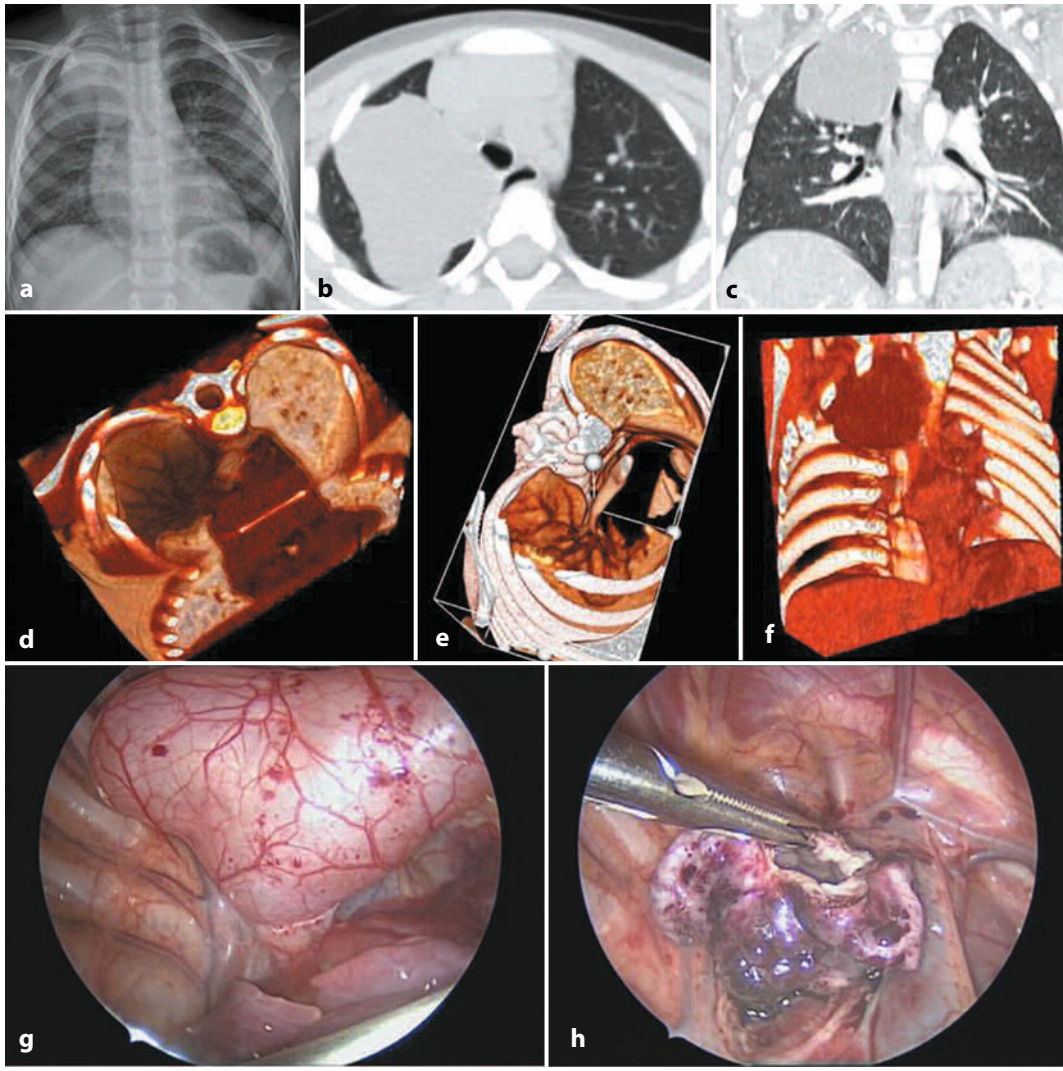

Fig. 24.2 A healthy 4-year-old male diagnosed with esophageal duplication after two episodes of pneumonia. Radiographs of the thorax, carried out after respiratory infections, showed persistent opacification of the superior right lung (**a**). Hence, he underwent CT of the thorax (**b–c**), which identified a cystic, fluid-filled mass in the subclavian right hemithorax. Three-dimensional reconstructions (**d–f**) were useful for planning surgery. After evacuation of its content, the foregut duplication was removed *via* thoracoscopic means without injuring the esophageal wall (**g–h**)

sound, chest radiography, computed tomography (CT) of the abdomen) [1]. In recent years, widespread use of prenatal ultrasonographic examination has permitted more affected individuals to be identified during pregnancy [4, 9, 11]. Fetal magnetic resonance imaging (MRI) (Fig. 24.1a) gives further information about the mass and surrounding structures (e.g., lungs, mediastinum) and can be useful for identifying fetuses at risk. In severe cases, invasive procedures are required and are carried out during intrauterine life (thoraco–amniotic shunting if there is a fetal hydrop or mediastinal shift).

After birth, ultrasound can be used to detect duplication cysts, especially if they are in the anterior mediastinum (bronchogenic cysts). The technique is less sensitive for pos-

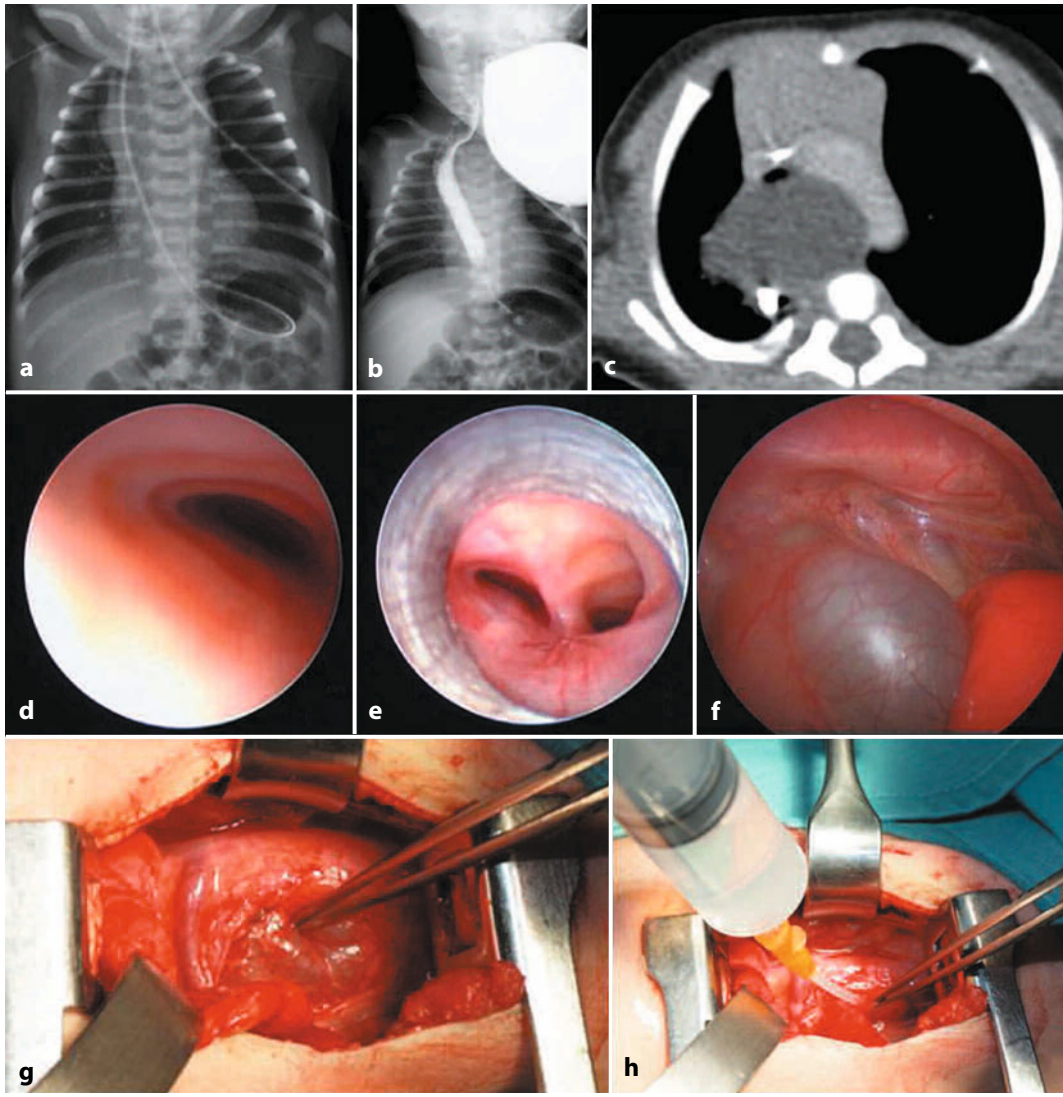

Fig. 24.3 Premature female infant with perinatal respiratory distress and vomiting due to a mediastinal cystic mass. After developing polyhydraminos during pregnancy, a Cesarean delivery was planned in a female fetus of g.a. 34 weeks. At birth, the baby developed respiratory distress and needed ventilatory support. The post-natal investigations were: ultrasound, radiography, contrast esophagography, CT and endoscopic procedures (esophagogastroscopy and tracheoscopy). A cystic mass (2.5×3.0×4.5 cm) was found in the posterior mediastinum (**a–c**). The left principal bronchus was displaced and occluded (**d–e**), which led to air trapping. The esophagus was pushed into the right thorax (**a–c**) and its lumen was compressed. The cyst was identified under thoracoscopic view (**f**) but conversion was required because of clinical instability and its large size. Complete resection of the cyst was possible after aspiration of the mucous fluid within it (**g–h**)

terior lesions [4]. The cysts appear as anechoic masses (if there is no bleeding) with a 2–3-mm wall formed by the mucosal and muscular layers. The inner mucus layer produces a characteristic echoic signal at the center of the cyst. This complex structure can be helpful in the differential diagnosis with other cystic lesions [3].

Radiography of the chest is the most used examination and is undertaken if the patient has respiratory symptoms. Radiography can be used to identify the lesions (radiolucent

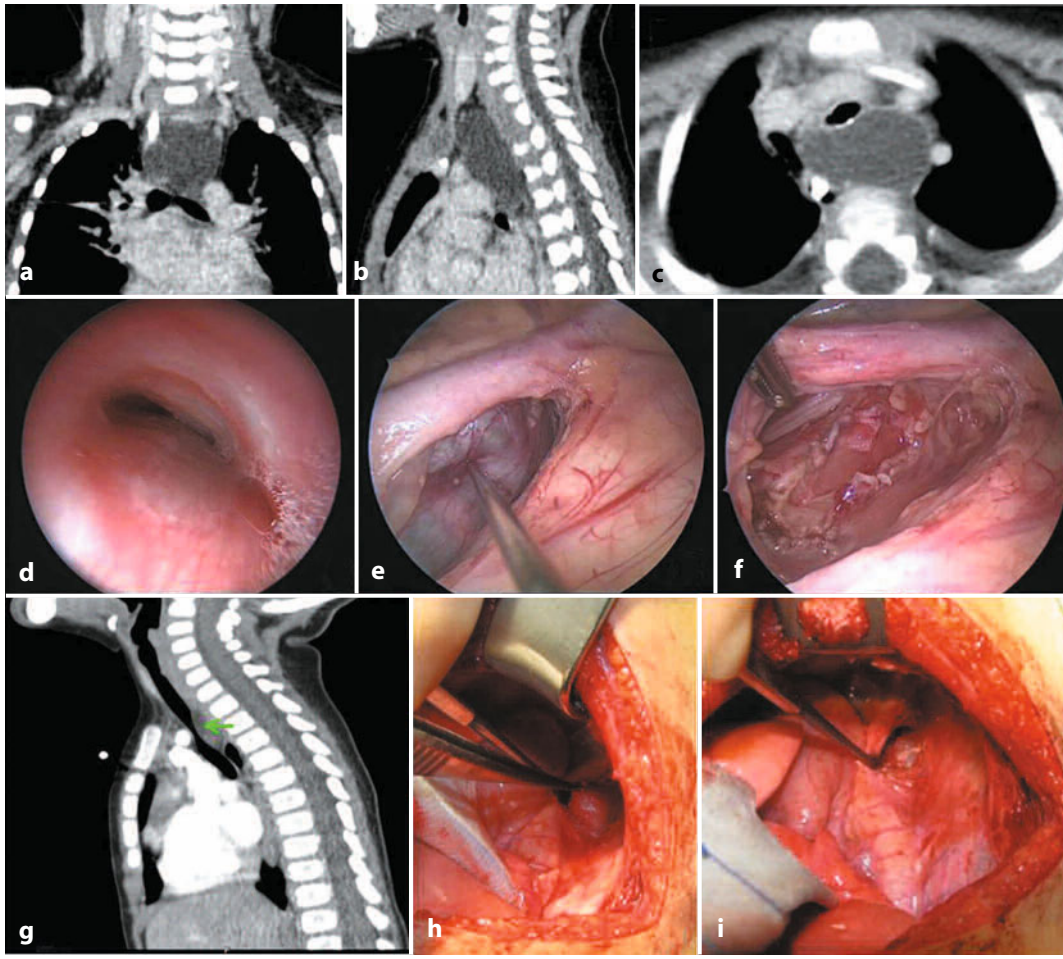

Fig. 24.4 Male infant affected by gastroesophageal reflux (GER), tracheomalacia and recurrent foregut duplication. Since his first days of life, the infant had several episodes of vomiting and dyspnea. He was diagnosed with gastroesophageal reflux disease. During radiological and endoscopic evaluations, a foregut duplication cyst was identified. CT (**a–c**) showed an oval fluid-filled mass (2×3×4 cm) in the posterior mediastinum that displaced the esophagus and the trachea, provoking a reduction of the size of their lumen (**d**). The mass was resected with a minimally invasive procedure. Five months later, the boy was admitted to hospital again for cough, stridor and dyspnea. A recurrent posterior mediastinal cyst was shown by CT. The fluid mass (*green arrow*; 1.4×2.0×2.0 cm) dislocated the esophagus and impinged the trachea (**g**). Open surgery allowed complete resection of the lesion (**h–i**)

masses above the diaphragm near the median line or clearly delineated masses at the level of the main carina) in >90% of cases [4]. Radiography can also be used to detect indirect signs of the presence of the cyst, secondary to the compression of adjacent structures by the mass (Fig. 24.1b).

CT and MRI are more accurate in the diagnostic process. These investigations show the anatomical features of the cysts and their relationships. They also allow three-dimensional reconstruction, which is useful preoperatively (Figs 24.2d–f). It is usually easy to distinguish these lesions from teratomas, cystic adenomatoid malformations of the lung and pulmonary sequestration. It is otherwise difficult to differentiate pulmonary abscesses because they both have wall reinforcement. CT and MRI can also be useful for evaluation of the abdomen and identification of abdominal cysts

(present in one-quarter of cases) [3]. MRI is the method of choice if spinal involvement is suspected. MRI is safe and non-invasive because it does not use ionizing radiation [3, 4]. The connections with the GI tract should be evaluated with contrast radiography, and they often require endoscopic evaluation that can also define extrinsic compressions (Fig. 24.1e). Scintigraphy with technetium 99m can identify ectopic gastric mucosa but is rarely used [10].

Differential diagnoses include conditions presenting with respiratory symptoms. These include post-infective pulmonary abscesses (that also have the radiographic features of bronchogenic cysts), bronchial asthma, pneumonia, pneumothorax (sometimes the pulmonary atelectasia obscures the duplication) as well as foreign bodies or vascular rings. Mediastinal masses should also be considered. The mediastinum is located in the central part of the thorax and delimited by the left and right parietal pleura (laterally), the sternum (anteriorly), the vertebral bodies (posteriorly) and the diaphragm (inferiorly). Anterior and superior mediastinal lesions can be lymphomas, teratomas, germ cell tumors, lymphangiomas, thoracic duct cysts, cystic hygromas and thymic cysts. A typical middle mediastinal cyst is the pericardium cyst. The posterior mediastinum can contain neurogenic tumors, meningoceles and foregut duplication cysts. Eventually, there are cystic malformations of the lung that can also be associated with foregut duplications ("hybrid lesions").

24.5 Management

Treatment of foregut duplications is surgical even in the absence of symptoms. It is thought that symptoms always arise sooner or later. In addition, they are associated with a higher risk of postoperative and intraoperative complications as shown in a study by St-Georges et al. In the adult population studied, clinical manifestations occurred in 82% of patients [11]. The prevalence of intraoperative complications increased up to 14% in these patients. Recently, the possibility of malignant degeneration of these lesions has also been described [2]. Moreover, complete excision permits the growing of lung parenchyma previously occupied by the cyst [12].

Over time, less invasive treatments have also been considered, such as sclerosing agents or simple aspiration of the cyst. However follow-up data for these patients are not available, and there are questions about the effectiveness of these methods [4].

Surgery should be undertaken when the clinical condition is stable. If complications are present, it is better to postpone the procedure. Infected cysts should be treated with a staged approach; it is important to primarily drain the cyst, treat the infection, and then return for definitive surgery [1–4]. The ectopic gastric mucosa can lead to acid secretion. These patients can have evident or occult bleeding, and they may benefit from the use of proton pump inhibitors [1]. The evaluation is completed with an upper endoscopy. Emergencies are rare. Instant surgical interventions are required in the presence of bulky masses that displace and compress the airways [3]. This condition is associated with respiratory distress and cyst decompression can be advantageous. Undertaking percutaneous puncture of symptomatic masses can threaten life. The emptying of the cyst should be done in the shortest time possible. Cyst marsupialisation, mucosal obliteration or cyst aspiration alone can be associated with a high risk of recurrence [2].

Open surgery enables removal of the cyst after posterolateral thoracotomy (Fig. 24.3). The patient lies on the right side if the lesion is in the middle esophagus or on the left if the lesion is in the distal esophagus or if it has an abdominal component [1]. The muscle-sparing technique provides for gentle separation and promotes rapid healing, along with a reduction of the risk of complications associated with classical thoracotomy. Resection should not involve the mucosa if the cyst does not communicate with the GI tract. The muscularis

layer is opened and later the margins are brought near again. When the lesion is removed, mucosal integrity is tested by air insufflation through a nasogastric tube. In some cases, it may be useful to introduce a flexible endoscope into the esophagus, whose light guides the process.

Over the last few years, there have been advances in minimally invasive surgery (MIS). MIS can also be used also in children thanks to the development of small instruments. Recent reports suggest that video-assisted thoracoscopic surgery (VATS) can be used to treat foregut duplications. VATS reduces postoperative pain and hospital stay and gives better esthetic results compared with standard thoracotomy incisions. The procedure permits identification of the exact localization of the cyst and to obtain information about its nature.

MIS also has therapeutic aims. The standard position during thoracic surgery is with the patient lying laterally on the operating table with the affected side facing upwards. The arm is raised above the head and the body rotated into a near prone position (because cysts are usually posterior). An axillary roll can be placed under the patient to obtain better exposure. The optic (5 mm/30°) is inserted inferior to the tip of the scapula. Lung collapse is obtained with low-pressure and low-flow of CO_2. Operating trocars (2 or 3 as appropriate) are positioned under vision to create a triangulation of instruments. When the mass is identified it should be prepared for dissection. Blunt dissection and cauterization are useful at this phase to expose the mass, which is usually easily isolated from the surrounding structures. The esophageal lumen must be preserved. This maneuver is not always easy, especially if the cyst and the GI tract are very close together. Esophageal duplications usually involve the esophageal submucosa, and their removal may leave a defect in the muscularis mucosae. The need to suture the esophageal wall at the end of dissection is controversial. The outer layers of the esophageal wall can be just approached if the mucosa is intact. Nevertheless, this maneuver may predispose to the formation of a pseudodiverticulum [2]. The defect in the esophageal mucosa (if there is one) should instead be repaired with wire-absorbable sutures. If the cyst is too large to be removed in its entirety through one of the ports it is advisable to puncture the mass to empty it. It is not recommended to carry out a small thoracotomy because it is rarely necessary [3, 10]. Decompression of the cyst is useful to ensure the best view. In this way, severe cases with mediastinal shift or abnormal locations (e.g., under the main carina) are not a contraindication to the execution of VATS. Difficult cases can be converted to a thoracotomy [2]. According to Bratu et al., the magnification provided by thoracoscopy is advantageous for the complete and meticulous excision of the cyst [2]. After the mass is resected (a stapler is helpful for this purpose in older patients) it can be removed *via* a port site, and the operative field should be inspected for hemostasis [10]. If the borders of the cyst cannot be removed entirely without leaking into the esophagus or the airways, they can be left and ablated using electrocauterization. The utility of placement of a drainage tube is questionable. After the removal of central mediastinal lesions, lesions of the thoracic duct may result [2].

A special mention should be made for cases with spinal or abdominal components. Thoraco-abdominal cysts are rare. They include lesions that cross the diaphragm and enter the abdomen. Communication with the GI tract can occur above and below the diaphragm. Connections with the stomach, duodenum, jejunum, ileum or pancreatic duct are possible. The surgical approach is twofold (thoracic and abdominal) and occurs in one or multiple stages [1].

Neuroenteric cysts (cystic lesions with an intraspinal component) are very rare and require a multidisciplinary approach (including a neurosurgeon). The mortality in these cases is very high. The first step consists of the removal of the intraspinous portion of the cyst (usually through laminectomy). Leaving the

neural portion can lead to meningitis and postoperative swelling. Recently, it was proposed that these lesions can be treated by robotic-assisted thoracoscopic surgery (RATS). RATS appears to achieve excellent vision of the operative field, a greater range of motion, and more precise and targeted movements with tremor filtration and motion scaling [13].

24.6 Outcome and Follow-up

The mortality related to the foregut duplications is greatly reduced thanks to early diagnosis and treatment. The outcome after surgery is, in general, excellent and the prevalence of recurrence very low (Fig. 24.4) [14].

Possible complications can be prevented by taking simple precautions. The complications related to thoracic surgery are pneumonia, wound infections, pain, pulmonary edema, arrhythmias, pneumothorax, pleural effusion and nerve injury (vagus nerve or phrenic nerve). Late musculoskeletal complications are related to the thoracotomy incision and decreased after extended use of MIS. Thoracoscopy also allows good control of pain through the intravenous and oral administration of painkillers. Respiratory physiotherapy should be initiated early and is helpful in preventing the onset of pneumonia and atelectasis. Excision of the mass is associated with esophageal and bronchial lesions or recurrences that are described in long-term follow-up, especially if the removal is incomplete. If an esophageal leak is suspected, the patient should undergo contrast radiography and a chest drain should be left. A chest drain is also useful for the identification of air leaks, which are usually self-limiting.

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Pneumothorax and Pneumomediastinum

25

Marcello Dòmini and Mario Lima

25.1 Pneumothorax (PNX)

PNX is a collection of air in the pleural cavity which leads to crushing of the lung and its consequent collapse [1]. Lung collapse may be partial or total and in some hypertensive forms it can also lead to the shift of the mediastinum towards the opposite hemithorax. PNX can be classified into four main groups [2]:

- spontaneous: with no apparent cause;
- secondary: the result of an underlying disease that may lead to the rupture of one or more pulmonary alveoli;
- iatrogenic: as a consequence of medical or resuscitation maneuvers that may cause air leakage from the lung;
- traumatic: caused by direct trauma to the open or closed chest.

A further distinction is based on the possible communication between the chest cavity and the external environment. It is of great importance, especially in the case of post-traumatic or iatrogenic PNX, and three forms can be recognized: closed, open or valve.

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25.1.1 Etiology and Pathogenesis

Spontaneous PNX (i.e., with no obvious underlying cause) is relatively rare in children [2]. It has a bimodal distribution by age with two peaks: one in the neonatal stage and the other during late adolescence [3]. The newborn may manifest PNX in three conditions.

- The first condition is spontaneous PNX. Spontaneous PNX occurs soon after birth (1% of births) due to the high transpulmonary pressure exerted during the first breaths. In addition, it is symptomatic in just 10% of cases (0.1% of newborns). It is nearly always normotensive and tends to resolve spontaneously (in the case of persistence or an increased need for drainage) [1, 2].
- The second condition is PNX during respiratory distress. Uneven alveolar ventilation, air trapping and lung hyperinflation lead to rupture of the alveoli with air accumulation inside the pulmonary interstices first and then inside the pleural cavity. It tends to restock and it is often hypertensive and drained (during mechanical ventilation PNX should always be drained).
- The third condition is PNX after attempts at central venous catheter (CVC) placement beneath the clavicle. In this scenario, puncture of the lung parenchyma occurs.

In the adolescent, spontaneous PNX is instead related to growth. The subjects most affected are mainly lean and apparently

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healthy. In this group, development has led to a rapid vertical growth of the chest as opposed to horizontal growth [1–3]. This discrepancy is responsible for an increase in the negative pressure at the apex of the lung that leads to the formation of subpleural bubbles (also air–fluid) which, once broken, will cause PNX.

25.1.2 Clinical Features

Air flow inside and outside the lungs (i.e., ventilation) is due to pressure gradients between the alveoli and the external or atmospheric air. Inspiration occurs if the atmospheric pressure is greater than alveolar pressure, causing a pressure gradient that moves the air inside the alveoli. Exhalation occurs if the pressure in the alveoli is greater than the atmospheric pressure, and this is considered to be a passive process because it does not require muscle contraction.

PNX leads to partial or total collapse of the lung parenchyma. If the lung collapses completely, intrapleural pressure is balanced with that of the atmosphere, and this pressure balance prevents the air entering the lungs *via* the airways from moving freely. This in turn disturbs the capacity of alveolar gas exchange because, as mentioned above, normal breathing occurs only if atmospheric and intrapulmonary pressures are different. This then results in breathing difficulties, which are proportional to the degree of PNX up to the point that it could turn into acute respiratory failure, so that the clinical manifestations are those of different degrees of dyspnea.

25.1.3 Diagnosis

PNX is diagnosed by chest radiography (Fig. 25.1). With large pneumothoraces, radiographic identification is easy. In many cases there is associated medial herniation of the pleural space across the anterior mediastinum, a finding that is especially useful in the identification of anterior PNX. In infants and toddlers, because they are lying flat, the free air collection is anterior to the lung. Confirmation of PNX can be obtained with lateral views.

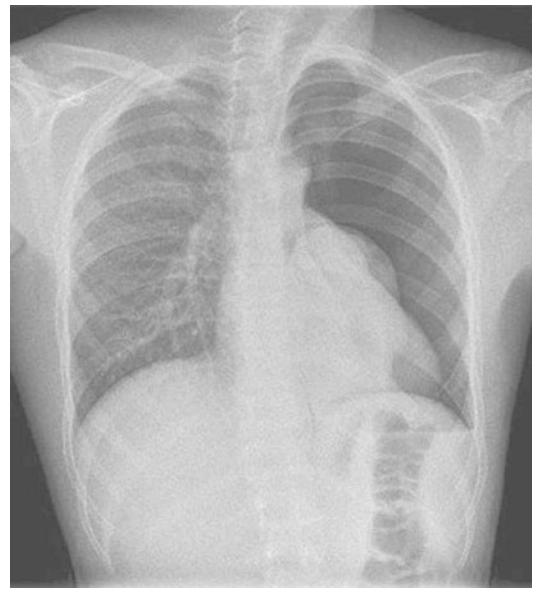

Fig. 25.1 Left massive PNX

Lesser-volume PNX is more difficult to identify. Knowledge of all areas of potential air collection is extremely helpful if a free lateral lung edge is not visualized. If a PNX collects medially the findings must be differentiated from pneumomediastinum (PM) or pneumopericardium (PE).

Patients in the scholar age with spontaneous and recurrent PNX must be evaluated with computed tomography (CT) (Fig. 25.2) to exclude a cystic lesion of the lung. Most patients with large cysts are usually detected in the prenatal age or present with respiratory distress in the neonatal period or shortly after. However, those with smaller lesions may present later because symptoms may take years to develop.

25.1.4 Management

Chest drainage is designed to restore ideal conditions in the pleural space by removing

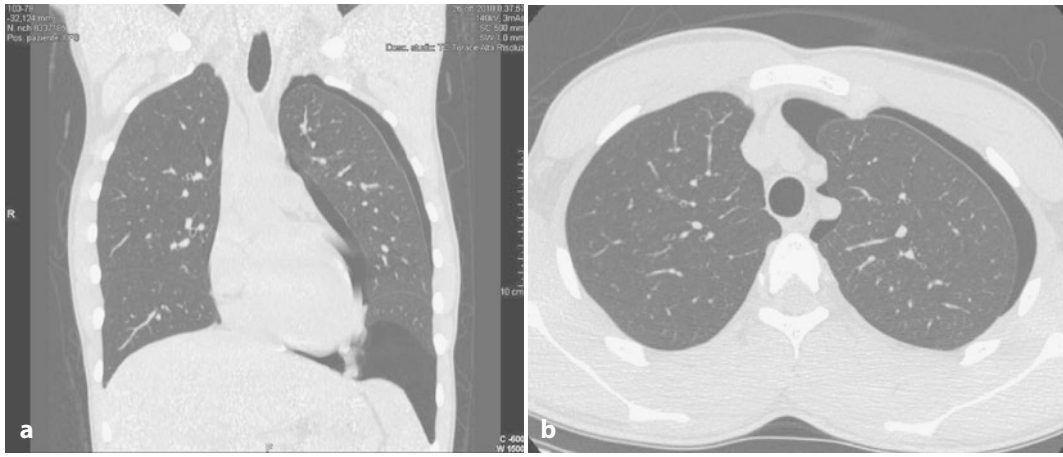

Fig. 25.2 Left PNX with thickening of the dorsal thoracic pleura of the inferior lobe. No pulmonary parenchimal lesions. At the apex of both lungs parenchimal air bullae can be observed (two in the right lung and one in the left one)

the causes of breathing difficulties (PNX, PE). The equipment for chest drainage is:

- drain tube with trocar for the insertion of different sizes (Fig. 25.3);
- Pleur-Evac®-type intake system;
- drainage and Pleur-Evac connection set;
- number 11 disposable scalpel blade;
- needle-holder, Klemmer-type forceps, sterile surgical forceps and scissors;
- sterile drape;
- 3-0 and 4-0 nylon sutures.

The type and location of the drainage tube will vary depending on the material (air or liquid) that needs to be drained from the pleural space. The air tends to collect upwards, the liquid downwards, so the drainage tube for a PNX should be directed towards the apex of the chest cavity and anterior part of the lung. *Vice versa*, for drainage of liquid collections, the drainage tube is directed to the diaphragm and the back of the lung. For children aged <1 year, who are predominantly in a supine position, directing the drainage tube anterior to the lung for the PNX and to the posterior in PE cases is sufficient.

If the collection inside the cavity is hematic or serous, the drainage tube must be larger to prevent the tube becoming clogged up by clots. If only air must be drained then a smaller-diameter drain can be used.

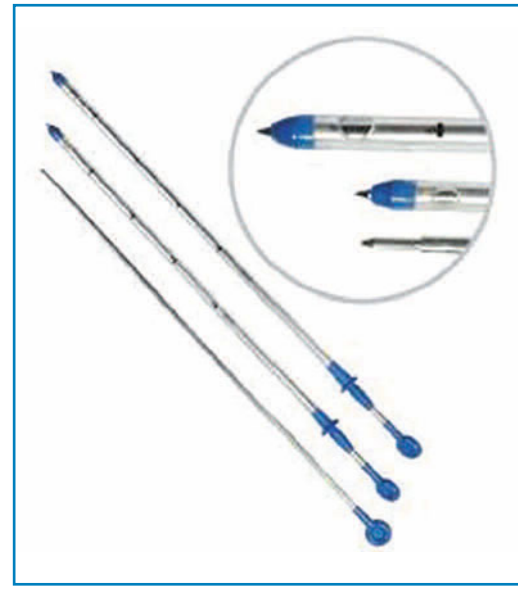

Fig. 25.3 Drain tubes with endoluminal trocar of different sizes. From [13]

25.1.4.1 PNX drainage

Patients must be distinguished according to their age and PNX severity. The first measure to be taken in case of a hypertensive PNX that causes an acute respiratory crisis is to remove the air from the chest as quickly as possible [2]. To achieve this it should suffice to insert a percutaneous type-18 Abbocath Ch venous catheter into the chest or a large needle attached to a

three-way stopcock and two 50-cm^3 syringes with which air will be drawn out repeatedly. During this extemporaneous procedure, conducted in an emergency, the nursing staff can prepare the equipment for the chest tube. Once all the equipment is ready, the needle will be removed, the patient will be examined and chest raiography will be done. After PNX has recovered a drainage tube using standard methods will be placed as described below.

The pleural drain can be placed along the mid-clavicular line in the second or third intercostal space [2], or in the axillary region in the third or fourth intercostal space along the mid- or rear axillary line. The choice of an intercostal space lower than the fifth intercostal space should be supported only by positioning *via* guided ultrasound or treatment to prevent injuries to the diaphragm or viscera immediately below (liver and spleen first and foremost). The choice depends on: patient age; the personal preferences of the operator; esthetic considerations (the axillary line is covered and recommended, especially for female patients); material to be drained (air alone, or air combined with effusion); and drainage management. Sometimes, if the collected material is mixed (air–liquid) it may be necessary to place two different drainage tubes.

Normally, if possible, the tube is placed along the anterior axillary line at the fourth intercostal space [2]. The skin incision for the entry hole can also be made in the intercostal space below, taking care to insert the drain through the chest wall in the upper space. This creates an inclined passage that helps to reduce the risk of accidental removal of the tube, as well as reducing other risks related to the entry of external air from around the drainage tube.

After local anesthesia, a skin incision is made ≈1–2 cm in the middle of the lower rib of the chosen space. Once the costal level is reached, the Klemmer curved forceps are introduced until the top edge of the rib is reached. Then, by blunt dissection through the muscle fibers, the pleural level is reached. After having created a space with the forceps, we insert the tube with a spindle, and by thrusting (keeping the index finger of the hand holding the drain against the chest wall to avoid sudden penetration of the chest with the spindle for a distance greater than its tip) (Fig. 25.4) we can penetrate the chest. At this point, the characteristic noise of air entering the chest

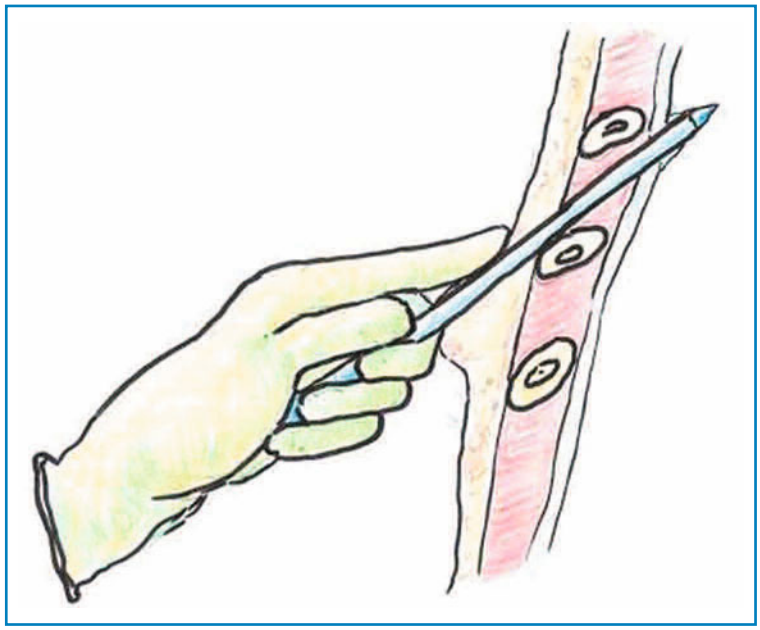

Fig. 25.4 Correct and safe way to hold the trocar. Note the index that reduces the risk of entering too deep with the sharp tip into the thoracic cavity provoking injuries to the lung, the heart or great vessels. From [13]

can be heard. Then the tube is directed up or from the back (depending on the drainage purpose). The rubber part is advanced up until the sign that had been previously chosen, taking into consideration the size of the child and the length of the drain; it is better to exceed slightly with the introduction of the drain and, if it is the case, to retract it after the RX control. This way a correct positioning is gained more easily. If too a little part is inserted, one has to insert the drain more after the X-ray, some minutes later, when the external part is no longer sterile.

Once the tube is placed and the spindle extracted, the junction is connected to the water valve and the wound is sutured with a non-absorbable suture so that it is closely adherent to the tube diameter. By means of a second non-absorbable stitch we make sure that the tube is attached firmly to the skin to avoid accidental removal ("spartan suture"). With a non-absorbable third stitch we place a "tobacco pouch" suture with which we close the drainage access hole definitively once the drain has been removed.

Once this has been done the wound is medicated, making sure to patch the tube to the skin and carry out chest radiography to check the position of the drain. Drains are made of polyvinyl chloride (which is radio-transparent) or silicone (which is radio-opaque), usually with a radiologically visible filament) (Fig. 25.5).

During all these procedures, while the drain is connected with the intake system, it is advisable to keep it clamped to prevent accidental introduction of external air through it.

25.1.4.2 PE Drainage

As mentioned above, because the liquid tends to collect downwards, the PE drain tube should be positioned from the posterior direction or possibly with the tip pointed towards the diaphragm. The rest of the maneuver is almost identical to that of placement of the drain for PNX drainage, possibly choosing the intercostal space to be underneath the one that would be used in PNX cases. It is also useful to execute the maneuver under ultrasound guidance.

With pleural empyema the simple chest tube is not decisive. If an empyema is established, the thoracic effusion is "organized" with the formation of fibrin agglomerates closely adherent to the parietal pleura. Very often the positioning of the drainage tube does not lead to leakage. If this occurs, the only possibility is video thoracoscopy. Video thoracoscopy is a minimally invasive surgical technique that allows for the removal of pleuroparietal adhesions. To flush the pleural cavity abundantly with the best possible bath for the pleural space, one (preferably two) chest tubes (apical and basal) under direct vision should be positioned [1, 2].

Closed suction system: Once it has been inserted, the chest tube must be connected to a collection system for draining the air or fluid from the pleural space. The basic requirement is that it must be unidirectional to prevent air or fluid going up into the pleural cavity accidentally (i.e., it is a closed circuit).

The concept of the closed suction system was established in 1872 when Playfair used a water valve to prevent air from going up into the chest through the drainage tube. However, the "father" of the modern chest drain is Gothard Bulau. The system of several bottles which he designed in 1891 still bears his name. He was the first to include the operation of negative pressure within the pleural cavity and to understand the importance of not avoiding contact between this and atmospheric pressure, thereby describing pleural empyema drainage by siphoning. It was during the Second World War that chest drainage and thoracentesis replaced thoracotomy which, until then, was largely routine for chest injuries.

Three elements have a fundamental role in the various types of closed drainage systems: gravity, positive pressure and suction.

- gravitational force causes the passage of air and liquid from a higher pressure level to a lower one. Hence, drainage should be in a lower position than the patient's chest to prevent the return of the drained material and the consequent risk of infection;
- drainage combines a higher pressure area

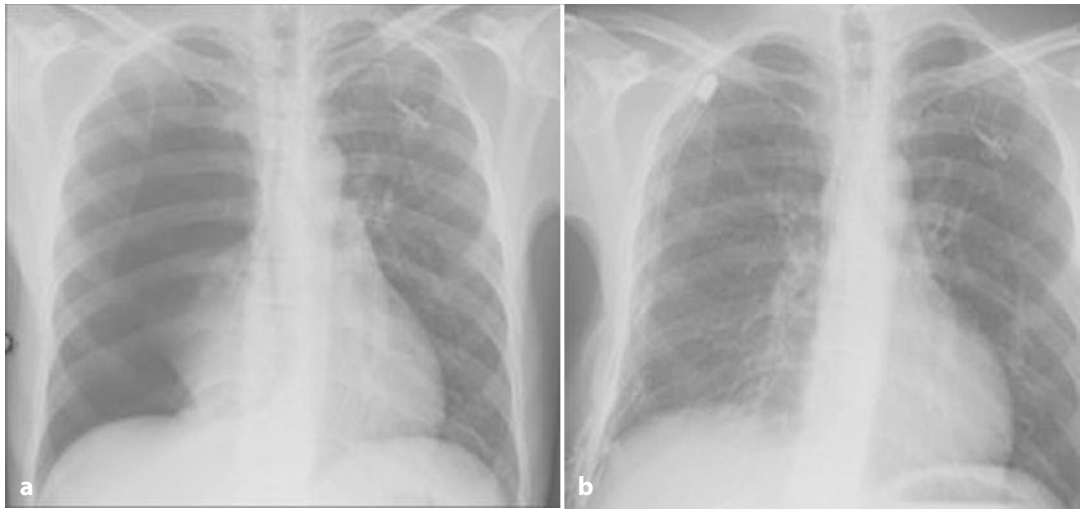

Fig. 25.5 a Right PNX; **b** quite complete resolution of the radiographic picture after the insertion of the drainage. From [13]

created in the pleural cavity due to the pathological presence of air or fluids (>762 mmHg) with a lower pressure (761 mmHg) so the material to be drained passes from the positive pressure area to that of lower pressure;

- addition of a suction system ensures a faster and more effective evacuation of gas and fluid.

The categories of collection systems which we referred to previously invented by Bulau are classified as the one-, two- or three-bottle methods. Glass bottles are used very rarely. Instead, there is another compact system, Pleur-Evac, named after the first manufacturer that made this system available on the market. However, the operating principle is the same as for the Bulau bottles.

In the one-bottle method (also called the "drop method"), the chest tube is connected to a drop tube that ends in a jar containing sterile distilled water. The cap that seals the jar is fitted with two stiff tubes. The first is a long tube, connected to the tube that goes to the patient, whose distal end is immersed in ≈2 cm of the distilled water at the bottom of the jar (which prevents further entry of air into the chest). The second is a shorter tube connected to the external environment, which allows air to escape from the evacuated pleural space and to be collected in the same bottle (Fig. 25.6).

The draft creates an evacuative one-way mechanism called a "water valve", which is essential for the removal of air and fluid in all the chest drainage systems used. This system serves three purposes, it: (i) ensures a unidirectional path for gas and fluid flowing from the thoracic cavity to the outside and not *vice versa*; (ii) ensures the display of air leaks; (iii) re-establishes a pressure difference between the chest cavity and the external environment.

During exhalation, when the pleural pressure becomes positive, the pressure in the immersed tube also becomes positive; if the pressure inside the tube is greater than the height of the immersed tube, the air or liquid penetrates the jar. During inspiration, when the pleural pressure is negative, a small quantity of liquid goes up into the immersed tube, without air return. The importance of this rise indicates endothoracic inspiratory depression, especially if the tube is equipped with a graduated scale (calibrated in centimeters), it becomes like a "pressure gauge" capable of measuring intrapleural pressure. These changes in pressure during respiration are responsible for fluctuations of 5–10 cm in the water valve column,

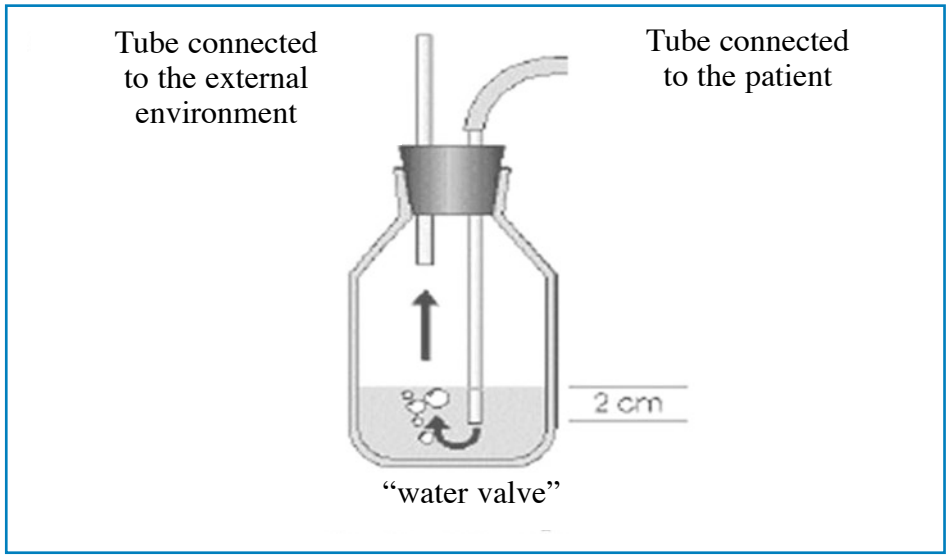

Fig. 25.6 The Bulau "one-bottle method". The distal end of the chest tube is immersed in 2 cm of distilled water, a second tube is connected to the external environment. Modified from [13]

and show correct functioning of drainage and the patency of the tube.

It is necessary to keep the immersion of the water valve connection at a level of 2–3 cm. If it is barely immersed (for instance, if the bottle is tilted while moving it) there is the risk of rising air. If it is over-immersed, a hydrostatic counter-pressure will occur, which will hinder the drainage of the pleural cavity (a phenomenon that also occurs with large amounts of drained material). The bottle should always be placed on the floor ≥40 cm below chest level because the gravitational force largely contributes to adequate drainage of the pleural space.

The two-bottle method always features a water valve chamber, complemented by a jar for liquid collection. The operation is similar to that for the one-bottle method, but in this case the valve system is not affected by the drained liquid (Fig. 25.7). Its use is advisable, especially for the drainage of substantial effusions. Its major drawbacks are the result of it being cumbersome (problematic for deambulation of the patient), and the large dead space.

The three-bottle method is similar to that of the two-bottle method. The addition of a third bottle allows control of the amount of aspiration. It is used if it becomes necessary to apply suction to drain significant air leakage (e.g., in the event of pulmonary resection or traumatic lung lesions).

The drained fluid from the pleural cavity flows directly into the collection chamber. The air then passes into the second bottle with the water valve, where bubbles are formed. Thanks to the connection in series between the second and third jar, the drained fluid reaches the third bottle, where it is evacuated through the suction system (Fig. 25.8).

The third bottle added to the drainage system limits the negative pressure transmitted to the patient's chest. It consists of: (i) a control tube, graduated, open to the external environment, passing through the cap of the bottle and immersed in sterile water to a depth of ≈20 cm; (ii) a shorter tube connected to the water valve bottle; and (iii) a tube that connects the third bottle to the suction source. Accurate adjustment of the aspiration level is required because if it is too high it may cause hematoma formation at the point of catheter insertion or invagination of tissue in the fenestrations of the drain tube.

In the three-bottle method, the maximum level of suction applied to the chest corre-

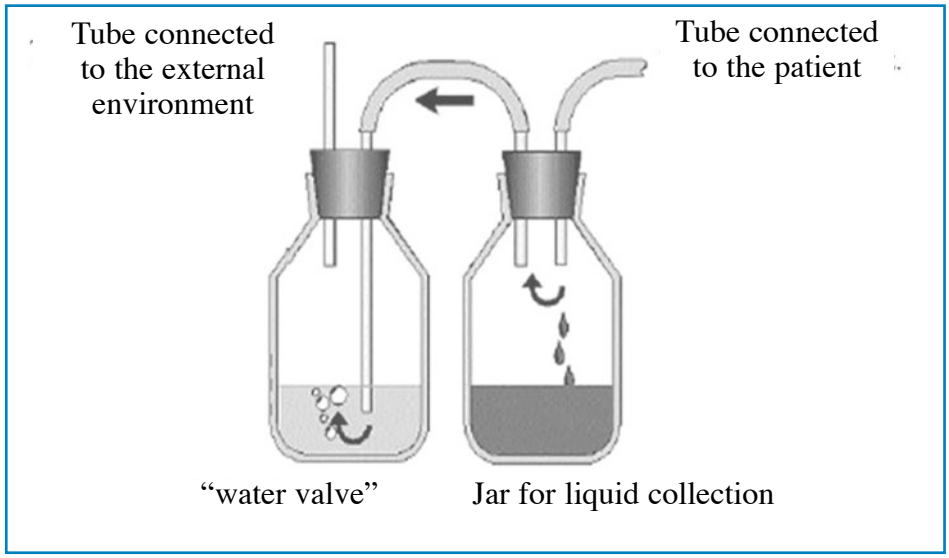

Fig. 25.7 The Bulau "two-bottle method". The concept is similar to that of the one-bottle method, but the valve system is not affected by the drained liquid. Modified from [13]

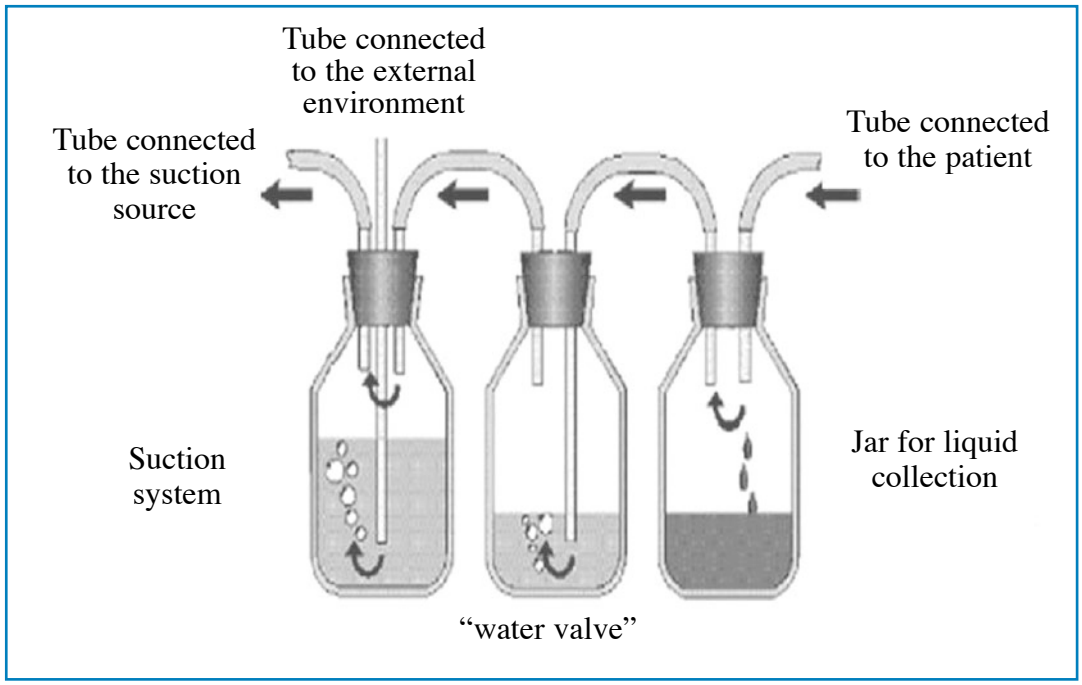

Fig. 25.8 The "three-bottle method". The addition of the third bottle control the amount of aspiration. Modified from [13]

sponds to the tube immersion depth: if the latter is immersed by 20 cm, the aspiration level will correspond to 20 cm of water. The central tube immersed in water therefore enables adjustment of the suction source applied to the pleural cavity. If the applied pressure is greater than the tube immersion depth, external air will enter the third bottle, forming bubbles in the liquid and balancing the pressure inside the jar.

The three-bottle method has been replaced by the sterile disposable device Pleur-Evac. It has the advantages of being less bulky, single-use (no need to empty the collection), unbreakable, compact, lightweight, as well as easy to move and operate [4]. It can be positioned on the floor or suspended next to the patient's bed, allowing accurate measurement of collected volumes without requiring maintenance during drainage. It also has dual protection against high positive or negative pressures.

The chambers of this device are equivalent to the traditional Bulau three-bottle method. They include a graduated collection chamber that measures the drained volume more accurately, a second chamber with a water or mechanical valve, and a suction chamber controlled by a water or mechanical control device (Fig. 25.9).

The collection chamber allows for the easy and accurate reading of the drained fluid. The nurse can record variations on a daily basis with a line inserted into a chart that indicates the time of the reading. Hence, any operator can assess (in real-time) the evacuated fluid from the chest during the postoperative hospital stay.

Fig. 25.9 The compact sterile disposable device Pleur-Evac has replaced the Bulau system. The chambers of this device are equivalent to the traditional three-bottle method (courtesy of Teleflex)

The water valve chamber is connected to the water collection chamber and ensures the unidirectional nature of the system. Pleur-Evac is also a diagnostic tool: the narrow tube is calibrated as a water manometer to measure variations in endopleural pressure. The drainage units are equipped with a protection device against high and negative pressures. They are equipped with an "anti-siphon valve". This is a floater at the top of the second chamber that protects the water chamber in the event of the tubes being squeezed or milked, thereby avoiding reflux in the collection chamber. Along with this valve there is an additional security system: a manual valve for high negative pressure. This valve enables evacuation of negative pressure through a temporary opening to the external atmosphere.

The suction control chamber is equivalent to the third bottle in the Bulau system. In the water-control system, the pressure suction is created by the height of the water column, usually regulated (as indicated above) at ≈20 cmH_2O. The third chamber, just like the second, has a "U"-shaped tube in which the shorter arm is connected to the external environment whereas the larger arm contains the water column. The total negative pressure transmitted to the patient is determined by the height of the water column in this chamber and not by the wall suction level.

The Thopaz drainage system (Medela AG, Baar, Switzerland) is a new compact digital reusable device that is not connected to the vacuum aspiration of the room's wall, and this feature gives the patients an unrestricted mobility. It makes the bed restriction unnecessary, permitting the early patient mobilization. Based on the patient's air leak, regulated negative pressure is applied close to the chest. A digital display shows actual and long-term data in real time as well as a 24-hour graph or the

Fig. 25.10 The Thopaz digital drainage system (courtesy of Medela AG). It permits the early patient mobilization. A digital display shows data and allow decisions in chest tube management by healthcare

air leak for easy tracking of therapy progress and timely and objective decisions in chest tube management (Fig. 25.10). In case of apical bullae, a segmental resection of the lobe can be done. The operation can be performed using a thoracoscopic approach using a stapler to resect the segment of the lobe (Fig. 25.11).

25.2 PM

PM, also known as mediastinal emphysema, is characterized by extraluminal air in the mediastinum [5.6]. PM, albeit very rarely, can be caused by various medical conditions and can often be accompanied by PNX, PC, pneumoperi-

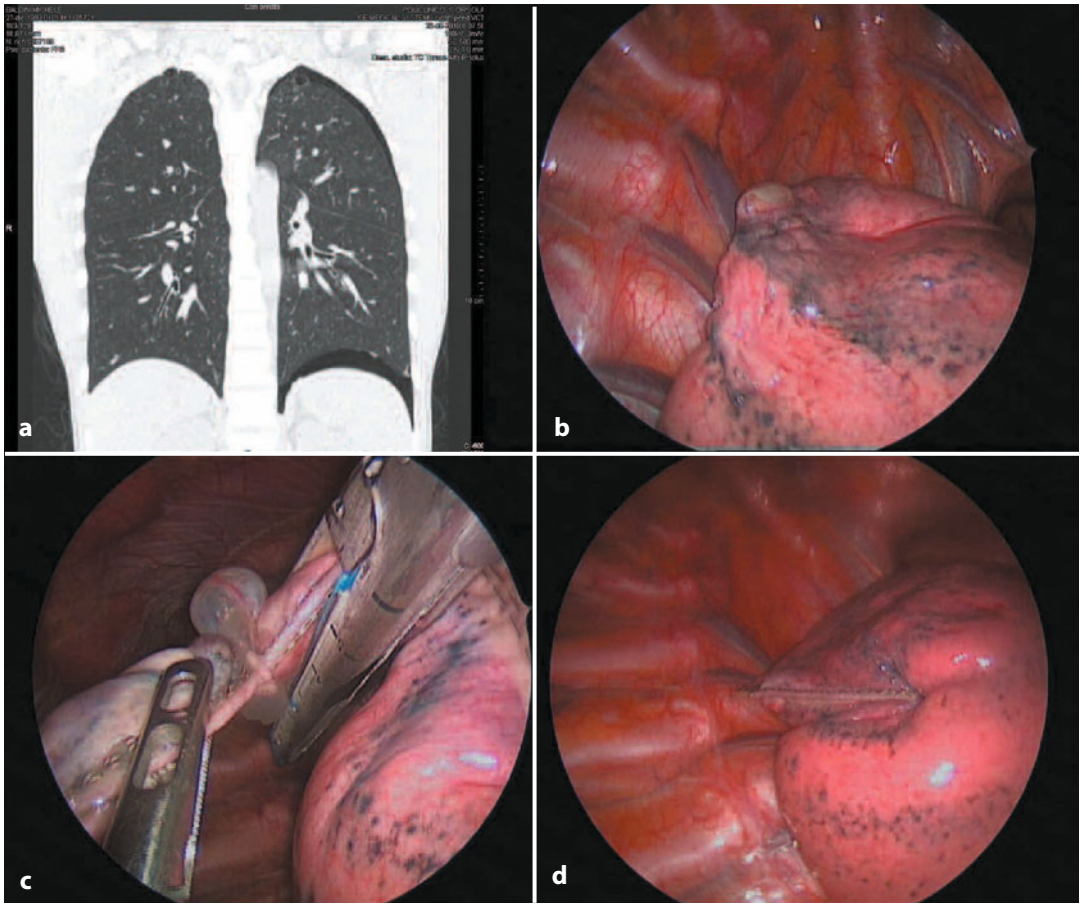

Fig. 25.11 a CT of subpleural apical bubbles complicated by pneumothorax; **b-d**, thoracic apical pulmonary resection

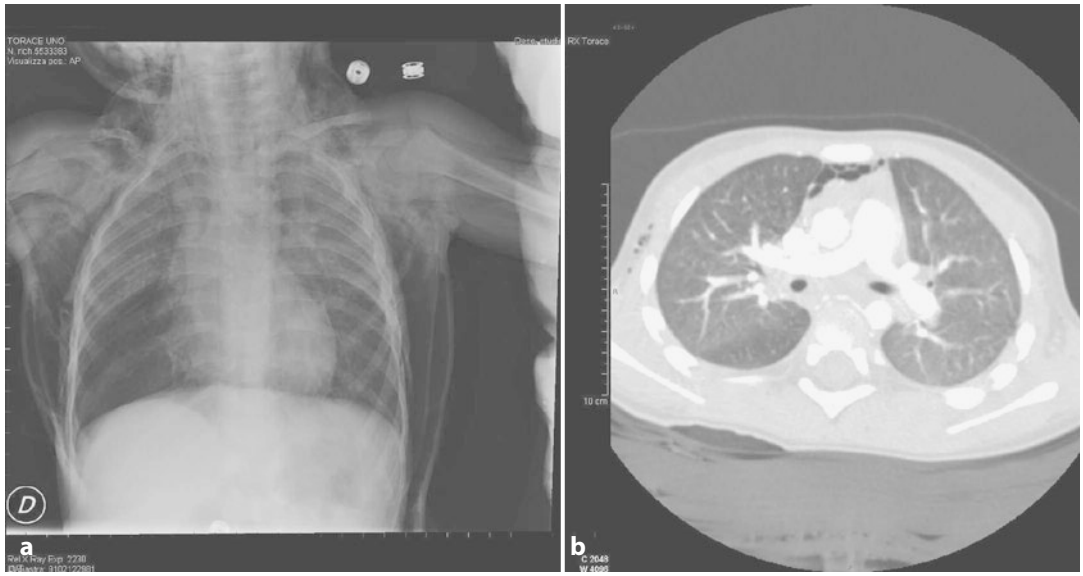

Fig. 25.12 a X-ray of left pneumothorax with pneumomediastinum; **b** CT of the pneumomediastinum

toneum or retropneumoperitoneum.

The air may collect in the mediastinum due to alveolar rupture, lacerations of the tracheobronchial tree, gastrointestinal (especially esophageal) ruptures, or direct passage through the cervical region, the retroperitoneum or the chest wall [7, 8].

25.2.1 Etiology and Pathogenesis

The most common cause is the rupture of alveoli, which occurs if there is high intra-alveolar pressure (obstruction of the airways, mechanical ventilation), or it may be due to lesions in the alveoli wall (pneumonia, emphysema, respiratory distress). Tracheobronchial lesions or perforation of the esophagus wall (spontaneous or iatrogenic) are less common causes of PM. Air can enter the mediastinum also from the head and neck (facial fractures, laryngeal injury, tracheostomy) [5].

PC is usually a result of penetrating trauma or cardiac surgery. It can rarely be caused by the same mechanisms that cause PM but in this case much higher pressures are required. However, it arises with PM [7].

25.2.2 Clinical Features

PM is usually asymptomatic. It can rarely cause chest pain or dyspnea. Stretching of the mediastinal pleura due to PM can lead to PNX. In exceptional cases, mediastinal pressure may be such as to lead to unconsciousness or hypotension due to decreased cardiac venous return [9].

At times, PM is the first clinical manifestation of a pathological disorder arising in the mediastinum. In this case surgical exploration of the abdomen is not advisable unless it becomes necessary in cases of doubt [10].

25.2.3 Diagnosis

PM is diagnosed directly by an experienced radiologist using chest radiography [7, 11]. It shows characteristic signs caused by the abnormal distribution of the gas formed around the organs in the mediastinum (Fig. 25.12). Free extrapleural air at the lung apex can easily be confused with PNX, as can back sternal PM extension. It is always useful to carry out chest radiography in two projec-

tions. Pneumomediastinal air collections tend to elevate and outline the thymus gland, whereas with PC air usually surrounds the heart (including the inferior aspect) and the pericardial sac is visible as a white line. These differentiating points are very useful if bilateral medial PNX occur.

Thus, we can identify a continuous diaphragm sign (air between the diaphragm and heart), Naclerio's V sign (the air draws the lateral margin of the descending aorta, predominantly but not specifically, in the case of esophageal rupture), the ring sign around the artery (air that surrounds the extracardiac mediastinal portion of the pulmonary artery), the extrapleural air sign (rounded air bubbles between the parietal pleura and diaphragm) and the spinnaker sign [7, 12]. A chest CT may be required to resolve diagnostic uncertainty [7].

Note The contents of this chapter are partially based on *Drenaggio pleurico e mediastinico nei versamenti pleurici e nello pneumotorace* (Lima M, Dòmini M, Gregori G, Randi B) in: Mirabile L, Baroncini S (2012) Rianimazione in età pediatrica, Springer, Milan, pp 599-611.

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Part VI

Chest Wall

Malformations of the Chest Wall

26

Michele Torre, Giovanni Rapuzzi, Patricio Varela and Vincenzo Jasonni

26.1 Introduction

Chest-wall malformations (CWMs) have a relatively high incidence and an unsuspecting impact on the quality of life of patients. Besides a minority of symptomatic cases, most patients seek medical advice for psychosocial concerns. These concerns can be severe, and are usually due to: poor cosmetic appearance; aversion to undertaking sporting activities: aversion to being seen in public.

CWMs are often misdiagnosed or neglected by physicians, thereby resulting in a significant delay or mistakes in the diagnostic work-up or management. Since the introduction of the Nuss technique for pectus excavatum (PE) [1], however, interest from the scientific community about CWMs has increased dramatically.

CWMs are represented by a wide range of malformations; some are very well defined and others are part of a wide spectrum of deformities. However, the literature relating to their nomenclature and classification is confusing. In our opinion, the classification is of paramount importance because of the treatment implications. Other controversial issues are the treatment options: many surgical techniques or other therapeutic alternatives have been proposed (especially in the last decade), so it can be difficult for a pediatrician (or even a surgeon) to advise patients about the possible correction techniques. In this chapter, we describe the different types of CWMs, their diagnosis and treatment and classify them into four types according to their embryology (Table 26.1).

26.2 Type I: Cartilaginous Anomalies

26.2.1 PE

26.2.1.1 Epidemiology

PE is the most common thoracic malformation, with an incidence of about 1/300 live births, and represents 90% of all CWMs [2, 3]. PE is characterized by the presence of a sternal depression associated with a malformation of the lower condrosternal joints.

26.2.1.2 Etiology and Pathogenesis

In most cases PE occurs during or after the pubertal spurt (though it can occur in a neonate). Older patients can have a association with malformations of muscular connec-

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Table 26.1 Modified version of the Acastello classification of chest-wall malformations according to their embryologic origin

Type I: cartilaginous	PE PC type 1 True PC type 2	
Type II: costal	Simple (1 or 2 ribs)	Agenesis, hypoplasia, sovrannumerary, bifid, fused, dysmorphic, rare (always complexes)
	Complex (≥3 ribs)	
	Syndromic (always complex)	Jeune, Jarcho-Levin, Cerebrocostomandibular, others
Type III: chondro-costal	PS	
Type IV: sternal	Sternal cleft (with or without ectopia cordis) CS syndrome	

PE, pectus excavatum; *PC*, pectus carinatum; *PS*, Poland syndrome; *CS*, Currarino–Silverman

tive tissue, such as the Marfan and Ehlers–Danlos syndromes [2–6]. The etiology of PE is not clear, and many hypotheses have been proposed [5]. Deficiencies in vitamins or nutrients are probably not involved, but disorders of connective tissue and genetic predisposition could have a role [6]. Overgrowth of costal cartilage could be the pathogenetic mechanism leading to the development of PE [2, 5]. Examination of costal cartilage has demonstrated type-II collagen in PE patients, as well as overexpression or downregulation of collagen genes, matrix metalloproteinases, tumor necrosis factor-alpha, and filamin [2]. Forty percent of cases are familial [5]. Moreover, PE patients can have siblings with other CWMs, such as pectus carinatum (PC). The main transmission pattern seems to be autosomal dominant, but families with autosomal recessive and X-linked patterns have been documented [7].

26.2.1.3 Clinical Features

Often, PE patients are tall and slim, with some degree of joint laxity, a kyphotic habit with rounded shoulders and a "pot belly" [4]. In fact, 15–50% of cases have associated spinal deformities such as scoliosis or kyphoscoliosis. These malformations are often mild and usually do not require treatment. Apart from prolapse of the mitral valve, associated cardiac anomalies are not common [6]. We observed an association with congenital diaphragmatic hernia or airway anomalies in infants and children with respiratory obstruction (e.g., hypetrophic tonsils). PE associated with airway anomaly is the only one that can ameliorate significantly or disappear during infancy [5]. In most cases, PE is mild at birth and worsens over time, progressing and causing symptoms (especially during the pubertal spurt). When the deformity is very deep, patients may manifest pulmonary symptoms (dyspnea, lack of stamina), cardiologic symptoms (palpitations), thoracic pain or psychological discomfort [1–5, 8]. Sternal depression can displace the heart leftward and cause compression of the right-heart chambers with different degrees of dysfunction on echocardiography. The inferior vena cava can also be compressed. Some degree of dysfunction can also be evident on lung function tests, with more dysfunction upon stress conditions than at rest. The most common pattern of PE is restrictive, but obstructive or mixed patterns are not uncommon, whereas asthma induced by exercise is rare. Esthetic factors can affect self-esteem and self-image in most of the patients, who are usually extremely shy and refuse to practice any activity that may involve exposing their chests (e.g., swimming, going to the beach).

Table 26.2 Classification of pectus excavatum according to morphology

- Grand Canyon (Fig. 26.1) refers to a deep and severe excavation with a long canal in the sternum. Thoracoscopic correction is extremely difficult, especially if the thorax is largely ossified and sternum extremely rotated. A higher prevalence of complications after correction is reported compared with the other types. In these cases, modified open procedures can be a valid option for correction.
- Punch or cup shape (Fig. 26.1): PE is localized (usually on the inferior part of the sternum) and is symmetric. In our opinion, correction can be very difficult at any age and sometimes the outcome is partially successful.
- Saucer type (Fig. 26.1) can be symmetric or asymmetric. It is the most common of all PE types and the thorax is usually quite flat, along the complete anterior chest.
- Transversal PE: The depression is transversal and below the sternum.
- Eccentric PE: The sternal depression is eccentric to the midline. It is the highest degree of asymmetric PE.
- PE with flaring chest (Fig. 26.1): The main feature of this type of PE (but sometimes this is an isolated malformation without associated PE) is the flaring chest at the level of the final ribs.
- Pectus excavatum-carinatum is a combined malformation with a sunken chest and cartilage protrusion beside the sternal edge.
- Superior PE is very rare and localized to the upper part of the sternum and cartilage ribs. The lower sternum is normal.

26.2.1.4 Diagnosis and Classification

Each PE patient is unique, so it is important to assess the severity to select the best treatment. The depth of the excavation can be measured by calipers [4] or a pulvimeter [2] but the most important index, the Haller index, can be evaluated by computed tomography (CT) [9]. This Haller index is the most widely accepted index, and is based on the division between lateral and anteroposterior thoracic diameters. Index values >3 or 3.25 indicate surgical correction. Another important feature is PE symmetry. Asymmetric excavations (usually more depressed on the right side due to a variable degree of sternal rotation) can compromise or influence the final result. In females with asymmetric PE, the sternum is usually rotated towards the right side and the right breast seems hypoplasic, mimicking the Poland syndrome (PS).

Evaluation of the shape of PE is crucial for determining the type of surgical approach and its prognosis. We can classify PE according to morphology as shown in Table 26.2 [2, 5, 10] and with reference to Figure 26.1.

26.2.1.5 Management

Patients are selected for surgical correction if they meet two or more of the criteria shown in Table 26.3 [5]. The ideal age for correction is controversial [3, 10]. Open and thoracoscopic procedures are feasible and elicit good results [11]. However, it is widely accepted that surgical correction should be done before complete ossification of the thorax. Surgical correction in the first years of life is probably unnecessary and can carry the risk of relapse [10] or severe postoperative complications such as acquired Jeune syndrome [12]. A good age for correction with the Nuss procedure is considered to be 9–15 years of life [10].

The main procedures for PE repair are the Ravitch procedure (and its modifications) and the Nuss procedure. The Ravitch procedure was first described in 1949 [13]. It comprises resection of all deformed costal cartilages. Subsequent modifications preserved the perichondrium to facilitate rib regeneration and fixation of the sternum to reduce the risk of a flail chest and recurrence. Initially, this procedure was done with a bone graft and later with a steel bar passed posterior to the sternum. Many means of sternal fixation have been proposed during the following years, some of them absorbable. In 1970, Wada introduced a totally new concept: he described a method involving a “sternal turnover” in which the sternum was completely detached and removed, rotated by 180°, and then sutured back to the ribs. Another approach, attempted in mild cas-

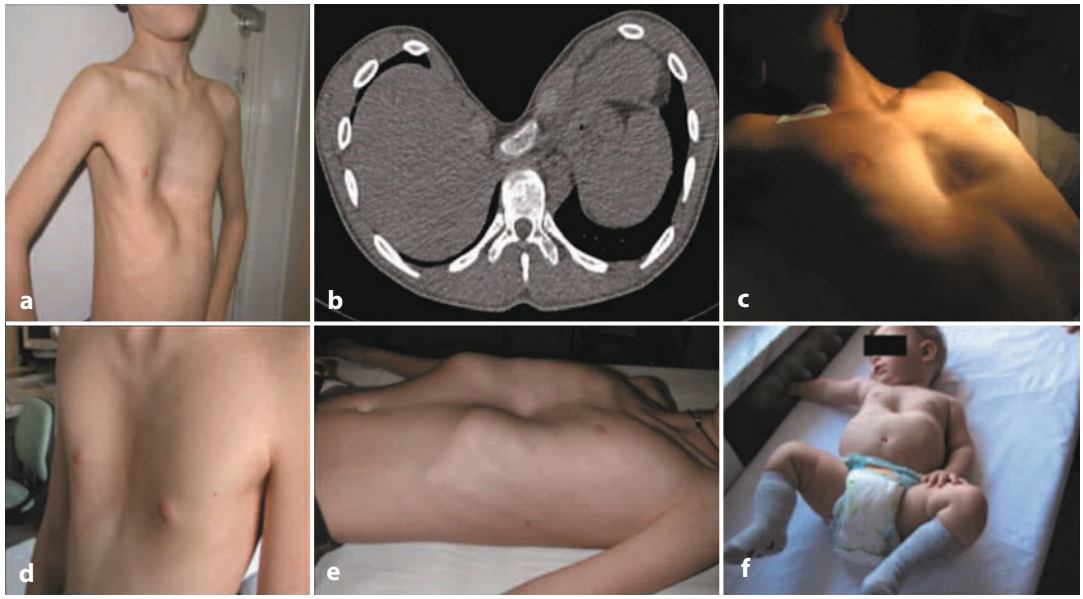

Fig. 26.1 First row: Grand Canyon-shapes PE (**a**). CT of the thorax showing a Grand Canyon-shaped PE with sternal rotation (**b**). Punch-shaped PE (**c**). Saucer-shaped PE (**d**). PE with flaring chest (**e**). Congenital punch-shaped PE (**f**)

Table 26.3 Criteria for surgical correction of pectus excavatum [5]

- symptoms (cardiologic, pulmonary or psychological);
- history of evolution;
- paradoxical movement of the chest wall;
- Haller index >3.25;
- cardiac compression and/or consequent cardiac disease;
- compression of the vena cava or pulmonary veins;
- significant restrictive disease on pulmonary function studies;
- history of failed previous repair;
- severe disturbance of body image.

Patients are selected for surgical correction if they meet two or more of these criteria.

es, and proposed for the first time in 1972 by Standford, was carried out by filling the concavity of PE with prosthetic material (e.g., Silastic®; Dow Corning Corporation) or other subsequent modifications (e.g., omental flap) [14].

In 1997, Nuss and colleagues proposed a revolutionary new method, and published it after 1 year [1]. The method involves implanting a retrosternal metallic bar which is bent and rotated at 180° to obtain immediate correction of the deformity. This metal bar is inserted through small lateral incisions and neither costal resections nor sternotomy are required. The long-term efficacy of the Nuss procedure is shown by the principle of thoracic cage remodeling determined by the retrosternal bar. Hence, the bar should remain for ≥3 years and is subsequently removed through an outpatient procedure. To avoid dislocation, the bar is fixed to the chest-wall muscles and stabilized *via* a lateral device that avoids slippage. Initially, the retrosternal tunnel for the bar was created blindly but, with the advent of thoracoscopy, the tunnel is now created under direct vision. In our opinion, thoracoscopic

aids are crucial because the bar must pass very close to the heart, which can be very closely attached to the sternum. Other, less frequently adopted conservative procedures have been described. They are based on suction devices (vacuum bell) [15] or magnetic forces [16], and attempt to correct PE without surgery, but evidence of efficacy is lacking.

26.2.1.6 Outcome and Follow-up

All major series have reported [3, 8, 10, 17] good results in >80–90% of cases depending on the severity and type of PE and the patient's age at correction. The largest series consisted of 1,215 patients and was reported by Nuss and colleagues [18]. With respect to the procedure, they reported a prevalence of 95.8% for surgeon satisfaction, 93% for patient satisfaction and 92% for parent satisfaction. There is ongoing debate between proponents of the Nuss procedure and proponents of the Ravitch procedure to define which is safer and can guarantee better results. However, the Nuss procedure is used more often because it guarantees minimal access and does not leave anterior scars.

The complications observed in open and minimally invasive procedures are: wound infections; hematomas; bar dislocations; pneumothorax requiring thoracic drainage; transient Horner syndrome; major bleeding; overcorrection/ mild correction [3, 8, 10, 18–19]. Complications specific to an extensive open procedure (particularly at early age) are floating sternum and acquired Jeune syndrome [12]. Complications specific to the Nuss procedure are pericarditis and allergy to nickel (component of the metal bar) [10]. During the Nuss procedure, very few heart lesions and deaths were reported; most of them occurred when thoracoscopy was not used [10, 20]. In case of infection due to the Nuss bar, this can be managed successfully conservatively [21]. Recurrence in 2–5% of cases has been reported [3, 18]. In our experience, in case of suboptimal results, one or more treatments with lipofilling into the residual excavation can improve the final outcome significantly, but published series are lacking. In females, Nuss or open procedures alone can correct the breast aspect but, if some degree of asymmetry persists, breast augmentation may be required, preferably after PE repair [22].

26.2.2 PC

26.2.2.1 Epidemiology

After PE, the second most frequent malformation is PC. The incidence of PC is estimated to be five-times less frequent than that of PE [2, 4] with a major predominance in male patients. PC comprises a protrusion of the sternum and chondrocostal joints (Fig. 26.2).

26.2.2.2 Etiology and Pathogenesis

The etiology of PC is not known, but the pathogenetic mechanism could be (as for PE)

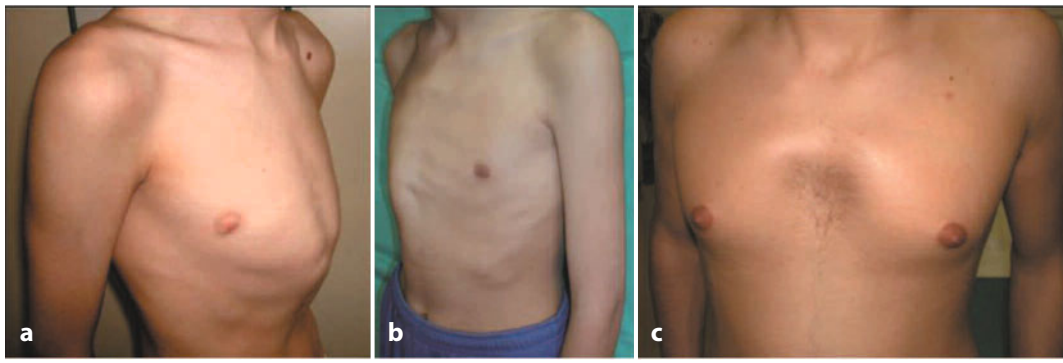

Fig. 26.2 Types of PC. Type 1 (inferior) PC (**a**). Unilateral PC (**b**). Currarino–Silverman syndrome (**c**)

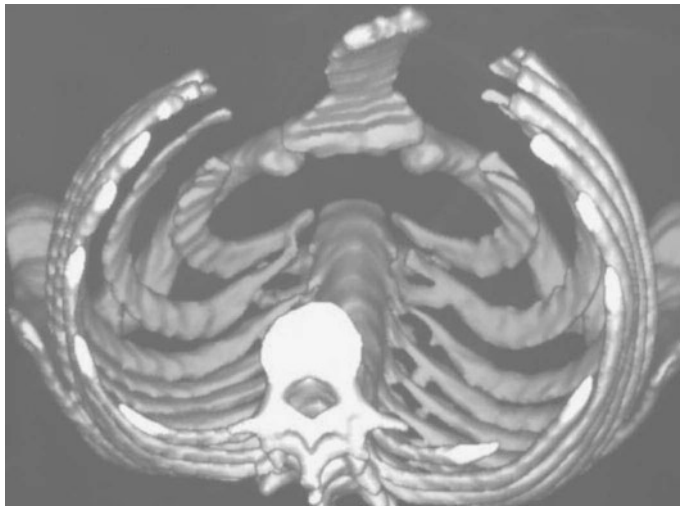

Fig. 26.3 CT reconstruction showing asymmetric unilateral PC

an overgrowth of the ribs. PC patients report anomalies of costal cartilage similar to those seen in PE patients [2]. Familial cases are not uncommon [2, 23] and it is possible to observe PC and PE cases in the same family [23]. Seldom associated with PC are connective-tissue disorders, Noonan syndrome and cardiac anomalies [6].

26.2.2.3 Clinical Aspects

PC usually has a later onset when compared with PE, occurring mainly during pre-puberty or puberty. However, in some cases, it is possible to observe infants or children with this anomaly. As with PE, PC protrusion rapidly increases during the growth spurt. The same symptoms as PE can be observed, with thoracic pain being more frequent than respiratory or cardiologic complaints [4]. In fact, cardiac and pulmonary functions are less involved than in PE [2], whereas psychological effects can be severe: they are the main indication for surgical correction.

26.2.2.4 Diagnosis and Classification

PC can be classified according to localization and symmetry into two types [4]:

- type 1: chondrogladiolar (Fig. 26.3) is the most frequent type and is more often symmetric. Sternal protrusion is located in the inferior or mid-sternum. The lower ribs can be depressed on lateral aspects;
- type 2: chondromanubrial is much less common. The sternum has a normal length and is not depressed in the lower third. This anomaly is probably due (similarly to inferior PC) to a cartilage anomaly.

A particular form of CWM is the Currarino-Silverman syndrome [24] (also called Pouter pigeon breast). Originally placed within the PC family [8], it instead must be distinguished from type-2 PC (though these variants share some features). This is a sternal malformation characterized by premature fusion and ossification of the manubriosternal joint and sternal segments. This results in a superior symmetric carinatum chest deformity with a short thick sternum excavated in the lower third (Fig. 26.2). The sternum on the lateral view is S-shaped. In our opinion, it should be part of sternal anomalies because of the sternal origin of the anomaly (see Table 26.1). Other types of PC described are:

- Lateral or unilateral PC [2]: asymmetric, consists of a protrusion of some costal cartilages on one side (Fig. 26. 3). The sternum can be rotated towards the opposite side.
- Reactive PC [25] is a complication of PE correction. It is more frequent in patients with connective-tissue disorders.

To best assess the severity and asymmetry of PC, some radiological indices have been proposed [26] that are measurable on CT but which in clinical practice are used less often than the Haller index is for PE. CT remains the "gold standard" imaging evaluation for PC.

26.2.2.5 Management, Outcome and Follow-up

As for PE, the standard correction is through costal excision surgery. Ravitch in 1952 was one of the first to describe the surgical technique for PC, whereas Howard introduced the principle of sternal osteotomy, which is usually required to correct the defect. There are many ways of carrying out an osteotomy; on the anterior sternal plate it can be done in a transverse approach, whereas in the case of asymmetric PC it can be undertaken in an oblique fashion. Recently, some modifications to the Ravitch procedure were proposed [27, 28]. They attempted to reduce its invasiveness as well as the extent of resection of muscle and cartilage. In case of the Currarino–Silverman syndrome, the best treatment is the open procedure, whereas alternatives (such as minimally invasive or conservative techniques) have been proposed recently for type-1 PC, with good results, as discussed below.

The orthotic brace system, proposed in 1992, gained popularity only recently [29]. This system is based on the principle of reshaping the thorax during puberty, thanks to its malleability (as in the Nuss procedure for PE), by applying dynamic compression upon it. Martinez-Ferro et al. [23] added to this system the possibility of measuring the pressure necessary for the correction and regulating it (dynamic compression system (DCS)). Good results were seen in a large proportion of patients, especially if the brace was used for most of the time during the day and night. A significant proportion of patients (13.8%) abandoned treatment, and some minor complications (hematomas, ulcerations, back pain) were reported in 12.5% of patients [23]. Moreover, this approach cannot be used in adults due to the ossification of the thorax, so it can be applied only to adolescent patients.

The intrathoracic compression (Abramson's) procedure [30] is based on same principle as the one for bracing. A metal bar is placed surgically in the presternal space through two lateral incisions under the pectoralis muscles and fixed to lateral stabilizers. It is like a "reverse Nuss procedure" and has an age limit. The advantage is obtaining the result immediately without wearing an external brace. In the series reported by Abramson et al., the results at 5 years were good; the bar is usually removed after ≥2 years [31].

Thoracoscopic cartilage resection [32] was described recently. It is undertaken under thoracoscopy and consists of cutting the anomalous costal cartilages unilaterally or bilaterally (according to the type of defect) without damaging the internal thoracic vessels. In severe cases, it can be associated with an intrathoracic compression procedure according to the Abramson procedure to better stabilize the sternum.

Thoracoscopic complete cartilage resection with perichondrium preservation (CCRPP) [33] has been reported by our research team. It is different from the procedures described above because cartilages are isolated laterally and medially to the internal thoracic vessels, up to the chondrosternal joints. Internal thoracic vessels are coagulated and cartilages excised completely, leaving the anterior perichondrium intact.

Minimally invasive submuscular dissection involves dissection of the pectoralis muscle and is carried out by insufflating CO_2 in the submuscular space. Resection of the ribs, sternal osteotomy, and insertion of trans-sternal steel struts are undertaken through a sagittal pre-sternal incision under endoscopic view. Recently, some technical variations have been reported [34]. The pre-sternal incision was abandoned and a major submuscular dissection was carried out with two lateral incisions between the anterior and middle axillary lines. These modifications should allow for the creation of a submuscular and presternal tunnel to implant a Nuss metal bar presternally.

However, special eight-hole stabilizers are required.

Minimal access treatment involves a bar being inserted (as in the Abramson procedure) through two lateral incisions above the sternum. However, the bar passes on both sides into the thoracic cavities; thoracoscopy can be used.

Reactive PC after the Nuss procedure can be corrected by withdrawing the bar. An open procedure is advised only in the case of failure or in other cases. Alternatively, a minimally invasive procedure can be attempted.

26.3 Type II: Costal Anomalies

26.3.1 Dysmorphic and Non-syndromic

Cartilaginous ribs are malformed and the consequence can be a unilateral or bilateral depression in the thoracic wall. The treatment of these malformations comprises excision of the anomalous ribs. A rare malformation belonging to this group is the "intrathoracic rib" (Fig. 26.4) and is classified into four types [35]:

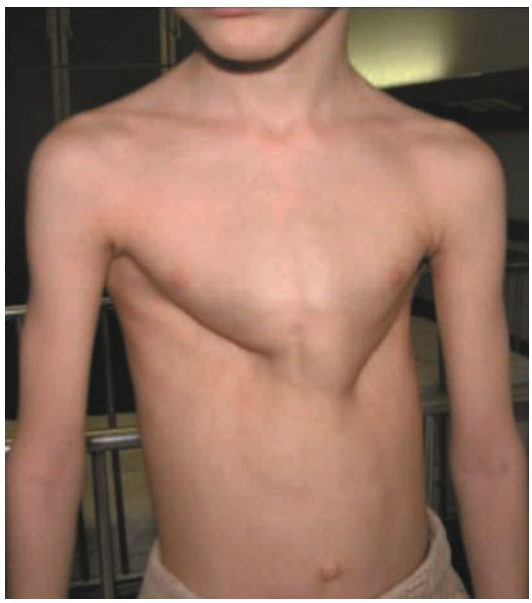

Fig. 26.4 Bilateral type-III intrathoracic rib

- type Ia is a supernumerary rib articulated with a vertebral body;
- type Ib is a bifurcated ("bifid") rib taking its origin close to the vertebral body;
- type II a bifid rib arising more laterally;
- type III is a non-bifid rib depressed into the thoracic cavity.

Another malformation is flaring chest, which comprises hypertrophy or fusion of the cartilaginous ribs in the lower costal margin. Open resection of all malformed ribs is an option. Other frequently observed malformations are cartilage rib asymmetries. They appear as an isolated protrusion of the cartilage ribs and, in most cases, the ribs are fused.

26.3.2 Syndromic Anomalies

26.3.2.1 Jeune Syndrome

Jeune syndrome (also known as asphyxiating thoracic dystrophy) is an autosomal recessive disorder. It was originally described by Jeune in 1954 in a pair of siblings. The frequency of the condition is rare, with an overall incidence estimated between 1/100,000 and 1/30,000 live births. Jeune syndrome is characterized by severe bone abnormalities. Usually, the affected patients have a long, narrow thorax with a reduced thoracic capacity, leaving the lungs with insufficient room to expand and grow. Both thoracic diameters (anteroposterior and lateral) are reduced, causing severe respiratory distress. Patients who develop respiratory symptoms during the first months of life have a poor prognosis, usually resulting in death during infancy.

All patients have small chests with short, wide and horizontal ribs (Fig. 26.5). Clinical and imaging aspects of this malformation vary between patients, and two variants exist:

- the severe variant represents ≈70% of cases. It is usually lethal during infancy. The thorax is extremely small, leaving the abdomen with a prominent aspect; respiratory failure is the rule.
- in the mild variant, the ribs are less affected (≈30% of patients), respiratory symp-

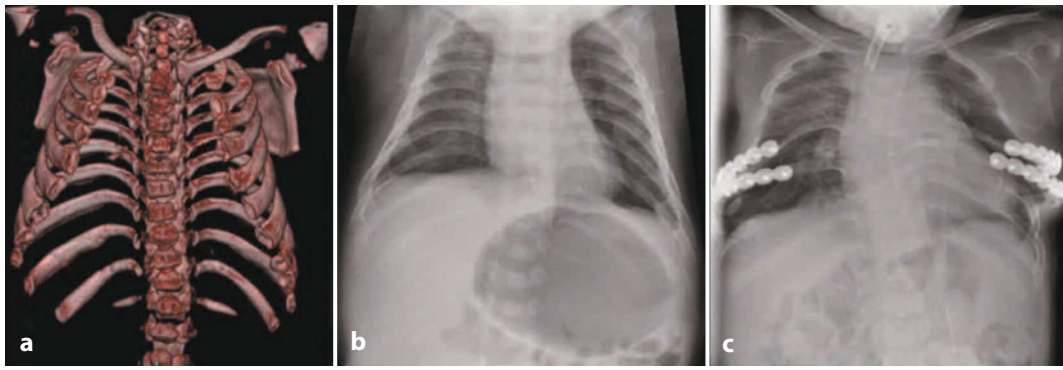

Fig. 26.5 Jeune syndrome. CT reconstruction showing short, wide and horizontal ribs with reduction of intrathoracic capacity (**a**). Chest radiograph demonstrating the disproportion between the thoracic and abdominal diameters and the rib anomalies mentioned above (**b**). The result of bilateral thoracic expansion (**c**)

toms are manageable and survival is prolonged. Renal or liver dysfunctions can be present, and can lead to death.

Surgical repair methods typically involved median sternotomy (with graft interposition), resulting in poor outcomes [36]. Other methods have been proposed: lateral thoracic expansion realized by rib incisions that are sutured in a staggered fashion or, more recently, a vertical expandable prosthetic titanium rib (VEPTR). Both of these methods seem to offer good results. Sometimes, the mild type of Jeune syndrome may not require treatment.

26.3.2.2 Cerebrocostomandibular Syndrome

Cerebrocostomandibular syndrome is such a rare entity that there is no clinical experience of it in the world. We diagnosed 1 case in the last decade: the main feature was a lack in development of the rib cage. Affected patients have only costal vestiges, the chest has a flail aspect, and mechanical ventilation is required from birth. In some cases, the thoracic cage agenesis can be unilateral. This defective costal development can also be associated with features of the Pierre–Robin anomaly. Cerebral maldevelopment or malfunction is also common [37].

26.3.2.3 Costal Agenesis

Costal agenesis is usually limited to some ribs and is not syndromic. These are also rare conditions. Lung herniation may occur, requiring thoracoplasty using the same technique used for Poland Syndrome (PS).

26.3.3 Rare type-II CWMs

There is a series of CWMs that are rarely observed and not included in standard classifications. They differ from each one from other so treatment must be personalized.

26.4 Type III: Chondrocostal Anomalies

26.4.1 Poland Syndrome (PS)

PS occurs in around 1/30,000 live births [38]. It is characterized by the absence or hypoplasia of the pectoralis major muscle, which is often associated with other ipsilateral abnormalities of the chest wall, breast and upper limb [5, 39]. The defect is essentially unilateral and, in most cases, right-sided, although very rare bilateral cases have been described [40, 41]. There is a male preponderance (2:1). Its etiology is not known, but the most accredited hypothesis is interruption of the vascular supply in subclavian and vertebral arteries during embryonic life, leading to different malformations in the corresponding districts. According to this, PS could be interpreted being a sequence.

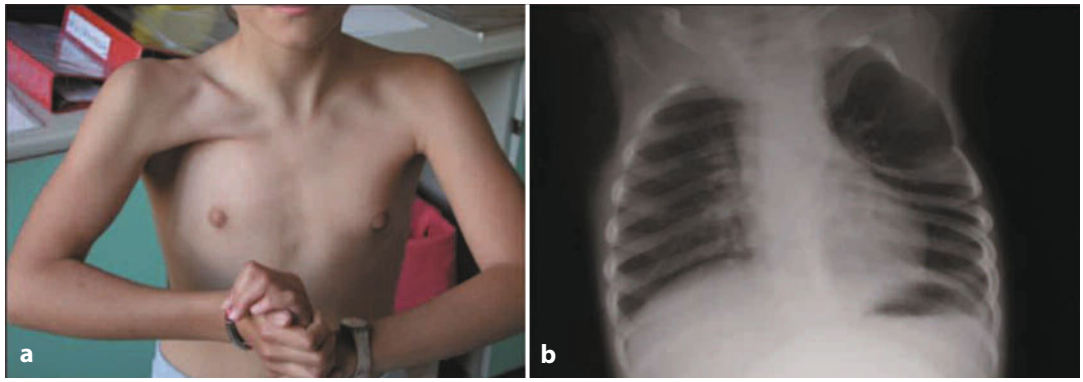

Fig. 26.6 Poland syndrome. Agenesia in the left major and minor pectoralis muscle (**a**). Agenesia in the left upper ribs with lung herniation (**b**)

PS is usually sporadic. However, in 4% of cases, there is familial recurrence, and in 8% of patients some upper-limb or thoracic anomaly (not classifiable as PS) is present in a family member [42]. Possible transmission with an autosomal dominant pattern has been hypothesized. Association with other anomalies (e.g., Moebius, Klippel–Feil syndromes, Sprengel anomaly) [41] has been reported.

The PS phenotype is extremely variable. The thoracic defect is usually evident at birth, but can pass undiagnosed until the child gets older. In fact, the pectoralis muscle deficiency causes an asymmetric aspect, more evident if there are associated costal anomalies (Fig. 26.6). In case of rib agenesis, particularly if multiple (the most affected ribs are the third and the fourth) with a wide defect, lung herniation and paradoxical respiratory movements are evident. Ribs can also be hypoplasic or anomalous (Fig. 26.6). Other CWMs such as PE or PC can be associated, but surgery is required in <10% of cases. A wide spectrum of defects ranging from a mild degree of breast hypoplasia to complete absence of mammary glands is a constant feature. Other uncommon anomalies are cardiac and renal defects, as well as scoliosis. Dextrocardia is reported frequently, always associated with left PS, and seems to be caused by mechanical factors during embryonic life in patients with multiple left rib agenesis [43]. Patients are asymptomatic, and usually do not suffer any limitation due to muscle defects. The upper limb is frequently involved, ranging from the classical symbrachydactyly to split hand or other defects.

The main indication to carry out a thoracoplasty is cosmetic. Usually, it is undertaken at puberty and is rarely necessary during infancy. There is no evidence of the utility of any surgical procedure to guarantee protection against thoracic traumatic injuries in children with rib agenesis. In case of surgical correction in the pediatric age, some options are available, from costal transposition, to a prosthetic repair [44, 45]. According to some authors [8], costal transposition and the consequent stabilization of the thorax can prevent the progression of thoracic deformity, but there is no consensus about this concept. Most authors [45] prefer to wait until puberty and later to correct, in one or more stages, the thoracic flail chest and pectoral defect. In female patients, the most frequent issue is breast and pectoral reconstruction. Correction with prostheses alone or associated with other surgical procedures (transposition of the latissimus dorsi muscle or rectal abdominal muscle; lipofilling; omental flap) has been advocated [45]. Each surgical approach must be tailored to the patient. In males, the same methods can be applied, but the indication for the surgical procedure needs to be evaluated case by case because the esthetic defect is less important. Recently, Martinez-Ferro described transposition of latissimus dorsi muscle flaps using a minimally invasive approach [46]. Usually,

the approach is multidisciplinary (pediatric, thoracic, plastic surgeons), thereby providing the best chance of a successful outcome.

26.5 Type IV: Sternal Anomalies

26.5.1 Sternal Cleft (SC)

SC is a rare idiopathic defect in fusion of the sternum. Acastello et al. found that SC accounts for 0.15% of all CWMs [47]. Also, the HOXB gene might be involved in the development of SC. In our opinion, the clearest classification has been proposed by Shamberger and Welch [48] and involves four types:

- Thoracic ectopia cordis: the heart is ectopic, uncovered by skin, and usually has intrinsic anomalies (majorly when anterior) and kephalic ectopia. The sternal defect can be superior, inferior, central (rare) or total. Abdominal-wall defects can be associated. The thorax is hypoplasic, so surgical correction is usually not sufficient to save life (though isolated survival after surgery has been reported).
- Cervical ectopia cordis is the rarest type. The heart is cranial, sometimes with the apex fused with the mouth. Maxillofacial anomalies are common. The prognosis is always poor.
- Thoracoabdominal ectopia cordis: the heart is covered by a thin membranous or cutaneous layer. The sternal defect is inferior. The heart (located into the thorax or in the abdomen) is not rotated as in the types described above, but intrinsic anomalies are common. This type of anomaly is, in general, found as part of the Pentalogy of Cantrell [49]. If surgically repaired, the prognosis can be good.
- SC is the most common of this group of CWMs, comprising a congenital malformation of the anterior thoracic wall, arising in a deficiency in the midline embryonic fusion of the sternal halves. The incidence is unknown, but it is more common in females [8].

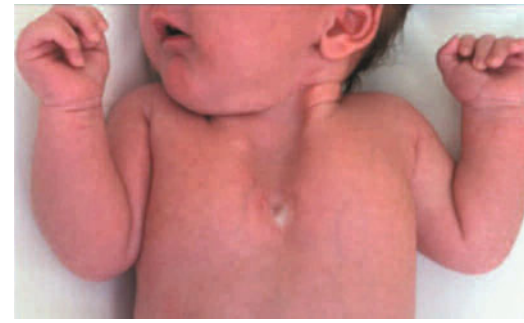

Fig. 26.7 Total sternal cleft in a newborn (note the congenital connectival nevus)

SC can also be classified as "partial" or "complete" (Fig. 26.7). The partial deformity can be located superiorly or inferiorly. The inferior variety is less common and is often associated with a thoracoabdominal ectopia cordis, whereas the more frequent upper partial cleft can be an isolated abnormality. Sternal clavicular joints are displaced laterally, but the clavicles have a normal length. Thoracic viscera bulge in the midline across the defect, which is more evident during forced expiration. A complete form (also described) is much less common. There is a total lack of fusion; it produces an even bigger paradoxical movement than partial cleft and can cause respiratory distress.

Moreover, SC is frequently associated with other defects (82%) [50]. These must be carefully looked for before any surgical procedure because they can lead to major complications. Some of them are evident on physical examination (e.g., maxillofacial hemangiomas) [51], cleft lip or cleft palate, PE, connectival nevi [50], supraumbilical raphe, or gastroschisis. Other defects must be ruled out, such as cardiac defects, aortic coarctation, eye abnormalities, posterior fossa anomalies, and hidden hemangiomas (cerebral or subglottic in particular).

In some cases, SC is also part of clinical conditions. These include: posterior fossa malformations–hemangiomas–arterial anomalies–cardiac defects–eye abnormalities–sternal cleft and supraumbilical raphe syndrome

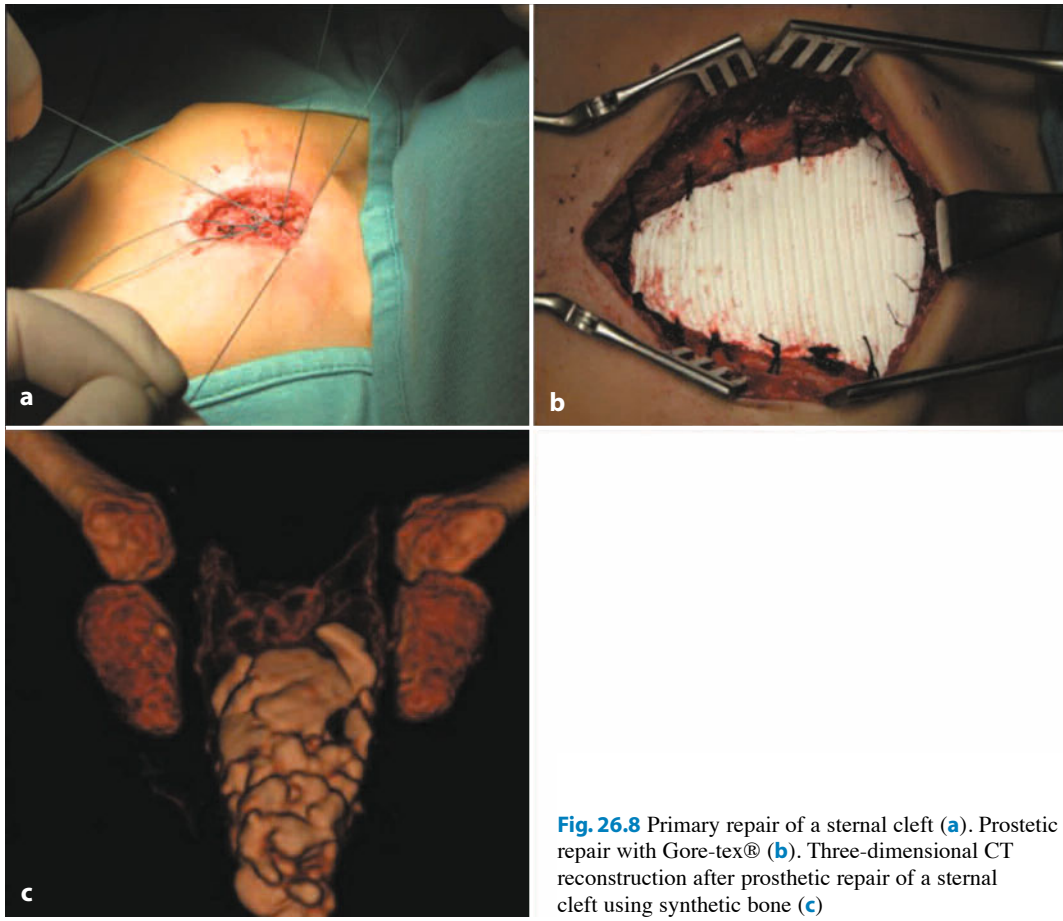

Fig. 26.8 Primary repair of a sternal cleft (**a**). Prostetic repair with Gore-tex® (**b**). Three-dimensional CT reconstruction after prosthetic repair of a sternal cleft using synthetic bone (**c**)

(PHACES) [52]; sternal malformation/vascular dysplasia; midline fusion defects; pentalogy of Cantrell.

The treatment of SC is surgical. Surgery is crucial: to re-establish the bony protection of the mediastinum; to prevent paradoxical visceral movement; to allow normal growth of the thoracic cage; for cosmetic reasons. Ideally, it should take place during the neonatal period or in the first months of life [8, 53, 54]. The reason for preferring an early surgical approach is that primary closure is easier and there is no need for a big procedure (which may be necessary at older ages). In fact, later in life, primary closure (Fig. 26.8) could require: sternoclavicular disarticulation; sternal isolation; inferior sternal osteotomy and medialization of the neck muscles after separation of their sternoclavicular attachments laterally [47]. Moreover, because it can carry the risk of circulatory impairment due to cardiovascular compression, in some cases primary sternal suture may not be possible and prosthetic or autologous closure [54] may be preferable because it is less invasive (Fig. 26.8). Sometimes, partial thymectomy can be useful to reduce the pressure on thoracic vessels [53]. Several prosthetic materials have been described for SC repair. We closed an upper cleft in one 8-year-old female with artificial bone tissue and had an excellent outcome. Complications are not common, but PE can occur later in life in patients who undergo surgery for SC. In case of prosthetic repair, there is an increased risk of infections and recurrence.

26.6 Other Anomalies

26.6.1 Postoperative Surgical Deformities

This category includes cases in which thoracic deformities develop after correction of other CWMs. We have experience of a few cases of these types of anomalies (Fig. 26.9). They can be due to multiple resections of cartilage during open surgery for a young patient with PE or due to previous thoracotomy (Fig. 26.9) or sternotomy (Fig. 26.10) for other reasons and finally result, after many years, in a thoracic deformity that requires surgical revision. As discussed above, the optimal age for PE repair is controversial [3, 10]. Repair in early childhood is easier but carries a high risk of causing restrictive growth patterns in the chest wall. Acquired Jeune syndrome is associated with open repair in young children, usually <4 years of age, with extensive resection of ≥5 ribs [12] and damage to the cartilage growth centers [55]. For these reasons, most authors postpone open surgical repair until after the patient is >10 years of age [3,10].

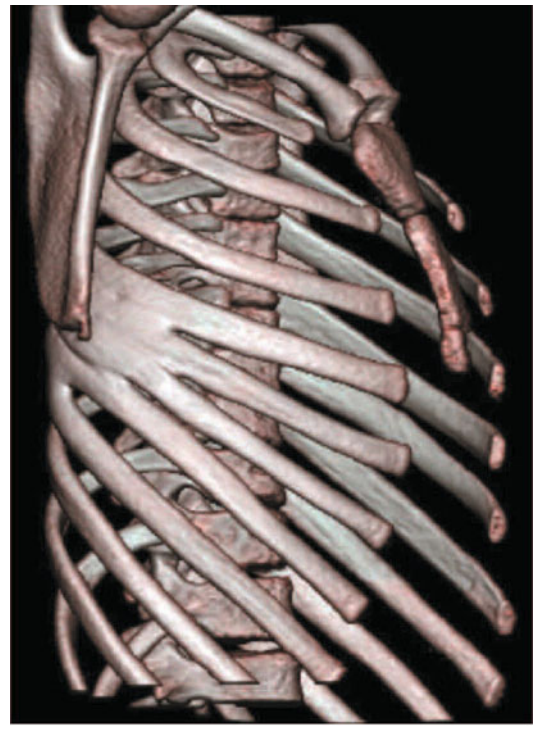

Fig. 26.9 Post-thoracotomy deformity. The ribs from the fourth to eighth rib are fused, causing scoliosis and reduced lung-function volumes. This female underwent three previous right thoracotomies for complicated esophageal atresia

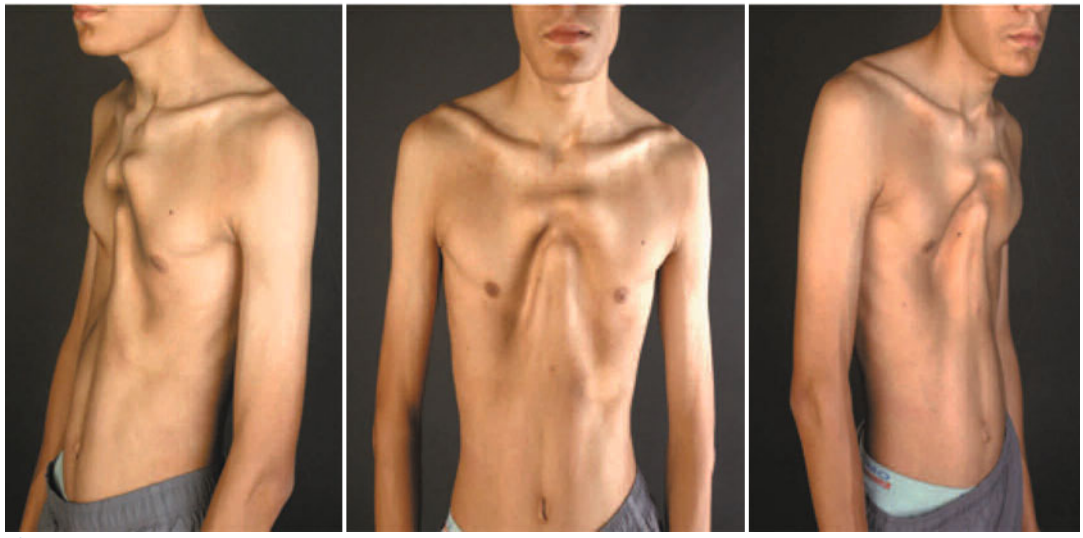

Fig. 26.10 Post-sternotomy deformity in a boy who underwent surgical treatment for tetralogy of Fallot

26.7 Conclusions

CWMs are a wide spectrum of anomalies. The etiological and genetic implications of CWMs are poorly characterized. Precise identification of a single malformation, its embryological classification, and an accurate diagnostic assessment are the first fundamental steps. Identification of familial cases, possible associated syndromes and anomalies, clinical symptoms and psychological implications, must be considered. Among the therapeutic armamentarium, classical methods and new approaches allow the most appropriate method for the individual patient to be chosen. This choice is according to the experience and preference of the surgeon but is achieved by tailoring the treatment to individual clinical and psychological needs. A multidisciplinary approach is advisable to manage CWMs in all their complexity.

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Breast Disorders

27

Maria V. Romanini, Simonetta Franchelli, Pierluigi Santi and Vincenzo Jasonni

27.1 Introduction

Breast anomalies in the pediatric population are not uncommon [1]. Until a short time ago, patients usually presented at the end of puberty, but in the current cultural environment, they address earlier to the surgery. These physical deformities are often a significant source of psychological distress for adolescent male and female patients, who feel alienated from their peers [2]. For this reason we should ideally correct these disorders before they become a significant psychosocial problem for the patient.

Breast deformities in the pediatric population represent a significant challenge for the reconstructive surgeon, who must respect the physiology and normal growth of the mammary gland, providing at the same time a satisfactory esthetic and functional outcome. Accurate diagnosis and counseling should be provided and the timing of surgery planned to optimize functional, psychological and esthetic outcomes, thereby alleviating the sense of deformity and unattractiveness that is often present.

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27.2 Embryology and Anatomy

Development of the breast begins during the seventh week of gestation from ectodermal cells along the "milk lines" or primitive mammary ridges, extending along both sides of the body, from the axilla to the groin. By the tenth week of gestation, the main part of the mammary line disappears. However, a small part invaginates in mesenchymal tissue at the level of the fourth interspace. It forms 16–24 sprouts, evolving into solid buds. The epithelial sprouts are canalized and form the lactiferous ducts, whereas the buds form the small ducts and alveoli of the gland. Initially, the lactiferous ducts open into a small epithelial pit that, shortly after birth, evolves into the nipple [3]. The nipple is located at the fourth intercostal space in men and women before puberty. At the onset of puberty, hormonal influence results in breast-tissue growth. Puberty begins at 10–12 years as a result of hypothalamic gonadotropin-releasing hormones secreted into the hypothalamic–pituitary portal venous system. The anterior pituitary secretes follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH causes ovarian follicles to mature and secrete estrogens. Estrogens stimulate the longitudinal growth of the breast ductal epithelium. As ovarian follicles become mature and ovulate, the corpus luteum releases progesterone

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which, in conjunction with estrogen, leads to complete development of the mammary glands [4].

Tanner describes five stages of breast development [5]:

- stage 1: pre-adolescent elevation of the nipple, but no palpable glandular tissue or areolar pigmentation;
- stage 2: glandular tissue in the infra-areolar region; nipple and breast project as a single mound;
- stage 3: further increase in glandular tissue with enlargement of the breast and nipple but a continued contour of the nipple and breast in a single plane;
- stage 4: enlargement of the areola and increased areolar pigmentation with secondary mound formed by the nipple and areola above the level of the breast;
- stage 5: final adolescent development of a smooth contour with no projection of areola and nipple.

27.3 Clinical Features

A multidisciplinary team (including a pediatrician, psychologist and endocrinologist) should evaluate any child for general and sexual development to exclude instances of precocious puberty or delayed appearance of secondary sexual characteristics. The plastic surgeon must also define the involved anatomy: musculature of the chest wall and breast position on the chest wall; size, shape, proportion, consistency, definition, symmetry and skin features of the breast [6].

27.4 Classification

Several classifications for breast anomalies have been proposed. Sadove and van Aalst identified three categories: hyperplastic, hypoplastic and deformational [1]. Pryor and Lehman added a further category: acquired anomalies [7]. We propose a simpler and more practical classification that identifies two categories of breast anomalies: congenital and acquired.

27.4.1 Congenital Anomalies

27.4.1.1 Supernumerary Nipples (Polythelia)

Polythelia is the most frequent breast disorder in the male and female pediatric breast. The prevalence is 0.22–5.6% and is dependent upon sex, ethnic group and geographical area [8, 9]. This condition can be associated with nephro-urologic defects [10, 11]. Accessory nipples can occur more frequently in the axillary region and inframammary region, but also anywhere along the mammary line (Fig. 27.1). The differential diagnosis is with pigmented lesions. Treatment is resection.

27.4.1.2 Supernumerary Breasts (Polymastia)

This condition occurs if a residual original mammary line develops into a complete breast. The presence of a supernumerary mammary gland can occur anywhere along the embryologic milk line [3] (Fig. 27.1). An inframammary breast is often confluent with the lower pole of the primary breast, with or without an associated nipple–areola complex. This condition can occur as an isolated finding or be associated with congenital renal anomalies. It can appear sporadically or with a familial recurrence [12]. The diagnosis is made by clinical evaluation. Treatment is excision of the ectopic tissue because of the possibility of breast cancer. Extreme caution should be taken when excising ectopic tissue in this region in patients with developing breasts to avoid a breast deformity (especially at the lower pole).

27.4.1.3 Inverted Nipple

An inverted nipple is a congenital or acquired anomaly in which the nipple, instead of pointing outward, is retracted into the breast. It is a relatively common esthetic problem present-

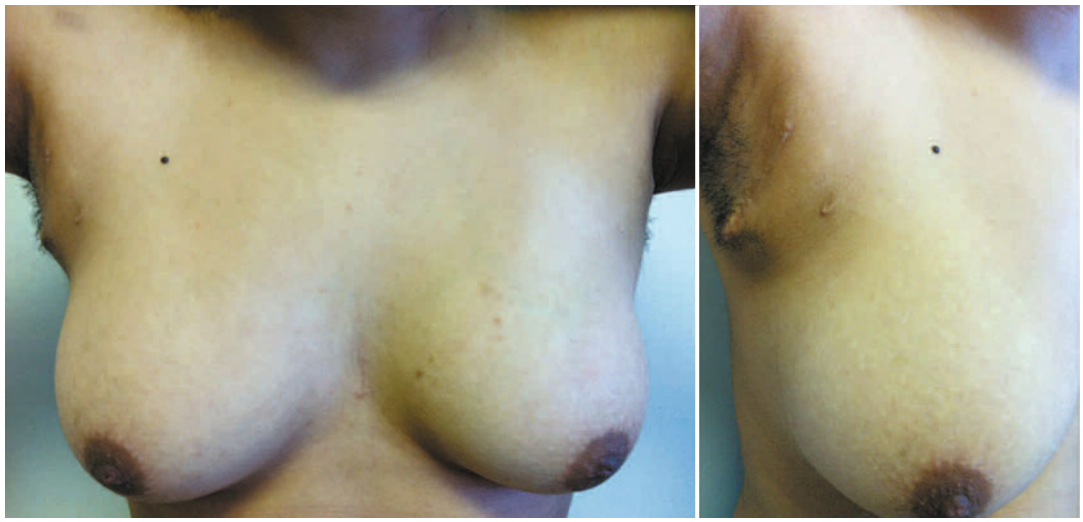

Fig. 27.1 This patient presented with bilateral polymastia and polythelia. She underwent surgery but was concerned about the superior scar and wanted excision of the polythelia

ing to a plastic surgeon (1.77–3.26%) [13]. After a few months of life, the nipple cannot evert because of the failed proliferation of mesenchymal tissue around the lactiferous ducts. This breast anomaly is classified into grades 1, 2, and 3 based on the following parameters: feasibility of keeping the nipple everted after traction; degree of fibrosis; damage caused to the lactiferous ducts. It causes three types of problems: esthetic; hygienic (due to repeated irritation and inflammation); functional (difficulty in breast feeding). Nevertheless most patients seek intervention because of the abnormal appearance.

Several surgical procedures have been described, suggesting that no procedure is universally successful. They can be divided into two main groups based on invasiveness. The first (less invasive) includes some procedures that: preserve the lactiferous ducts; do not require special postoperative care; leave minimal scars; do not affect the sensitivity and function of the nipple. For these reasons they are bettered suit to young patients. In this group, one procedure involves releasing the fibrous tissue around the lactiferous ducts and keeping the nipple in the everted position with a bolster suture and milk-suction pump [14] (Fig. 27.2). The other procedures employ local dermal flaps of different shapes: triangular [15], rhomboid [16] V–Y [17] and star-shaped [18].

In more severe cases (second group), to avoid recurrence and to obtain the perfect shape of the nipple, it is necessary to section the galactophorous ducts and surrounding fibrous tissue through a periareolar incision. These techniques lead to a lack of nipple function and are better suited to older patients [19, 20].

27.4.1.4 Poland Syndrome (PS)

PS is a congenital unilateral anomaly of the thoracic wall characterized by a variable degree of hypoplasia or agenesis of the pectoralis major muscle (particularly the sternocostal head), pectoralis minor muscle, breast, nipple, subcutaneous fat, axillary hair, with or without rib and upper-limb anomalies [21, 22]. The epidemiology, etiology and pathogenesis are reviewed in Chapter 26. S presents a wide spectrum of anomalies and severity varies greatly among individuals (Fig. 27.3). In female patients, a certain degree of breast anomaly is always described, ranging from a mild breast asymmetry to complete agenesis with absence of breast and nipple. An association with tuberous breast may be present. The diagnosis is based on the

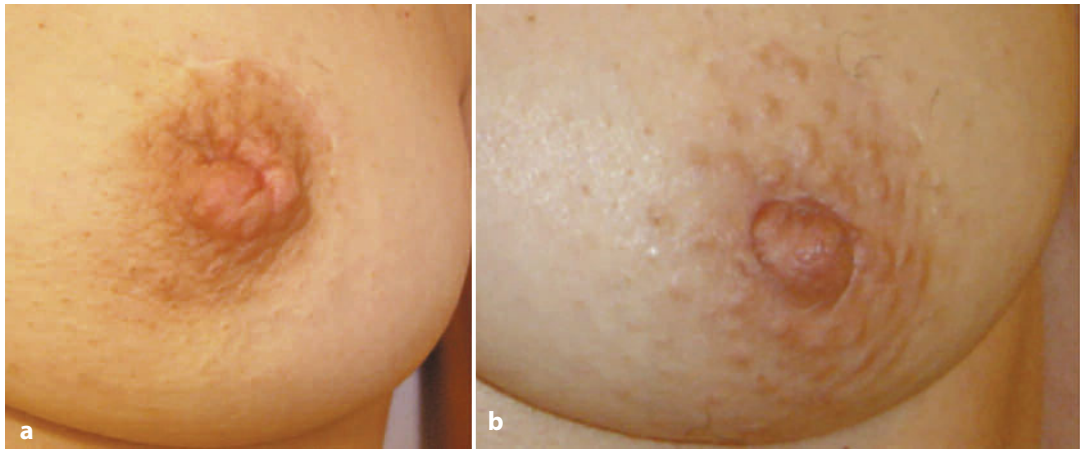

Fig. 27.2 Inverted nipple before surgery (**a**). Same patient 2 years after surgery with a less invasive procedure (**b**) (courtesy of Dr Maria Stella Leone)

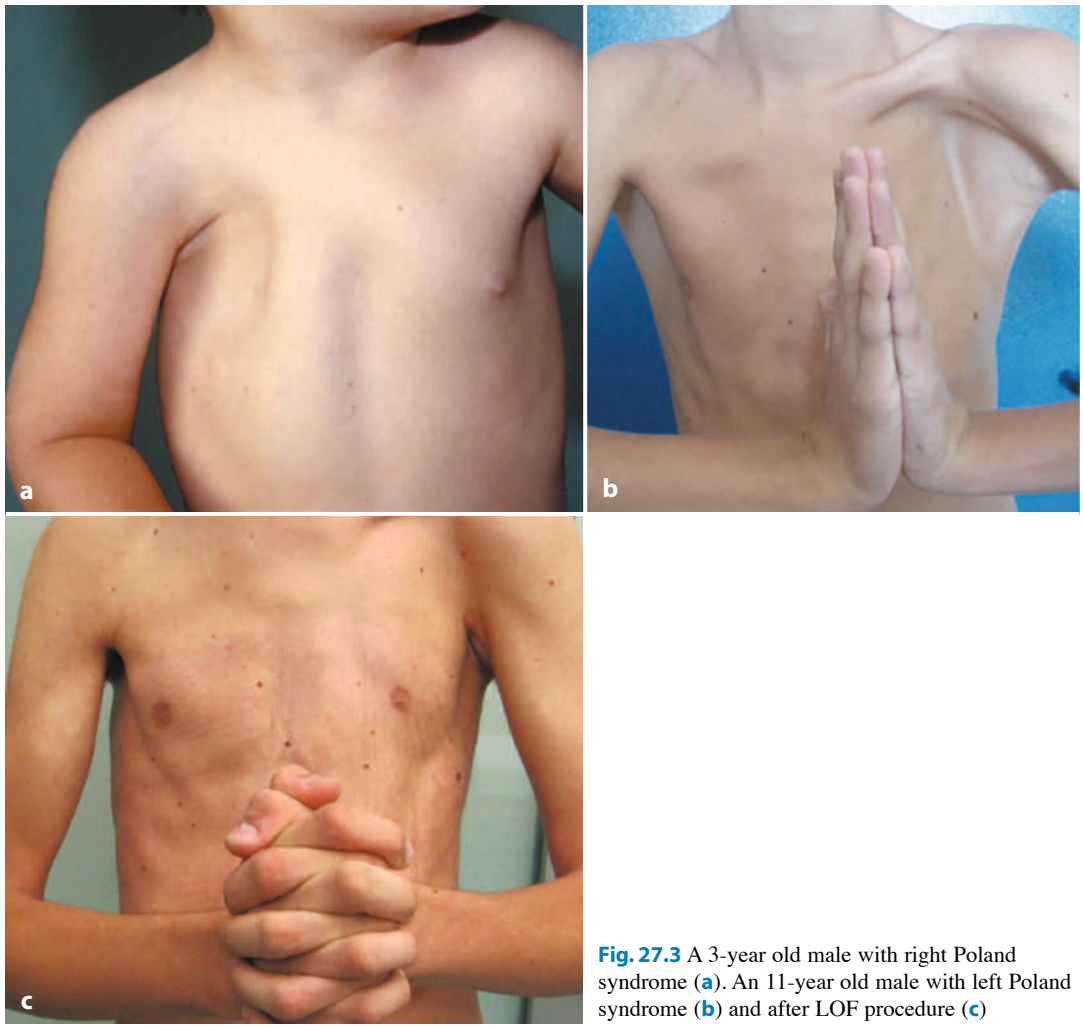

Fig. 27.3 A 3-year old male with right Poland syndrome (**a**). An 11-year old male with left Poland syndrome (**b**) and after LOF procedure (**c**)

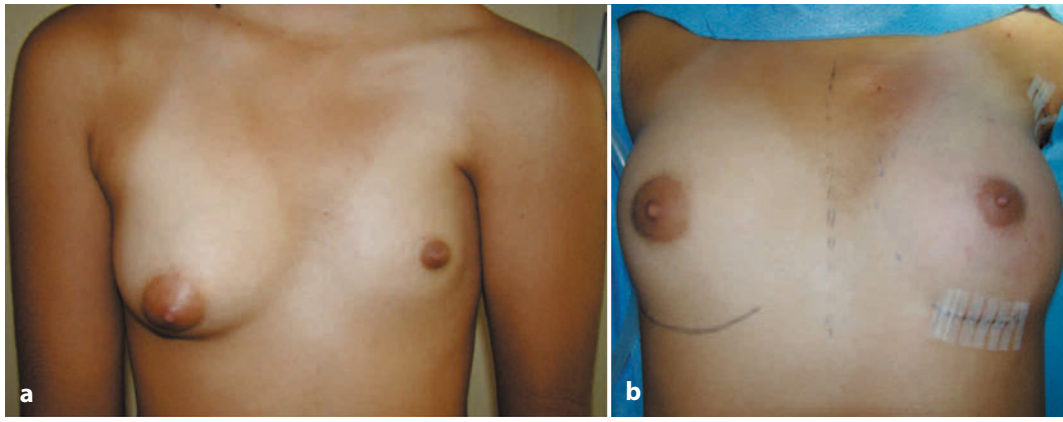

Fig. 27.4 A 15-year-old patient with PS before surgery (**a**). Same patient immediately after surgery with a LOF (**b**)

hypoplasia or absence of the pectoralis major muscle as revealed clinically and by imaging (ultrasonography, computed tomography (CT) of the thorax).

In the case of rib agenesis, chest reconstruction is described elsewhere within this book. Breast reconstruction in PS is particularly challenging for the plastic surgeon, who must tackle the paucity of fat and skin tissue as well as the absence of a muscular plane giving support to the implant. For this reason the use of prosthesis alone in most cases does not guarantee an optimal result. Many procedures have been utilized for the reconstruction of PS: muscular flaps; pectoral and breast implants; fat transfer; and omentum flap.

Muscular flaps include the latissimus dorsi flap (LDF) or rectal abdominal flaps. Although LDF reconstruction can give satisfactory results, providing muscular, fat and skin tissue to the breast area from the posterolateral thorax, it presents several disadvantages [23]. These include the: invasiveness of the procedure; resulting visible scar; removal of one of the major muscles of the shoulder and arm; possible loss of function of the donor muscle; risk of secondary atrophy. Moreover, the latissimus dorsi muscle is not always well represented in PS [24, 25] so the procedure is not always feasible. In an attempt to improve the esthetic result, some authors have proposed minimally invasive harvesting of the muscular flap using endoscopic methods [26].

Surgical correction in males includes the LDF, pectoral implants and, ultimately, fat transfer (lipofilling and lipostructure) carried out with the Coleman procedure [27]. This procedure, in mild-to-moderate cases, gives very good results after 2–3 sessions of lipofilling and is almost complication-free. Our research team is carrying out two-step surgery: (i) expansion of the skin using a tissue expander and (ii) replacing the tissue expander with fat transfer and pectoral implants when necessary. We have obtained satisfactory results.

In female patients, breast reconstruction is particularly challenging because of a cranial defect of the pectoralis muscles and partial/complete breast agenesis. The therapeutic alternatives include positioning a breast implant (generally associated with a rotational LDF to fill the infraclavicular defect) or a fat transfer in the pectoral region alone or associated with an implant. Recently, a laparoscopically harvested omental flap (LOF) has been described by two surgical teams [28, 29]. The first research team described breast reconstruction in adults with PS [28]. However, Morovic, in cooperation with our research team, also showed the feasibility of this procedure in teenagers [29]. Our indication for using a LOF is breast hypopla-

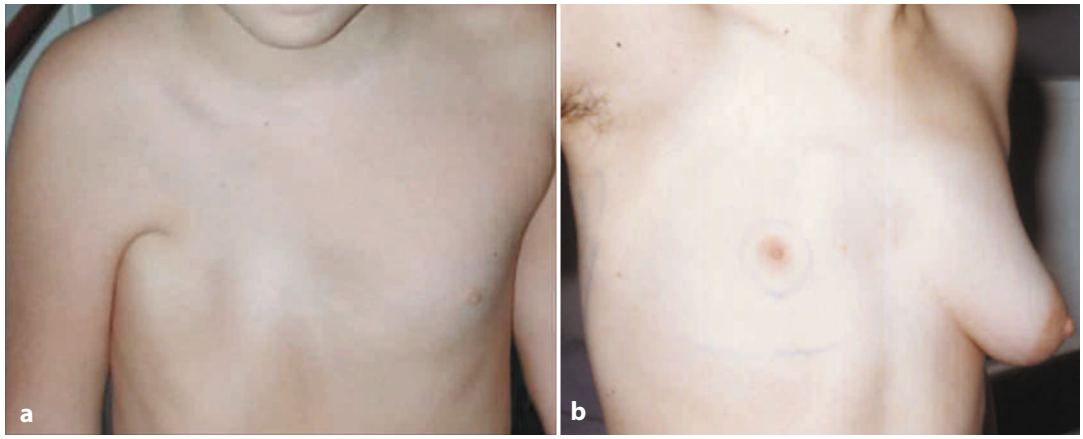

Fig. 27.5 Amastia in a 7-year-old patient with PS (**a**). Amazia in a 15-year-old patient with PS (**b**)

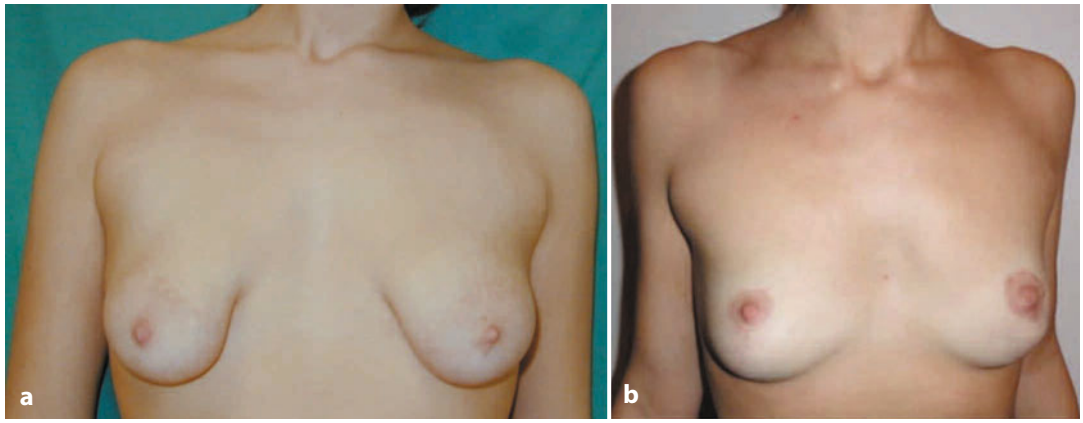

Fig. 27.6 A 17-year-old patient with a tuberous breast before surgery (**a**). Same patient 5 years after the Muti procedure without a breast implant (**b**)

sia without rib anomalies in patients with contralateral breasts reaching Tanner grade 4 or 5 (Fig. 27.4).

27.4.1.5 Amastia

Amastia is the absence of the breast and nipple–areola complex. It is a rare condition, wherein in normal growth of the breast and nipple does not occur because of a complete failure of mammary line development at 6 weeks of life. It has a male to female ratio of 1:5.

Amastia is usually unilateral and often associated with PS (Fig. 27.5a). Bilateral cases have been described making part of several syndromes [30–32]. The differential diagnosis is with amazia (absence of the breast but the nipple–areola complex (NAC) is present; Fig. 27.5b). The diagnosis is clinical at birth and at puberty.

Three-stage surgery is usually employed: At first, a gentle expansion of the skin using a tissue expander is carried out. Then a breast implant or fat transfer can replace the tissue expander. Finally the NAC is reconstructed with skin grafts or local flaps [33].

27.4.1.6 Athelia

Athelia is the absence of a nipple. It can be associated with breast hypoplasia or unilateral amastia in PS (Fig. 27.5a) or bilaterally in

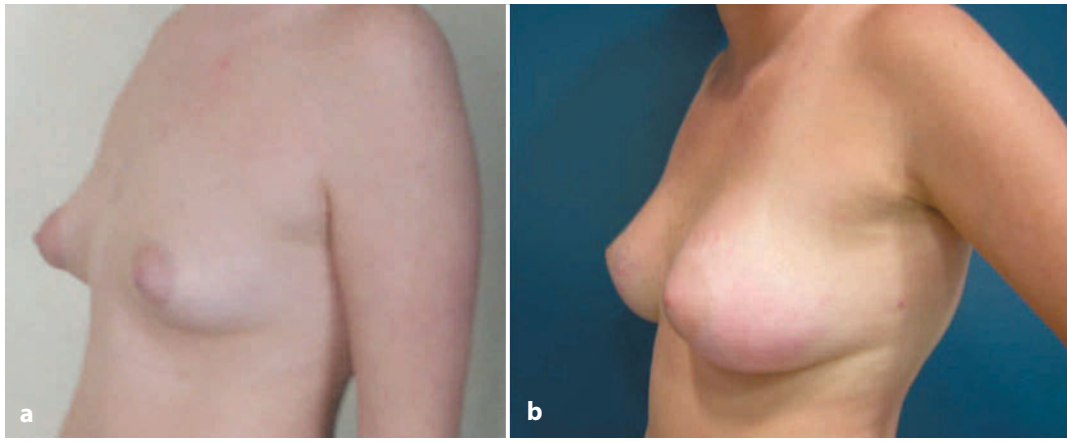

Fig. 27.7 A 16-year-old patient with a tuberous breast before surgery (**a**). See the alteration of the breast profile, which is typical of a tuberous breast. Same patient 1 year after the Muti procedure with a breast implant (**b**). The corrected breast profile is anatomical

association with abnormal development of the skin, teeth, nails and sweat glands like an ectodermal dysplasia [30, 34]. Treatment is reconstruction of NAC using skin grafts from the contralateral complex or a local flap.

27.4.1.7 Tuberous Breast

The term "tuberous breast" was first used by Rees and Aston in 1976. They described a congenital defect featured by the absence of a superficial layer of Camper's fascia in the area below the areola; however the superficial fascia was very thick in the lower pole of the breast. As a result, a ring around the NAC is formed that impairs normal development of the breast. The absence of the fascial layer results in a "zone of least resistance" so that the breast can herniate towards the NAC. The Muti classification [35] distinguishes three categories of defect:

- type I: the mammary parenchyma is herniated into an expanded areola containing the small ptosic breast; a cranial inframammary crease, tight and defined by a fibrotic ring surrounding a small base gland in a lateral position in the chest wall (Fig. 27.6);
- type II: An extreme breast ipoplasia with "solid skin", small areola; retro-areolar and sub-areolar gland protrusion that creates a typical deformity of the breast profile (Fig. 27.7); a flat lower pole with an almost non-existent inframammary crease;
- type III: Usually these are breasts of a morphological "tubular" type, the NAC points downward and there is a reduced NAC–inframammary crease distance; the position of the breast is not excessively lateral.

A tuberous breast may appear during puberty. It can be unilateral or bilateral and can affect the two breasts with different types. It is one of most serious breast deformities, causing profound psychological distress. Previously, surgical treatment was at an adult age, when development of the glandular tissues was complete, but now surgeons operate earlier [35]. The deformity is one of the most challenging congenital breast anomalies, and surgery should correct the multiple breast defects. Placement of an implant does not improve the appearance of a tuberous breast. To correct it, the surgeon must transform the hypoplasic tuberous breast into simple hypoplasia. That is: releasing the NAC from its constrictive envelope; replacing it in the right place in the chest; relocating the inframammary crease; and reducing the areolar diameter significantly without discarding gland tissue.

Two surgical methods appear to be sufficiently flexible to correct the various defects of this deformity. One method, described by

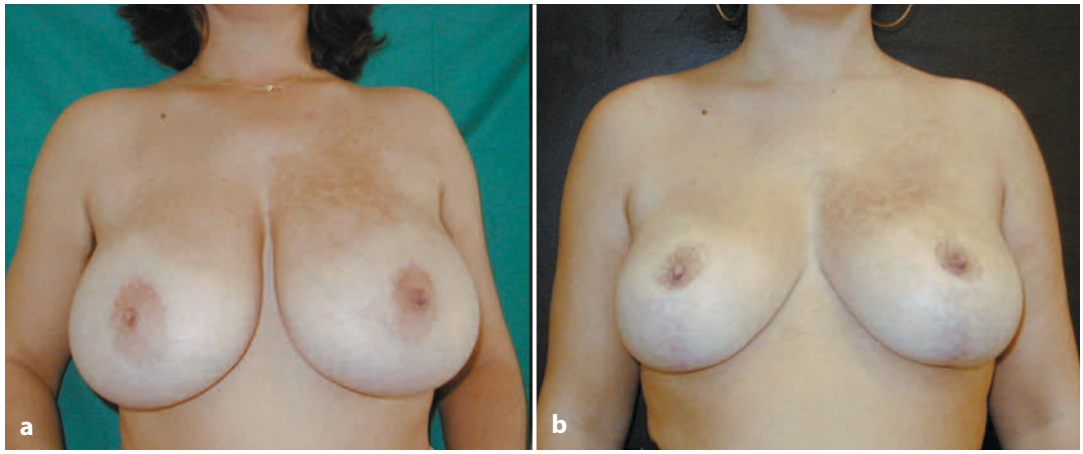

Fig. 27.8 An 18-year-old patient before surgery (**a**). Same patient 4 years after bilateral reduction mammaplasty (800 g for each side) (**b**)

Botti [36], proposes partial removal of the periareolar skin, the undermining of the lower portion of the breast from the skin as well as from the chest and the incision on the deep surface of the gland so that the gland can be freed and widened towards lower quadrants. A prosthesis, usually anatomically shaped, is placed in the suprapectoral space.

Another method, by Muti [35, 37], contemplates the use of a rhomboid glandular flap whose apex is above the nipple, carved in the middle of the lower pole of the gland and inferiorly tilted. The flap shape allows simultaneous reduction of areolar diameter. In this case too, surgery ends with placement of a breast implant (Fig. 27.7) anatomical or round-shaped. The latter versatile method has allowed us, in selected cases, to correct the deformity without the use of breast prostheses (Fig. 27.6b).

27.4.2 Acquired Anomalies

27.4.2.1 Juvenile Hypertrophy

Juvenile gigantomastia is a benign disorder of the breast which is rare. It is characterized by massive enlargement of one or both breasts in otherwise healthy adolescent girls. The etiology of this disorder remains unclear. To establish the diagnosis, all the other causes of gigantomastia must be excluded. Drug-induced gigantomastia (due to D-penicillamine, neothetazone, cycloprosin or protease inhibitors) must be ruled out. Pregnancy tests and serum levels of estrogen, progesterone, prolactin, and gonadotropins should be normal, as should urinary levels of 17-keto- and 17-hydroxysteroids (which are related to adrenal dysfunction). Juvenile gigantomastia is not associated with hormonal disorders. Imaging studies can rule out tumors such as fibroadenoma, juvenile cystosarcoma phyllodes, and malignant breast carcinoma (including lymphoma and sarcoma).

Endocrine therapy alone is rarely successful. Sometimes, after reduction mammaplasty, it is possible to observe recurrent hypertrophy. Indeed, juvenile gigantomastia is prone to recurrence, and several studies suggest that subcutaneous mastectomy provides definitive treatment. Other authors advocate the association of tamoxifen and reduction mammaplasty (Fig. 27.8) to obtain stable results. The age to treat these patients is very variable (13–14 years to 17–18 years) and is dependent on psychological discomfort. However, some authors suggest that only older patients can be treated definitively with reduction surgery alone [38].

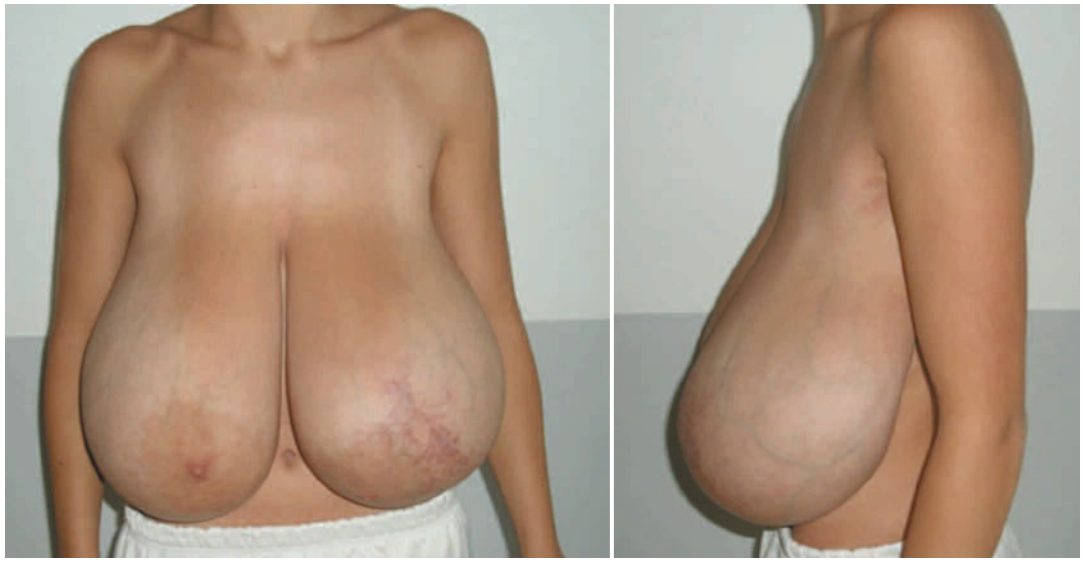

Fig. 27.9 A 17-year-old patient with gigantomastia. Almost all the breast tissue was replaced with fibroadenomas

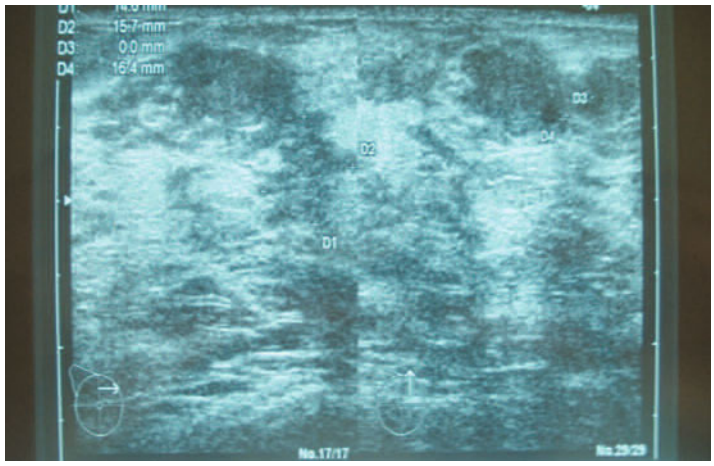

Fig. 27.10 Ultrasonography of the breast showing multiple hypoechoic masses with smooth margins and partially lobulated margins

27.4.2.2 Gigantomastia (Fig. 27.9)

The causes of macromastia in pubertal and para-pubertal females vary. They include endocrine changes and childhood obesity; sometimes idiopathic forms are possible. It is important to know the etiologies and pathophysiology to make a precise diagnosis and consider the true surgical indication *versus* medical treatment. The body mass index (BMI) should be recorded every time a patient is applying for breast reduction; the BMI is >30 in most cases. These patients should be referred to a dietician before surgery to avoid the recurrence. The main symptoms are: pain in the neck, back, and/or shoulder; intertrigo, shoulder grooving. Many patients complain of difficulty in finding brassieres and participating in sports activities; social distress is also a problem. Preoperative evaluation with ultrasonography is essential to assess glandular tissue (Fig. 27.10).

Gigantomastia is often associated with

Table 27.1 Etiologic factors for gynecomastia

• Idiopathic (most common);
• Physiological (neonatal): circulating maternal estrogens *via* placenta
• Pubertal: relative excess of plasma estradiol *versus* testosterone
• Age: decrease in circulating testosterone, peripheral aromatization of testosterone to estrogen
• Pathological: cirrhosis, adrenal tumors, hyperthyroidism, adrenal hyperplasia, congenital or acquired hypogonadism, testicular tumors
• Pharmacological: marijuana, calcium-channel blockers, spironolactone, cimetidine, ketoconazole, anabolic steroids

severe breast ptosis. We evaluate the distance between the sternal notch and NAC before implementing the chosen breast reduction procedure. The vitality of the NAC is dependent upon its vascular supply. Our first choice is the superior pedicle because of its reliability and long-term results.

If the amount of breast tissue to be removed is >500 g for each side, we can use inferior pedicled reduction mammaplasty. In some selected cases (especially if the normal parenchyma is replaced partially or completely with benign neoplasms such as fibroadenomas) the amputation–graft procedure can be used after careful explanation of the disadvantages to the patient and parents.

27.4.2.3 Gynecomastia

Gynecomastia is benign, excessive development of the male breast. The overall incidence is 32–36% (≤40% in autopsy series). Up to 65% of adolescent boys are affected. It usually develops during mid-puberty (14 years) and is self-limiting, with an average duration of 1–2 years. During middle age, approximately 30–36% of men develop gynecomastia, with the prevalence gradually increasing to >70% in the seventh decade. It is bilateral in 75% of cases. In unilateral cases, the right side is affected more often that the left side. Sometimes, it is the symptom of other, more severe disorders such as hermaphroditism, testicular tumors and Klinefelter's syndrome.

The etiology of gynecomastia is multifactorial and is most commonly idiopathic. However, the pathophysiological mechanism involves a relative or absolute excess estrogen action, decreased levels of circulating androgens, or a defect in androgen receptors [39]. The potential causes of gynecomastia are detailed in Table 27.1 [40].

The histological classification of gynecomastia is according to the degree of stromal and ductal proliferation [41]:

- florid: increased budding ducts and cellular stroma;
- intermediate: overlapping florid and fibrous patterns;
- fibrous: extensive fibrosis of the stroma with little ductal proliferation.

The proliferation of ductal and stromal tissues leads to increased breast volume. If this lasts >1 year, fibrosis and hyalinization prevail over epithelial growth. In these cases, surgery can become an irrevocable option. The risk of malignant transformation is real only in patients with Klinefelter's syndrome (1:1,000 cases to 1:400).

The classification of gynecomastia by Simon and colleagues [42] distinguishes three degrees of illness. In our opinion, it is a very useful clinical classification that supports treatment planning. In the first degree, a minimal increase in breast volume is evident. In the second degree, breast volume is increased significantly with cutaneous excess. In the third degree, a significant increase in breast volume leads to a variable degree of ptosis.

With regard to the diagnosis, initial evaluation involves differentiation between fatty tissue, increased mammary tissue and tumor. Pseudogynecomastia is a bilateral increase in

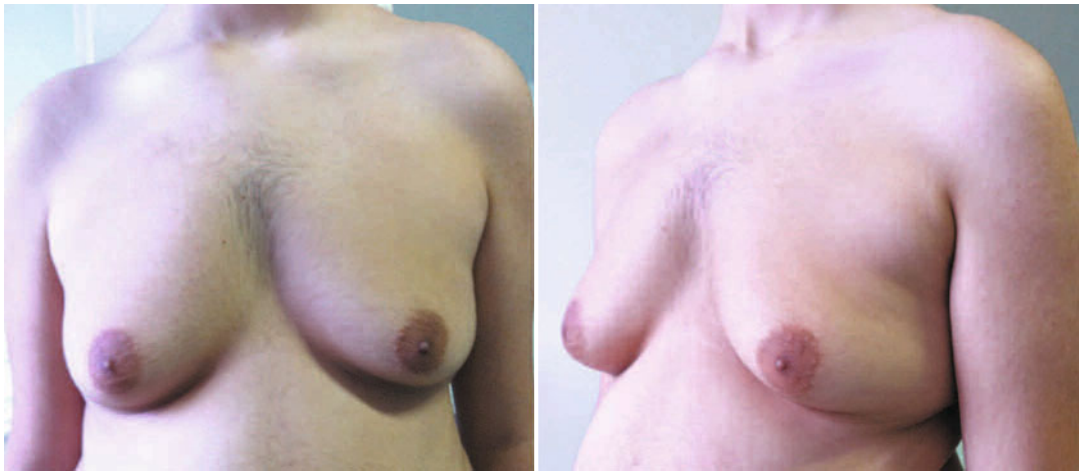

Fig. 27.11 A 14-year-old patient with Klinefelter's syndrome and severe gynecomastia

male breast size resulting from fat tissue. There is no hyperplasia of breast tissue. A complete physical examination must investigate: breast ptosis; skin excess; lack of male hair distribution; and feminizing characteristics. Testicular palpation is vital in patients with gynecomastia to rule out testicular tumors. Imaging studies such as mammography and/or ultrasonography, are useful. Biopsy may be applied in some cases (especially in Klinefelter's syndrome). Endocrine evaluation must be carried out before surgical treatment.

During adolescence, treatment should be postponed because gynecomastia can regress spontaneously. The choice between surgical approaches must be made with the help of clinical classification. Several procedures have been advocated to correct the different clinical aspects depending on the severity, ptosis and amount of fat tissue in the pectoral region. That is, periareolar or intra-aerolar incisions; all types of dermal and glandular pedicles for nipple relocation; free nipple grafting; and conventional and ultrasonography-assisted liposuction.

In mild and moderate cases, we usually carry out a mastectomy with a hemi-periareolar incision. In severe cases (Fig. 27.11) a mastectomy with a periconcentrical procedure or free nipple grafting is employed. The most frequently reported complications are: under-resection, over-resection, poor scarring and seromas [39, 43].

27.4.2.4 Synmastia

Synmastia is aberrant communication of the breasts (Fig. 27.12). It is usually a result of (i) technical complications after breast-augmentation surgery caused by over-dissection at the medial side of the pocket, over the sternum, in the subglandular plane or (ii) over-division of the insertion of the major pectoralis muscle along the sternum in the submuscular plane [44]. The most important rules to prevent synmastia are: accurate surgical planning, correct choice of implant size, and appropriate surgical technique. It is difficult to correct synmastia: additional procedures expose the patient to risks, cost, and dissatisfaction.

27.4.2.5 Asymmetry

Breast asymmetry can affect the wellbeing of young females. It is associated in 69% of cases with tuberous breast, whereas the remaining percentage can be due to PS, pectus excavatum, pectus carinatum iatrogenic factors (chest tissue biopsy) and scoliosis; sometimes asymmetry is idiopathic (Fig. 27.13). Correction of breast asymmetry may present a reconstructive challenge, especially in tuberous breasts. Tho-

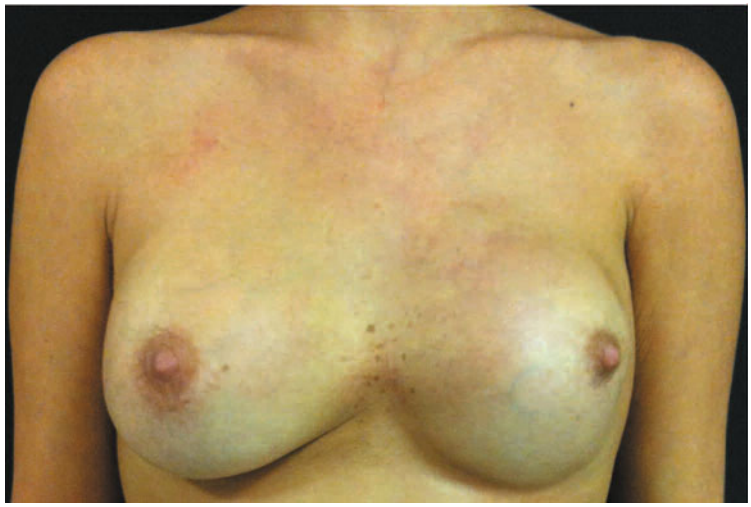

Fig. 27.12 Synmastia. Note the lack of separation or cleavage between the breasts

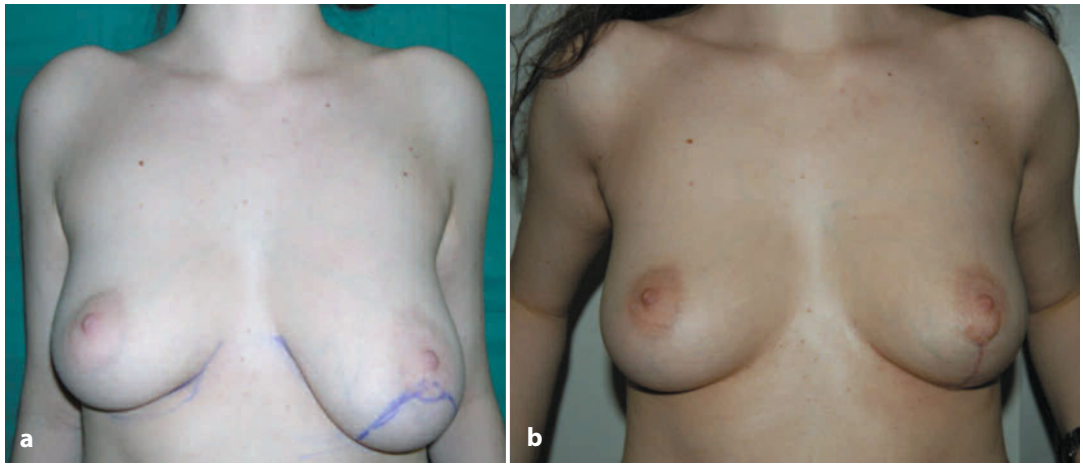

Fig. 27.13 Preoperative view of a 16-year-old patient with moderate asymmetry (**a**). Same patient 5 years after left reduction mammaplasty (**b**). The right breast did not undergo surgery

racic symmetry is the aim. The surgical modalities used include augmentation mammaplasty with or without tissue expansion, parenchymal scoring, NAC reduction, reduction mammaplasty and/or mastopexy.

27.4.2.6 Tumoral Lesions

Other minor diseases include breast atrophy, dysplasia, fibroadenoma, giant fibroadenoma, cystosarcoma phyllodes, intraductal breast papilloma, adenocarcinoma, mastitis, traumatic breast disorders, benign breast disease, fibrocystic change, mastalgia and galactorrhea.

27.4.2.7 Other Defects

Patients with a history of thoracotomy or tumor excision (Fig. 27.14) can present with breast deformities. Surgical procedures should be undertaken with great care in the vicinity of the breast bud. Inadvertent (and even apparently minor) trauma to the bud can result in profound disturbances in the growth and develop-

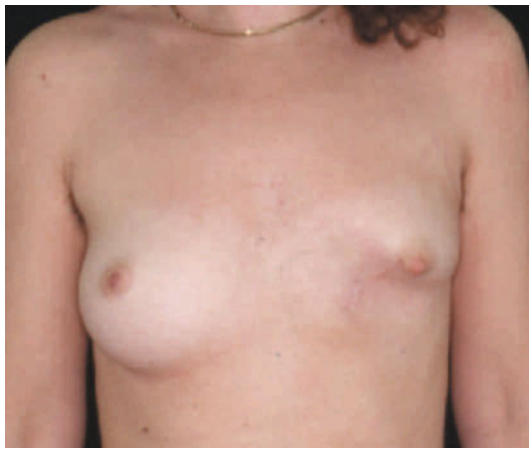

Fig. 27.14 A 16-year-old patient with an iatrogenic sequela of tumor excision at 4 years of age. Note the defect of the lower half of the breast

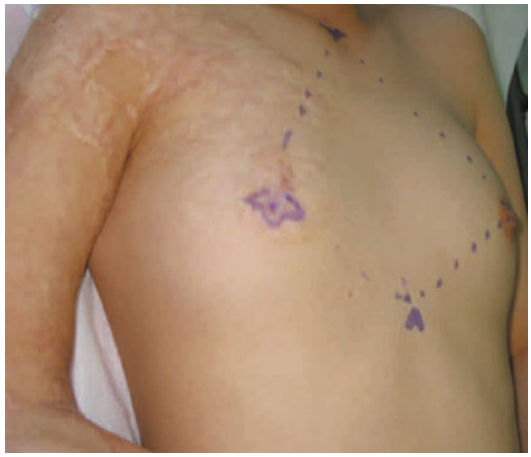

Fig. 27.15 A 12-year-old patient with burn sequelae in the right breast and ipsilateral arm. Reconstruction of the nipple is planned (preoperative design)

ment of the breast. Burns (Fig. 27.15) and traumatic injury can damage the breast bud and interrupt the normal development. All these patients may require breast reconstruction.

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Part VII

Infections

Thoracic Empyema

28

Francesco Molinaro and François Becmeur

28.1 Introduction

Empyema thoracis is an accumulation of pus within the pleural cavity. The correct definition of empyema is the presence of pus in the pleural space. There are various criteria to define and classify parapneumonic pleural effusions [1].

It may result from a direct extension of infective agents from the lung parenchyma or bronchial tree, ruptured intrathoracic abscesses, hematologic spread or contamination resulting from surgery or trauma and mediastinal sources (esophageal perforation).

Approximately 0.6% of pneumonia episodes in children are complicated by empyema. The incidence of parapneumonic empyema in children is 0.4–6 per 1,000 hospital admissions [2]. Moreover, the incidence of empyema thoracis in children has increased significantly in recent years in the western world. The incidence of empyema is around 3.3 cases per 100,000 children [1].

The microbiology of childhood empyema dictates appropriate antibiotic selection. *Haemophilus influenzae*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* remain the most common pathogens cultured in empyema [3].

Empyema can been divided into three stages. In stage 1 (exudative stage), there is a simple parapneumonic effusion with normal levels of glucose and a correct pH in pleural fluid. In stage 2 (fibrinopurulent stage), there is an increase in fibrin levels and the number of polymorphonuclear leukocytes. At this stage, the fluid in the pleural space begins to loculate. There also are associated changes in the chemistry of pleural fluid: glucose levels and the pH decreases and lactate dehydrogenase (LDH) levels increase. In stage 3 (organizing stage), fibroblasts grow from both pleural surfaces, forming an inelastic pleural "peel" or "rind". This results in entrapment of the involved lung [4].

Physical examination and laboratory analyses of pleural fluid aid the diagnosis. CT of the chest frequently provides others information. Recently, the use of ultrasonography has become increasingly helpful, but remains operator-dependent. Radiological images can define the pleural rind and locate its cavities.

The morbidity and mortality of this condition have undoubtedly improved over recent years, the nature and timing of surgical intervention is controversial.

In the past, empyema was treated with antibiotics, prolonged drainage of the chest

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and, if this failed, open thoracotomy for debridement. This was associated with long hospitalizations and significant morbidity due to the delayed referral to a surgeon and to the surgical procedure. With the expanded use of endoscopic techniques, thoracoscopy has been increasingly used in the treatment of empyema and much earlier in the course of the disease [5].

The role of intrapleural fibrinolytic agents for the treatment of empyema is not well defined because this type of therapy could fail with more advanced disease. Some authors, because fibrinolytic therapy can be used to dissolve fibrin-produced loculations, suggest attempting this therapy before video-assisted thoracoscopic surgery (VATS). Flexible bronchoscopic evaluation with bronchoalveolar lavage fluid (BALF) can be undertaken before the surgical procedure to evaluate associated endobronchial lesions [6]. VATS enables the removal of pus, elimination of loculations, and insertion of a chest drain. The pleural effusion can be used to test for bacteria (aerobic and anaerobic) and fungal cultures.

Air leaks and residual pneumonia are the most common complications. The prevalence of mortality is 0–13%. Aggressive postoperative pulmonary therapy and increased activity benefit patients. The long-term outcomes of patients treated by VATS are encouraging [5].

28.2 Etiology

Usually, empyemas follow acute bacterial lobar pneumonia. Underlying conditions with associated immune suppression could predispose a child to empyema. The most common causative organism is *Streptococcus pneumoniae*; less common agents are Gram-negative bacteria and fungi [6].

Empyema can follow an infection from a traumatic hemothorax, lung contusion, a penetrating injury to the chest, or after infection in the pleural space following thoracotomy. A secondary empyema in children could follow intrathoracic rupture of the esophagus as a result of a leaking anastomosis or rupture after dilatation of an esophageal stricture. Peritonitis caused by acute appendicitis could lead to empyema as a result of reduced host resistance, postoperative pneumonia, or local spread of infection through the diaphragm. Sometimes, tuberculous effusions present with secondary bacterial infection. Similarly, hydatid cysts may rupture into the pleural space or become infected due to a secondary infection [7].

28.3 Pathogenesis

The variation in presentations of pleural empyema is dependent upon the virulence of the organisms, resistance of the host, and use of appropriate antibiotics and drainage procedures.

28.3.1 Stages

Exudative stage: The inflammation caused by pneumonia results in increased capillary permeability [8]. Accumulation of fluid and cells into the pleural space from the visceral pleura leads to the exudative phase of the empyema. The fibrinolytic system is activated by the products of inflammation, and capillary permeability is increased further [9].

Fibropurulent stage: The coagulation cascade is activated as inflammation increases with suppression of fibrinolysis, which favors fibrin deposition in the pleural cavity. A certain membrane called the "pyogenic membrane" proliferates due to the accumulation of fibroblasts, phagocytes, bacteria, and fibrin. This membrane initially covers the parities of the thorax but subsequently fibrin strands septate the empyema cavity and loculations form. This defines the fibrinopurulent phase of the disease [10].

Organization phase: Fibroblast proliferation leads to the formation of fibrous tissue. This process localizes the infection. The fibroblasts deposit layers of fibrous tissue (rinds) on the visceral and parietal pleura and

within the empyema cavity. The fibrous rind encases the collapsed lung and prevents it from re-expanding. As the empyema continues to organize, the fibrous rind thickens with further lung collapse and restriction of chest-wall movement [11].

28.3.2 Extrapulmonary Complications

Convulsions, osteomyelitis, toxic shock syndrome, disseminated intravascular coagulation, gastric hemorrhage, thrombosis, and multiple organ failure are extrapulmonary complications of staphylococcal and streptococcal pneumonia with overwhelming sepsis [12].

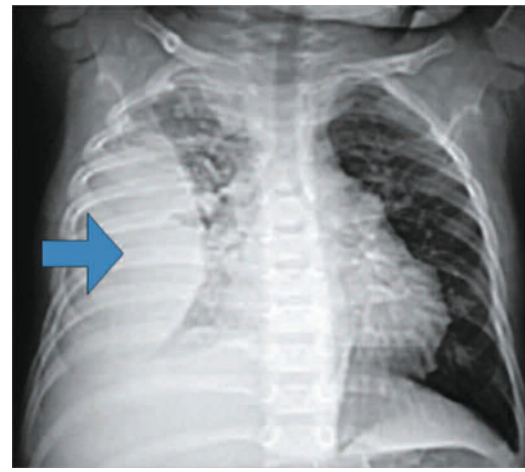

Fig. 28.1 Chest radiograph showing a right large pleural effusion (*arrow*)

28.4 Clinical Features

In children, symptoms related to pneumonia such as fever, cough, malaise, and loss of appetite, precede symptoms related to pleural empyema. Tachypnea, fever and lethargy can be the main early symptoms in younger children. Some children also complain of pleuritic chest pain or abdominal pain. Possible contact with subjects infected with tuberculosis should be examined. The possibility of an inhaled foreign body should not be forgotten [13]. Some children will be cyanosed and for this reason measurement of oxygen saturation (SaO_2) by pulse oximetry is particularly important.

The thorax can appear decreased in chest expansion, with stony dullness to percussion, and reduced (or absent) breath sounds. A mediastinal shift may be detectable by tracheal deviation and displacement of the apex beat to the opposite side. Consolidation of the underlying lung causes bronchial breathing and reduced air entry that is apparent on auscultation [14].

28.5 Diagnosis

Blood tests and radiological parameters are very important for the diagnosis. Neutrophilia is frequently present and is associated with normochromic normocytic anemia. Levels of C-reactive protein (CRP) and other inflammatory markers such as procalcitonin are also elevated. The serum albumin is invariably low. Coagulation abnormalities may be present and must be recognized prior to surgery.

A plain radiograph of the chest is usually the first imaging investigation. Pneumonic consolidation will be seen (Fig. 28.1). A mediastinal shift with large effusions can be present. Lung abscesses, pneumatoceles, and pyopneumothorax are all visible on a chest radiograph [15].

Ultrasonography is particularly valuable: ultrasound can be used to identify fluid in the pleural space. Ultrasound is most useful to ascertain if an effusion is loculated (Figs. 28.2 and 28.3). This examination is also useful for guiding insertion of a chest drain or carrying out thoracocentesis (Fig. 28.4) [16].

Contrast-enhanced CT complements ultrasonography for imaging children with complicated pneumonia. CT gives more important information about anatomical extension of the disease, clearly showing the lung parenchyma and pleural wall, a mediastinal shift, and bronchopleural fistulae (Figs. 28.5–28.7) [14].

Cultures of sputum, blood and, if possible, pleural fluid, can be carried out routinely.

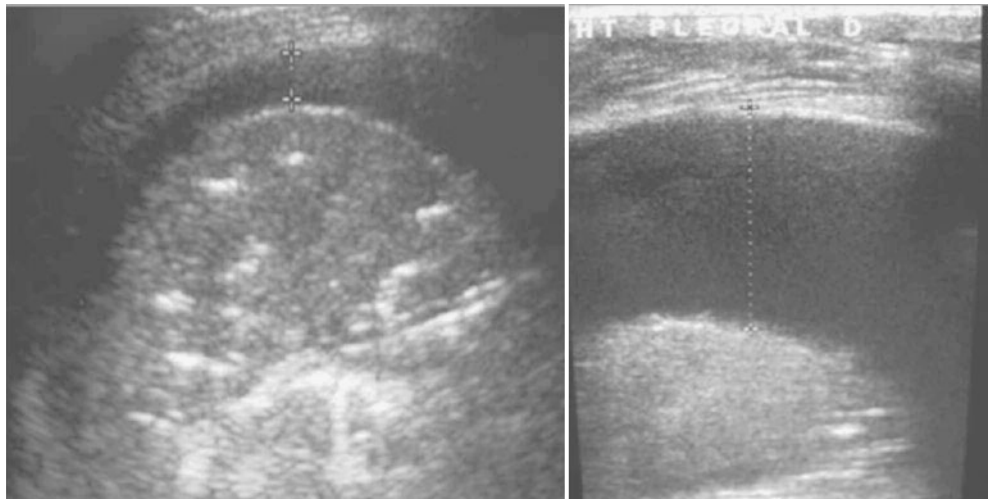

Fig. 28.2 Ultrasound evaluation showing an echogenic focus that has resulted in a pleural effusion

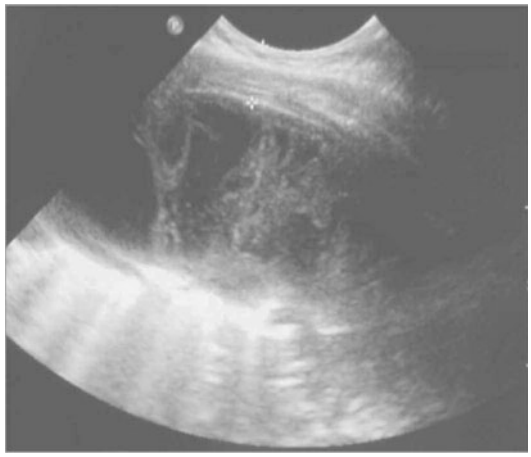

Fig. 28.3 Ultrasound evaluation showing a central zone which represents pus

Microbial cultures should always include tests for bacteria and tuberculosis. A Mantoux test should be carried out if tuberculosis is suspected [13].

28.6 Management

Early recognition and treatment of lobar pneumonia in children reduces the incidence of empyema. Appropriate antibiotic therapy is essential as a first step of the management of empyema in children. Response to antibiotics is dependant upon the pathogen involved, empyema stage, and immune status. In the early exudative stage, high concentrations of antibiotics alone may be effective treatment. However, antibiotics are unlikely to be effective in more advanced disease without surgical intervention [17].

Recommendations for antibiotic therapy for childhood empyema are lacking. A first-line treatment of a generic antibiotic is usually adopted (such as cephalosporin given intravenously). Therapy should then be altered depending on the sensitivity of the pathogen isolated [18].

Along with antibiotic therapy, medical support with humidified oxygen, fluids, analgesia and physiotherapy is required. Antipyretics should be given regularly. Children who fail to improve clinically and upon imaging findings should be referred to a center with expertise in the drainage procedures for empyema [17].

28.6.1 Surgical Management

28.6.1.1 General Principles

Thoracoscopic debridement has significantly changed the treatment of empyema in chil-

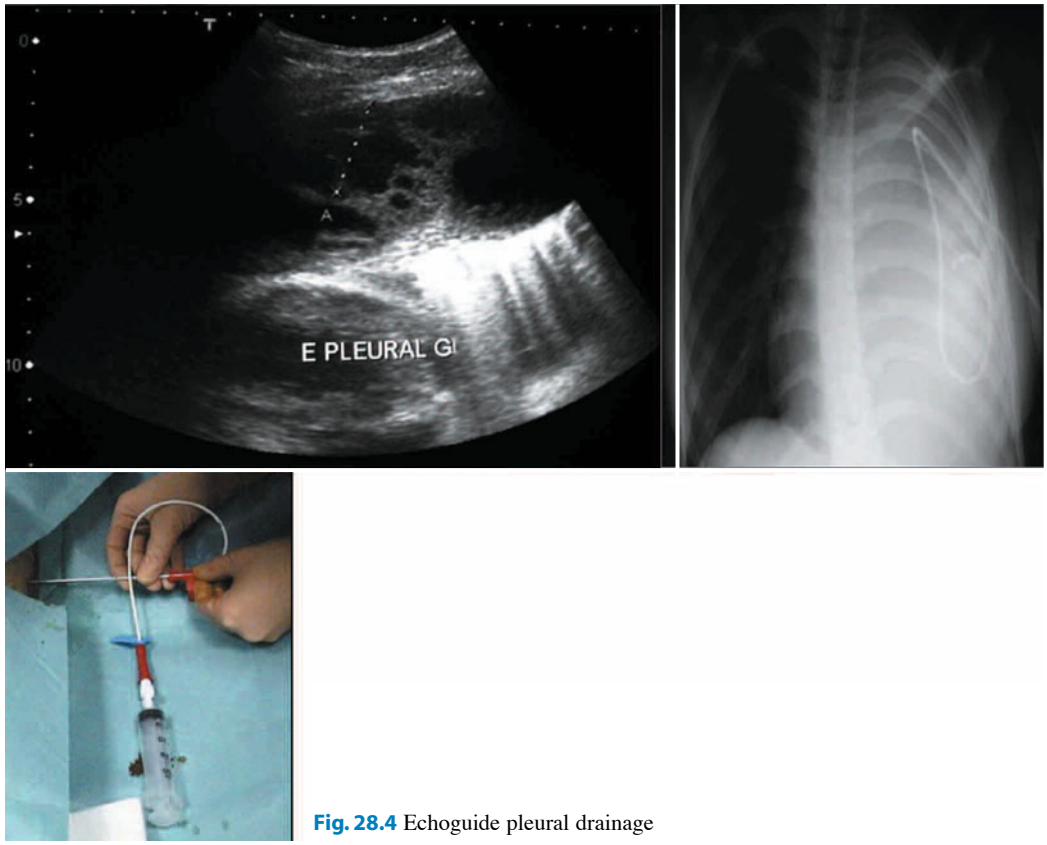

Fig. 28.4 Echoguide pleural drainage

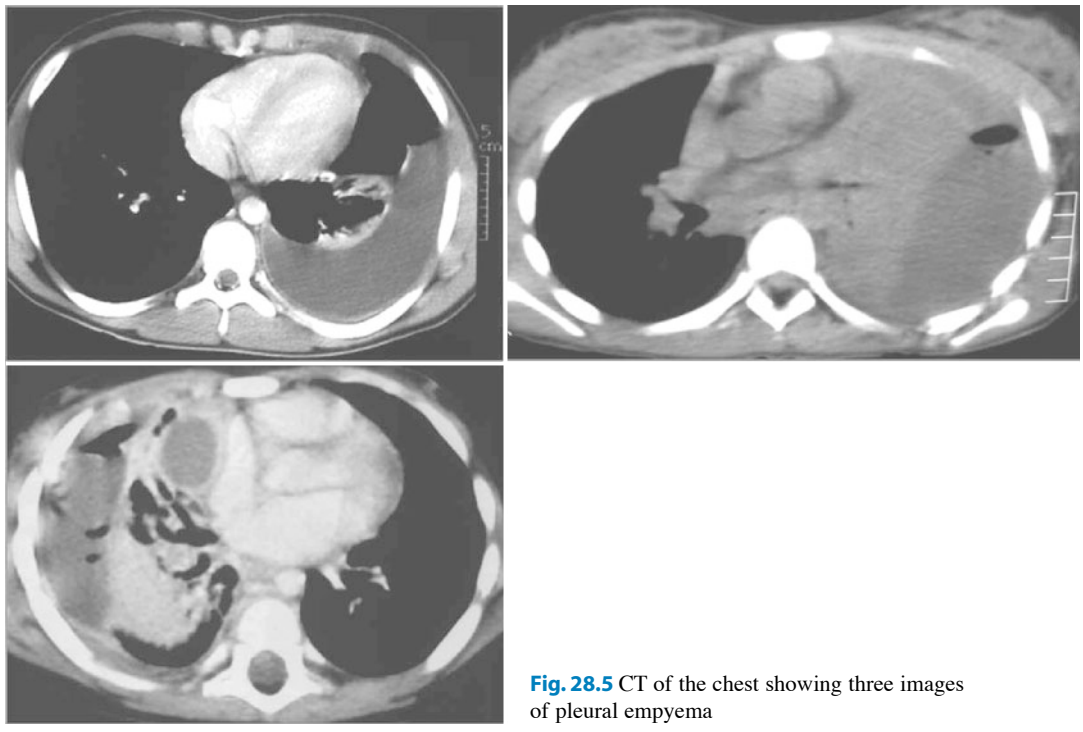

Fig. 28.5 CT of the chest showing three images of pleural empyema

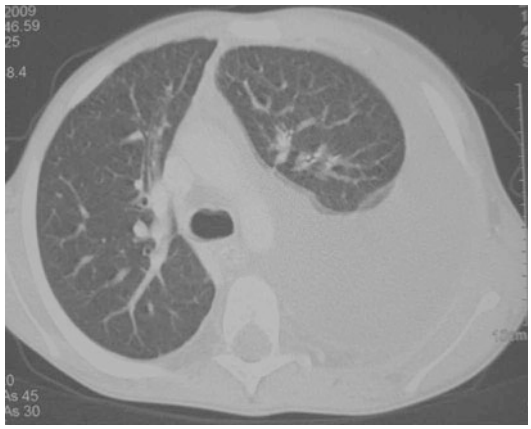

Fig. 28.6 CT of the chest showing a large mediastinal shift

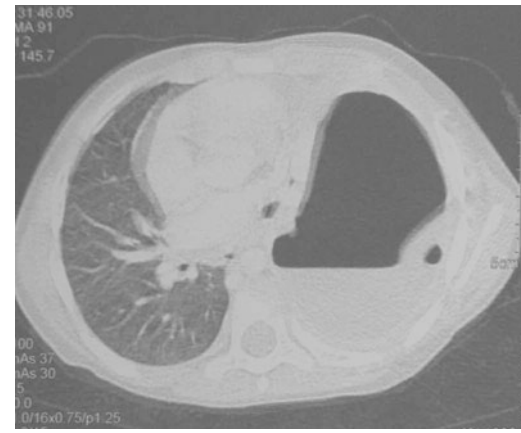

Fig. 28.7 CT of the chest showing a bronchopleural fistula

dren. The ability to quickly clean out infected fluid and debris through minimal incisions with minimal morbidity has lowered the threshold for intervention. In general, any child thought to need a chest tube for drainage of empyema is taken to the operating room for thoracoscopic debridement. Earlier intervention has resulted in quicker recovery with minimal complications [18]. The goal of surgery is to achieve full expansion of the lung and resolution of empyema. An added advantage of the procedure is that the lung parenchyma may itself be readily evaluated.

The time the child is brought to the surgeon is very important for the timing of surgery. In the fibrinopurulent phase, even drainage of the pus with lung expansion is imperative to reduce progression of the disease to the organization phase [19]. If surgical consultation is delayed for a prolonged period of time, thoracoscopic drainage and debridement may not be possible and open decortication may be the only option. This can, however, be assessed by thoracoscopy.

For these reasons, early definitive surgical intervention is highly effective in childhood empyema. Unfortunately, it is extremely difficult to predict which children will respond to simpler measures and avoid the need for thoracotomy [19, 20].

However, one of the major criticisms of an all-inclusive surgical approach is that children who may otherwise respond to less-invasive therapies (i.e., those with stage-I and -II empyema) are subjected to general anesthesia and surgery. Because of their active lung infections, these patients are an increased anesthesia risk (American Society of Anesthesiologists (ASA) class II and III). In addition, these children are catabolic because of stress, making recovery from surgery slower [18].

Successful treatment of empyema has also been described for some children receiving tube drainage alone or with adjuvant fibrinolytic therapy. Therefore, if some patients are treated successfully with these less-invasive methods and have comparable outcomes, then VATS can be reserved for patients truly needing this procedure.

Ultrasound can be used to characterize pleural disease. With higher sonographic grades of empyema, the chance of successful treatment with tube drainage and fibrinolytic agents decreases. As suggested by Gates et al., ultrasound characterization can help guide therapy (tube drainage *versus* surgical consultation). If the likelihood of resolution of pleural disease is low based on the characterization of solid peel, tube drainage should not be attempted [16]. However, if the pleural disease does not appear to be predominately organized, tube drainage can be done. There are conflicting studies concerning the use of intrapleural fibrinolytics. Fibrinolytic agents are

adjuncts used to improve drainage, and their use should not change the underlying principles of empyema management [19].

Chen et al. found that >70% of children with late-presenting empyema required surgery, and that more than half of the children received initial chest tube drainage. Delay in surgery was associated with more procedures, more radiographs, and an increased length of stay in hospital. Despite later intervention, patients undergoing surgery as an initial approach had the shortest length of stay in hospital. Early surgical intervention is indicated for most children referred with established empyema [20].

28.6.1.2 VATS

The use of VATS as an initial intervention in children with empyema has obvious diagnostic and therapeutic advantages. However, there remains strong opposition to this indication because of the lack of randomized trials. A multicenter prospective study is required to define the most effective method of assessment of pediatric parapneumonic empyema and the most successful treatment at each stage of the disease process.

Early VATS can give good lung re-expansion and improve drainage of the empyema. Loculi can be separated, allowing thick pus to drain effectively. Several series have shown reduced postoperative pain, shorter stay in hospital, and better cosmetic results when VATS is compared with conventional thoracotomy [21]. Although most studies have been retrospective with small cohorts of patients, VATS has proven effective, with minimal complications, and is well tolerated. Conversion to open thoracotomy is necessary if access to the pleural cavity cannot be achieved because of a thick pyogenic rind or excessive bleeding. Mini-thoracotomy and debridement or decortication in these instances is safer and curative [22].

Debridement using VATS: Patients are brought to the operating room. General anesthesia with simple or double-lumen endotracheal intubation is initiated, and patients placed in a full or semilateral position according to empyema location (Fig. 28.8).

Selective endobronchial intubation (or the use of bronchial blocker in young children if double-lumen tubes are not available) may be useful in selected cases to avoid contamination of the contralateral lung. If the patient already has a chest tube *in situ*, this can be removed prior to positioning and preparation of the patient. Also, the site may be used for placement of one of the ports. A suction trap should be prepared to obtain a sample of pleural fluid for cell counting, Gram stain, and culture if this has not been done previously [20].

The surgeon may stand on either side of the patient. The surgical assistant is usually positioned on the other side of the table to hold the camera. The scrub nurse is toward the patient's feet, on either side.

The thoracic area is prepared and draped for possible open thoracotomy. The first 5-mm port is placed on the estimated location of fluid. A sample is collected for biochemical and cytologic examination, as well as bacterial, mycobacterial, and fungal smear and culture. This port is usually inserted in the fifth or sixth intercostal space in the posterior axillary line. Creation of a working space is essential (Fig. 28.9). A 0° telescope is usually employed for visualization and insufflation with CO_2 at a pressure of 5–8 mmHg. The VATS approach to empyema uses one scope port with or without an additional port to three working port(s) or utility incision. The thoracoscope with a working channel or angled end-viewing thoracoscope is used to facilitate initial dissection or examination. A second port for instrumentation is placed under thoracoscopic visualization. Two ports are usually sufficient if debridement is done early. Figures 28.10–28.12 show the three stages of empyema using VATS.

Laparoscopic instruments are used for the lysis of adhesions from the chest wall and breakage of fibrous septa. Sometimes, a thick membrane is seen encasing the lung and inhibiting expansion; a peanut sponge is used to gently peel the membrane off the visceral

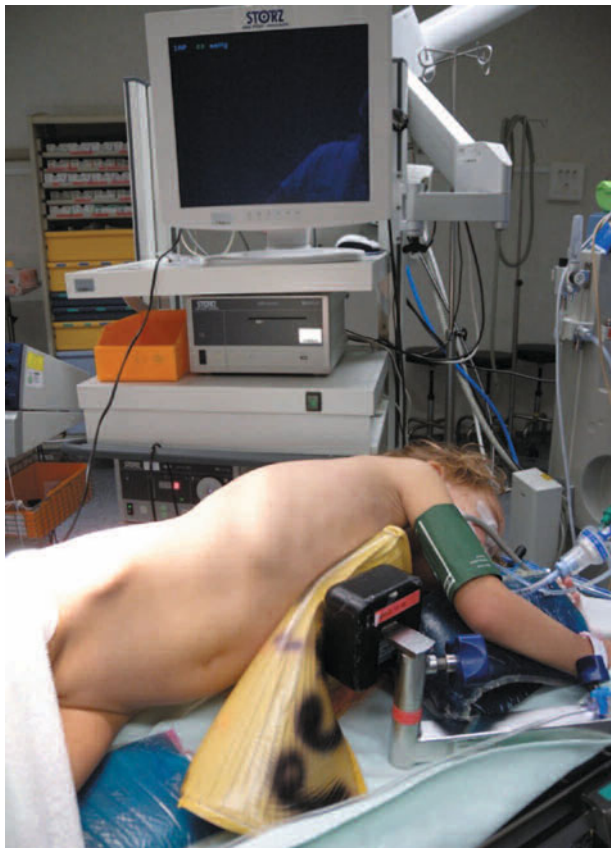

Fig. 28.8 VATS: patient positioning

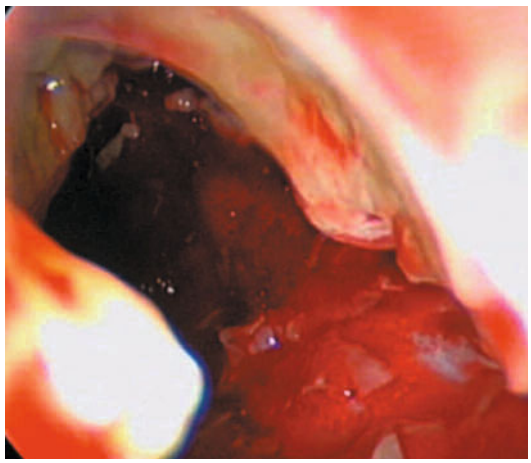

Fig. 28.9 VATS. Intraoperative image: creation of working space

pleura. A curved large-bore suction tube with or without connection to a 32-F chest tube is introduced into the chest cavity for suction. Peels on the parietal or visceral pleura are removed for re-expansion of trapped lung and for debridement (decortication) (Fig. 28.13). Pleural or lung biopsy is done if the underlying cause is in doubt [20, 21].

Most children can be managed safely on a pediatric surgical ward postoperatively with nurse- or patient-controlled analgesia. Chest radiography is repeated the following day to confirm lung expansion and assess the extent of lung consolidation.

The chest drain should remain *in situ* until the losses reduce to <30 mL/day and become clear. The child is kept in hospital on intravenous antibiotics until afebrile for ≥24 h. Chest radiography should be carried out after drain removal [20].

Conversion to open thoracotomy is indicated for failure of separation of the fibrous rind from the visceral pleura after thoracoscopic

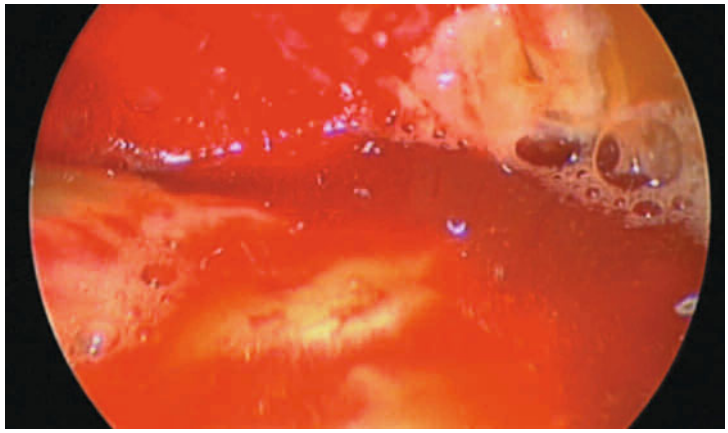

Fig. 28.10 VATS showing stage 1 of empyema: exudative stage

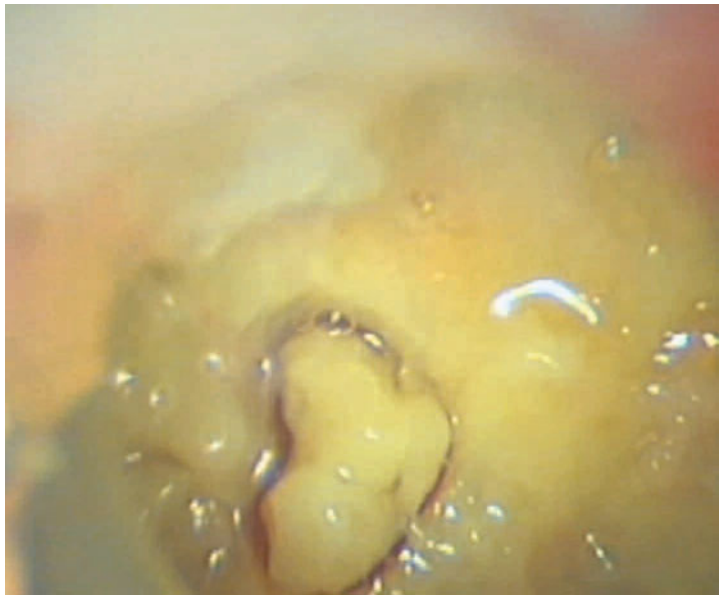

Fig. 28.11 VATS showing stage 2 of empyema: fibropurulent stage

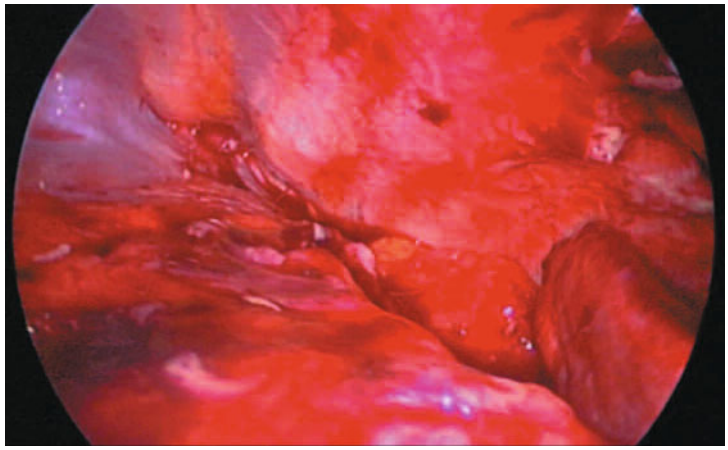

Fig. 28.12 VATS showing stage 3 of empyema: organization stage

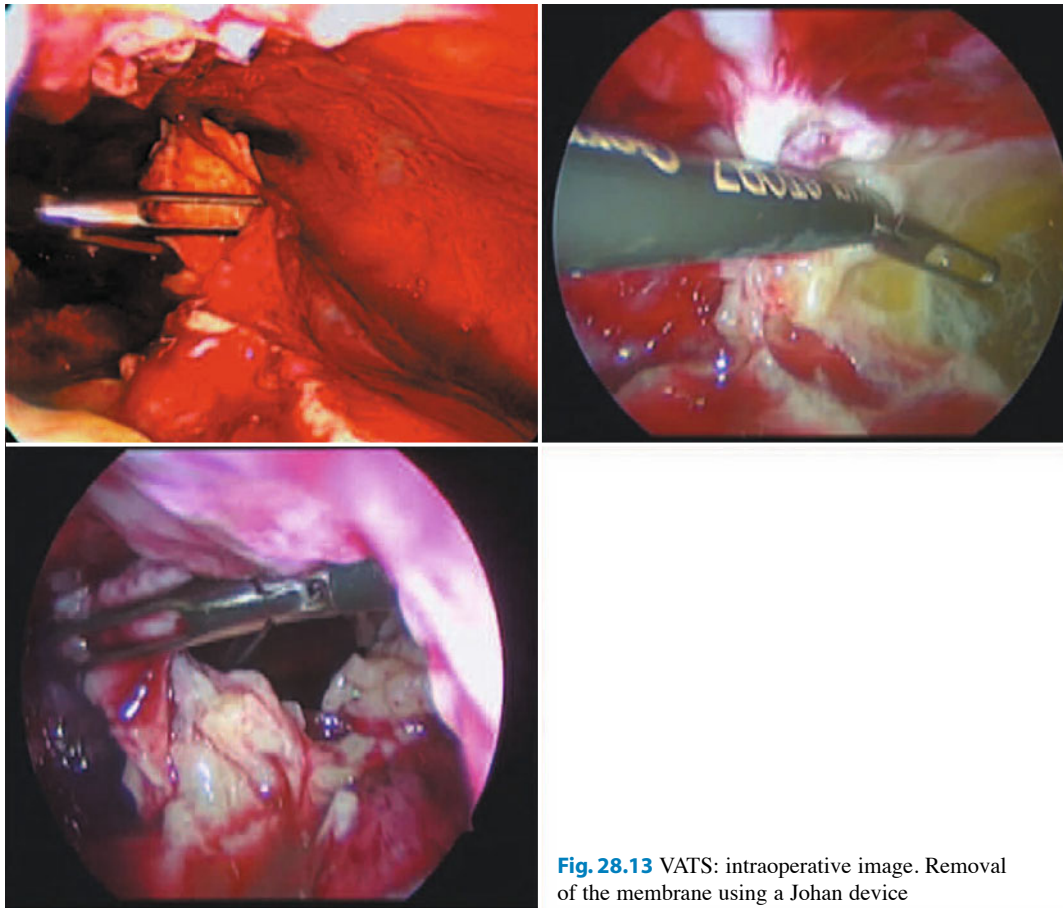

Fig. 28.13 VATS: intraoperative image. Removal of the membrane using a Johan device

maneuvers, excessive bleeding, inadequate visualization, and failure of lung re-expansion [23].

28.6.2 Management of Complex Empyemas

28.6.2.1 Bronchopleural Fistulae

A spontaneous bronchopleural fistula occasionally complicates necrotizing pneumonia (Fig. 28.14). Management of a bronchopleural fistula poses a major challenge and is associated with high morbidity. An air leak into the pleural cavity and persistent contamination of the pleural space hinder lung re-expansion. Aspiration of infectious material may contaminate the opposite lung. Preoperative contrast-enhanced CT is essential to determine lung necrosis and lung abscesses. Conservative management of the fistula has been advocated in the past, along with various surgical approaches, but all are associated with prolonged hospitalization and morbidity. The optimum management of a spontaneous bronchopleural fistula is drainage of pus from the pleural cavity with liberation of the lung to achieve complete expansion. Sometimes, it is possible to suture the lung parenchyma to close the fistula (Fig. 28.15). Excision of the parietal pleura encourages the expanded lung to adhere to the chest wall and aids healing of the fistula [17].

28.6.2.2 Bilateral Empyema

Bilateral parapneumonic empyema is encountered occasionally in infants and immunocom-

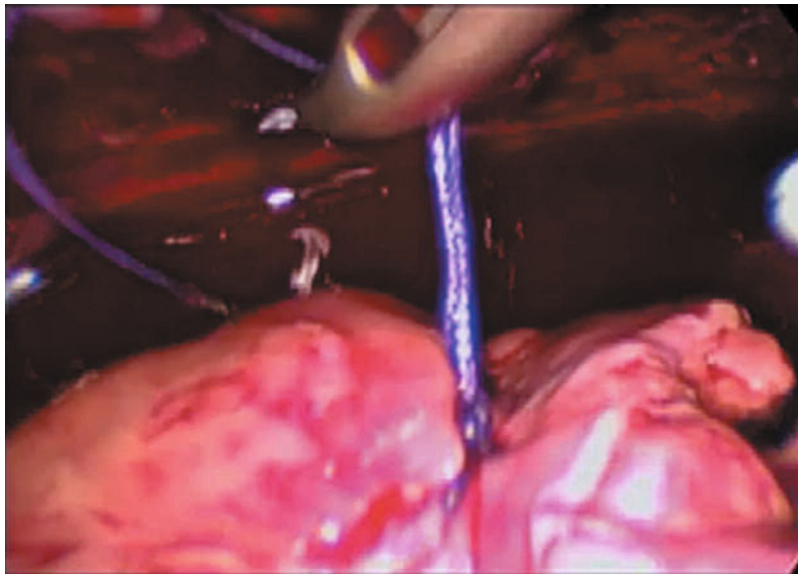

Fig. 28.15 VATS: intraoperative image. Closing of a bronchopleural fistula with a stitch

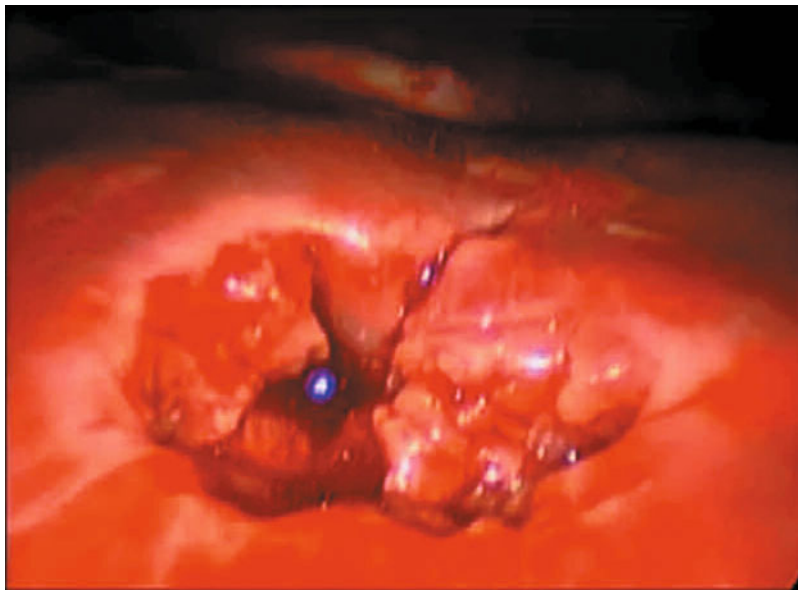

Fig. 28.14 VATS: intraoperative image. Bronchopleural fistula

promised children. However, the most common cause of bilateral empyema in children is esophageal injury, either a leaking anastomosis or perforation after dilatation of a stricture. Caustic strictures are particularly prone to perforation during dilatation.

Bilateral parapneumonic empyema is not common. The infective organism is usually staphylococcus, pneumococcus or, rarely, *Pseudomonas aerugenosa*. Staphylococcal infection is more common in malnourished children. Bilateral empyema is seen as a common complication of necrotizing mediastinitis. Necrotizing mediastinitis occurs as a result of descending infection from the retropharyngeal plane of the neck. Bilateral empyema has

been managed successfully with VATS debridement [24].

28.7 Follow-up

Children with empyema should be seen 4–6 weeks after hospital discharge, with subsequent follow-up depending upon improvement based on evaluation of clinical and findings. Attention to nutrition is essential. Iron supplements may be necessary if the child is anemic. Antibiotics (p.o.) should be continued for 4 weeks after discharge from hospital [18]. The long-term prognosis after treatment for empyema is excellent in most subjects despite the different methods of management. Complex empyema, however, carries a significantly higher morbidity and longer stay in hospital, and some of these children require prophylactic antibiotics during the winter months to prevent further respiratory infections [20].

28.8 Conclusion

The rapid identification of patients at risk of complicated parapneumonic effusions or empyema can improve outcome by allowing early drainage of the pleural space. The findings of chest radiography and CT as well as the characteristics of pleural fluid suggest that a parapneumonic effusion has a high likelihood of requiring drainage.

Use of VATS as the initial intervention in children with empyema has obvious diagnostic and therapeutic advantages. Adequate drainage of the abscess (empyema) within the pleural space and re-expansion of the collapsed lung are the fundamental principles of empyema management. However, there remains strong opposition because of the lack of randomized trials showing efficacy, which makes physicians reluctant to relinquish their patients to surgeons. A multicenter prospective study is required to define the most effective method of assessment of pediatric parapneumonic empyema as well as the most successful treatment at each stage of the disease process.

VATS is a safe and effective procedure for the treatment of complicated parapneumonic effusions or empyema. Earlier intervention using VATS to treat complicated parapneumonic effusions or empyema can elicit better results than the other methods. Additional prospective, randomized, or controlled studies should be carried out to identify the optimal timing and conditions of VATS for complicated parapneumonic effusions or empyema.

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Lung Abscess

29

Giovanni Ruggeri, Michela Maffi, Tommaso Gargano and Mario Lima

29.1 Introduction and Epidemiology

A lung abscess is a thick-walled cavity that contains purulent material [1–2]. It is a rare condition in children. It arises as a complication of a poorly controlled pneumonia, and has an estimated incidence of 0.7 per 100,000 hospital admissions/year. A lung abscess can be defined to be "primary" if it occurs in a previously healthy child or "secondary" if underlying conditions predispose to the onset of the abscess [1–8]. It can be "acute" or "chronic" if it has been present for >6 weeks [1, 9].

29.2 Historical Aspects

At the time of Hippocrates, a lung abscess was at least known as a pathologic entity burdened by high mortality, whereas aspiration of oropharyngeal secretions was recognized as a probable cause. Hippocrates also suggested external drainage as treatment [10]. In 1904, Guillemot [11] identified microbes normally belonging to oral flora in empyema thoracis, and assumed that aspiration was an important event in the pathogenesis of pulmonary suppurative disease [1]. In 1942, Brock [12] demonstrated a relationship between the position of the patient and the anatomical location of a lung abscess, thereby giving more weight to the theory of oropharyngeal secretions as sources of pathogens.

In 1936, Neuhoff and Touroff [8, 13] treated lung abscesses with one-stage external drainage with good results. In 1979, Welch [8, 14] reported a two-stage procedure in which the first step was used to stimulate pleurodesis and the second for drainage; the prevalence of mortality was 40%.

In the first half of the twentieth century, the surgical approach was preferred. With the introduction of antibiotics, conservative management gained wide acceptance. In the 1970s, some authors [15–16] suggested bronchoscopic drainage. However, this was identified as carrying a risk of microbial dissemination in the airways, so this procedure was abandoned. In recent years, image-guided percutaneous drainage [17–19] has become popular and is considered helpful for the diagnosis and therapy (especially in patients who do not respond to antibiotics).

29.3 Predisposing Factors

When an infective process in lung parenchyma is poorly controlled by bronchial defences,

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it can lead to progressive destruction of pulmonary tissue and abscess formation. This process is dependent upon several factors, including the pathogen involved (especially in a previous healthy child) and the underlying predisposing conditions.

Aspiration of oropharyngeal secretions or gastric contents is one of the most important predisposing factors. In particular, the number and volume of aspirated materials and impairment of normal clearance mechanisms contribute to abscess formation [2, 20]. Many authors have reported a correlation between the patient positioning during aspiration and the anatomical location of the abscess. In supine patients, the superior segments of the lower lobes are more commonly involved. If the child is in the right decubitus position, the right upper lobe is at risk; if he/she is in the left decubitus position, the apical posterior segment of the left upper lobe is the site of the abscess. The upright child aspirates into the basilar segments of the lower lobes, whereas in the prone position the anterior lobes are involved [2, 8, 12, 21, 22].

Aspiration is likely in children with neurodevelopmental disease (especially if associated with poorly coordinated swallowing and/or a depressed cough reflex) and in neuromuscular conditions such as myotonia or Duchenne dystrophy. In general, all the causes of reduction or loss of consciousness predispose to aspiration (e.g., anesthesia (especially in the postoperative period), sedation, epilepsy, trauma).

Gastroesophageal reflux is a source of aspirated matter. Any communication between the oesophagus and trachea and any esophageal motility disorder can lead to the passage of gastric content in the airways and to subsequent pulmonary infection. Localized structural lung abnormalities such as congenital cyst adenomatoid malformations, sequestration, bronchogenic cysts, bronchiectasis and, less commonly today, cystic fibrosis, may predispose to secondary infection. Bronchial obstruction due to various causes (enlarged mediastinal lymph nodes, neoplastic mass, aspiration of a foreign body) can induce distal infection which can evolve into an abscess [2, 20].

Pulmonary infections in children can have a worse course in "developing" countries, where human immunodeficiency virus (HIV) infection, tuberculosis and malnutrition have a high incidence. In "developed" countries, congenital immunodeficiencies, chemotherapies or other immunosuppressive therapies can depress the immune system of children.

Microbes from various sites of infection can reach the pulmonary parenchyma through blood or lymphatic flux. A lung abscess can be promoted by embolic phenomena such as may be seen in septicaemia, thombophlebitis and endocarditis. A lung abscess is more likely in children with heart-valve anomalies or those subjected to cardiac surgery or placement of a central venous line. Local extension from pharyngeal abscesses or abdominal collection is also possible [2, 18, 23, 24]. The most common causes of lung abscesses can be divided into gastrointestinal disorders, neuromuscolar disorders, pulmonary conditions, surgical causes, immunocompromise, and other causes [1, 2, 8, 18, 22, 25, 26], as shown in Table 29.1.

29.4 Pathogenesis

The pulmonary parenchyma is normally protected by different mechanisms of defence. Mucous secretions, a ciliated epithelium, branches of the tracheobronchial tree, and the cough reflex contribute to purify the inhaled air so that the lower airways are almost sterile. If microbes reach the distal airways, activated humoral and cellular systems (immunoglobulins, complement system, macrophages, neutrophils, lymphocytes) usually destroy them, producing an inflammatory response.

If these mechanisms are impaired, an infection may occur [1]. Aspiration of milk, food, oral secretions and vomitus is associated with aspiration of aerobic and anaerobic oropharyngeal bacteria. If sufficient clearance is not achieved, pneumonia can arise after a

Table 29.1 Most common causes of lung abscesses

Gastrointestinal disorders
Esophageal reflux
Esophageal motility problems (strictures, achalasia)
Tracheoesophageal fistula
Periodontal disease/caries/poor oral hygiene
Neuromuscolar disorders
Mental retardation
Cerebral palsy
Impaired swallowing mechanism
Loss of consciousness
Myotonic dystrophy
Duchenne muscular dystrophy
Pulmonary conditions
Congenital cyst adenomatoid malformation
Sequestration
Bronchogenic cyst
Bronchiectasis
Bronchial obstruction (extraluminal/intraluminal)
Aspiration of foreign body
Cystic fibrosis
Congenital ciliary dysfunction
α1-antitrypsin deficiency
Surgical causes
Aspiration during anesthesia
Lung damage during pulmonary surgery
Prolonged intubation
Prolonged tracheostomy
Immunocompromise
Congenital or acquired immunodeficiencies
Chemotherapy or immunosuppressive therapies
Malnutrition
HIV infection
Others
Bacteraemia
Endocarditis
Septic thrombophlebitis
Spread of a subfrenic infection or hepatic infection by the lymphatic system
Malignancy
Lemierre's syndrome

short latency period of several hours [18]. During this first period, the inflammatory response leads to an edema of the airways involved that can obstruct the natural drainage of secretions, whereas a ciliated epithelium is often damaged by microbes. Some children (especially those affected by predisposing conditions) are occasionally unable to eradicate the infection, which can progress to necrosis of lung tissue and formation of multiple small abscesses in 1–2 weeks [1, 27]. Timely intervention with appropriate antibiotics stops disease progression but, because the necrotic tissue is poorly perfused, antibiotics may not reach the affected tissue. Furthermore, microbes at the site of infection establish conditions that interfere with the normal function of white cells and with the activities of certain antimicrobial agents. Conversely, low pH and low oxidation reduction potential favors the multiplication of microrganisms (especially Gram-positive or Gram-negative anaerobic bacteria) [28, 29]. Hence, the microabscesses may coalesce to form a larger abscess that is more often localized peripherally. For this reason, lung abscesses are associated with empyema and bronchopleural fistulae if pleural rupture occurs. Another possibility is natural drainage of the purulent collection through communication with the airways. In this case, the patient presents with thick sputum, and an air–fluid level is visible on chest radiography. Natural drainage is more common in older patients due to a greater caliber of bronchi, but this mechanism is less effective in infants. Adequate drainage promotes healing, which is characterized by the appearance of granulation tissue and subsequently fibrosis, which progressively occludes the cavity. If not treated in a timely fashion and/or not treated correctly, an abscess can evolve to chronic disease. Conventionally, an abscess is defined to be "chronic" if present for >6 weeks. Histologically, it appears as a thick-walled cavity in which the mechanisms of destruction and repair of tissue act simultaneously, and the infection is limited by host response but is not eliminated [30].

29.5 Microbiology

The procedures required to obtain adequate material for culture are often invasive, so only a proportion of patients are subjected to these procedures. Moreover, the collection and

Table 29.2 Common bacteria involved in lung abscesses

Anaerobes	Aerobes
Fusobacterium	*Staphylococcus aureus*
Peptostreptococcus	*Streptococcus pneumoniae*
Prevotella	*Streptococcus pyogenes*
Porphyromonas	*Haemophilus influenzae*
Bacterioides	*Escherichia coli*
-	*Klebsiella pneumoniae*
-	*Pseudomonas aeruginosa*

transport of specimens (especially for anaerobic bacteria) require precision and clarity. Therefore, some bias may be present in the information obtained about the etiology of a lung abscesses. Nevertheless, it is reasonable to suggest that lung abscesses secondary to aspiration are caused by microbes inhabiting the upper respiratory tract [20, 27, 31].

Anaerobic bacteria are often involved. The most common ones are pigmented Prevotella, Porphyromonas, Bacteroides, Fusobacterium (all Gram-negative bacilli), Peptostreptococcus spp., microaerophilic streptococci and Veillonella spp. [18, 20, 22, 27, 32–39]. The predominant aerobic and facultative bacteria are shown in Table 29.2 [18, 32, 34, 36, 40, 41]. Rare causes of lung abscesses include *Mycoplasma pneumoniae* [18, 42–50] and some reports have described lung abscesses caused by Salmonella organisms [22, 51–53] or *Yersinia enterocolitica* [22].

Lung abscesses are rare in neonates and may be associated with predisposing factors such as lung cysts, pneumonia or insertion of a central venous catheter [2, 54–56]. In this age group, the microrganisms involved may be *Staphylococcus aureus*, group-B streptococci, *Escherichia coli* and *Klebsiella pneumoniae* [2, 20, 55, 57]. Intubated children may present with pulmonary infection caused by a mixed flora of oral anaerobes and nosocomial pathogens [18, 32] whereas in cystic fibrosis *Pseudomonas aeruginosa* or *Staphylococcus aureus* may be the cause [18, 57, 58].

29.6 Clinical Features

The most common symptoms caused by a lung abscess are fever, cough, dyspnea, chest pain, productive sputum, malaise, anorexia, weight loss and chills. Infrequently, diarrhea, vomiting and irritability may be present. Minor hemoptisis is uncommon as a presenting feature (unlike the situation in adults). The physical signs include tachypnea, frequent expiratory grunts, dilated nostrils, flushed cheeks, cyanosis, rales, fine crackles, diminished breath sounds, dullness to percussion, retractions, decreased movement of the chest, bronchial breathing and prolonged expiration [1, 2 ,8, 18, 20, 22, 27, 28]. Laboratory findings are not specific: leukocytosis is common and mild anemia may be present [8, 18, 20, 22, 59]. Sometimes, the clinical course is more aggressive: it may be characterized by apnea and hypotensive shock [18–20]. Conversely, the course before medical intervention may be indolent and insidious with weeks-to-month of malaise, low-grade fever, cough, weight loss and anemia. Digital clubbing is rare. Amphoric or cavernous breath may be evident [1, 18, 20, 28]. Children with compromised immunity may have not have fever or a subnormal temperature. Neonates may show less specific signs of illness, such as apnea, grunting, respiratory distress, diarrhea and even hematemesis [1, 18].

29.7 Diagnosis

29.7.1 Imaging of Lung Abscesses

The basic diagnostic test for a lung abscess is chest radiography including frontal and lateral views [2, 22]. An abscess without communication with the bronchial tree appears as an opaque lesion. A cavitation becomes visible when air entering from a bronchus creates an air–fluid level which is usually present but can be missed if only a supine film is taken.

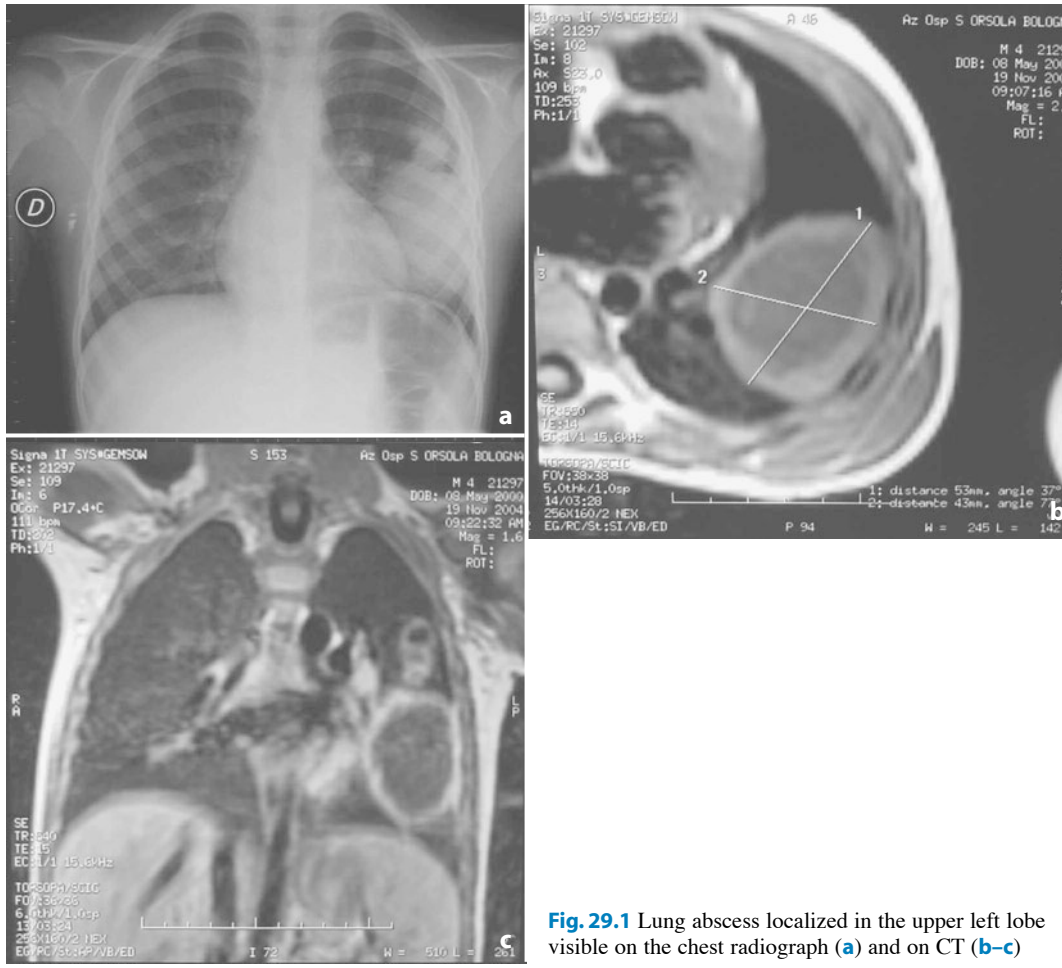

Fig. 29.1 Lung abscess localized in the upper left lobe visible on the chest radiograph (**a**) and on CT (**b–c**)

Abscesses can vary in size from 2 cm to 20 cm in diameter and the wall thickness can vary from 5 mm to 15 mm. Abscesses are usually uniloculated and surrounded by atelectasis. If the abscess is localized peripherally, the overlying pleura can be thickened and a small amount of pleural fluid may be seen [18].

The abscess must be distinguished from pneumatocele (a localized collection of intrapulmonary air that usually does not contain an air–fluid level) and from empyema (which has an air–fluid level) [8, 22]. The findings of air trapping may suggest the presence of a foreign body [27].

Contrast-enhanced computed tomography (CT) has become the most valuable investigation in the diagnosis and management for: small lesions; rare central abscesses obscured by infiltrates or pleural thickening; distinguishing an abscess from empyema, pneumatocele, bronchopleural fistula, congenital anomalies, pulmonary sequestration or (rarely) persistent pneumonia [8, 20, 60]. The diagnostic criteria for a lung abscess are: a well-defined mass; detection of a sharp angle between the lesion and pleura; density of the mass being greater than that of the water and normal pleural fluid; contrast enhancement in adjacent tissues (Figs. 29.1 and 29.2).

Magnetic resonance imaging (MRI) offers no diagnostic advantages over CT and is not routinely used (although it does not involve radiation exposure) [2, 18]. Conversely, ultrasonography is a useful tool for defining lung

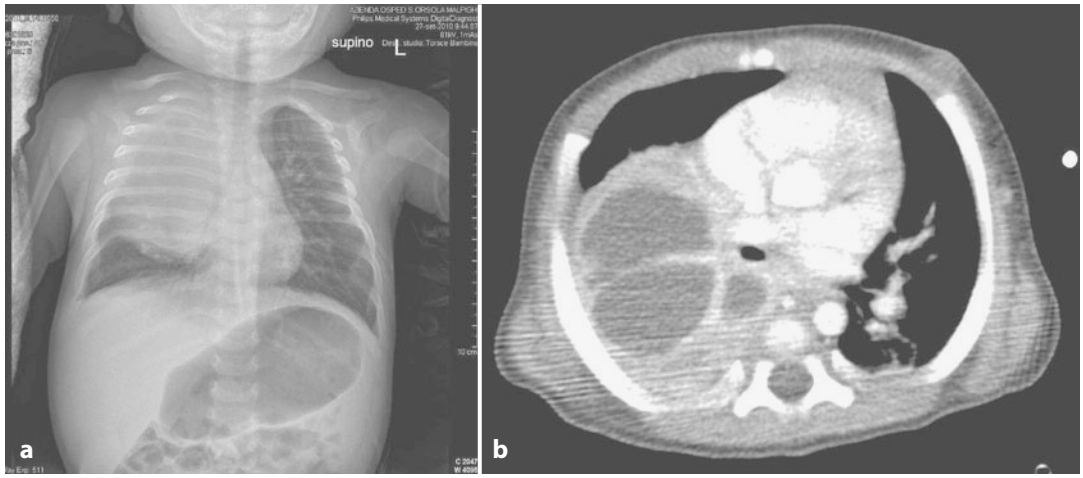

Fig. 29.2 Multiloculated abscess in the upper right lobe as seen by chest radiography (**a**) and CT (**b**)

abscesses. The advantages are a lack of sedation needed for the examination in infants, lack of radiation exposure, low cost [2, 61] and availability in emergency situations. With ultrasonography, a lung abscess appears as an avascular, hypoecoic mass with a thick, irregular wall and round/oval shape. CT and ultrasonography are useful for guiding drainage or transthoracic needle aspiration.

29.7.2 Microbiology

Identification of causative organism(s) has several advantages. Even if many common pathogens can be predicted by clinicians, unexpected micro-organisms should be considered. Microbiological diagnosis allows specific therapies, improves bacterial eradication, and reduces the development of resistance. Futhermore, some organisms influence the prognosis, (e.g., isolation of *Burkolderia cepacia* complex in a child with cystic fibrosis) or can help elucidate a clinical problem (e.g., isolation of *Fusobacterium necrophorum* in unsuspected Lemierre's syndrome) [41].

However, defining the organism(s) involved poses practical problems. Blood cultures are rarely positive in lung abscesses, particularly primary abscesses [41, 62]. Sputum cultures are unlikely to be useful because of the high incidence of lung abscesses in preschool children who cannot expectorate successfully. Expectoration can be achieved only in children aged ≥8 years. Inhalation of nebulized hypertonic or isotonic saline solution enables the production and subsequent expectoration of sputum, and has been used effectively in children as young as 2 years of age. A quite high sensitivity can be reached if specific criteria are used (e.g., >25 neutrophils/low power field, <10 squamous epithelial cells/low power field, or >50 organisms/oil immersion field with intracellular organisms in at least one field) [41, 63]. Nevertheless, even when available, sputum culture may reflect pharyngeal flora. Appropriate material for culture should be obtained by methods that bypass the upper airways [18]. Transtracheal aspiration provides specimens that are not contaminated and may be used to obtain a microbiological diagnosis but is unsuitable in small children for technical reasons [20]. Bronchoscopy with biopsy, brush sampling or bronchoalveolar lavage can also be used to obtain uncontaminated specimens and is useful to identify an obstruction due to a foreign body or malignancies, but the possibility of flooding of the airways should be considered [1]. Direct transcutaneous aspiration is the most reliable indication of the etiologic agent and may be diagnostic and thera-

peutic, but it is difficult to carry out if the abscess is not peripheral. Complications may occur, in particular pneumothorax and empyema. Whatever the method used, the specimens obtained should be collected anaerobically, transported to the laboratory without delay and handled quickly to improve the possibility of microbiological identification.

29.8 Differential Diagnoses

The differential diagnoses of a lung abscess include pneumatocele (which usually presents as a thin-walled cavity without an air–fluid level), congenital cyst, cystic adenomatoid malformation of the lung, traumatic pseudocyst, infected hydatid cyst, and cavitating post-primary tuberculosis. If the lesion has a homogeneous density, simple pneumonia, a neoplasm, lymphoma, loculated empyema, embolism or infarction should be considered.

29.9 Treatment

29.9.1 Medical Treatment

Treatment is conservative, and the aims are to obtain drainage and administer antibiotics. Chest physiotherapy is useful in children who can cough and consists of inhalation of a bronchodilator followed by percussion and postural drainage. Physiotherapy is contraindicated in children with an impaired cough reflex because it may result in "flooding" of the tracheobronchial tree with infected material [22].

Antibiotics are administered intravenously initially without waiting for a microbiological diagnosis. The selection of antibiotics is usually empirical and should include broad-spectrum aerobic and anaerobic cover and a penicillase-resistant antistaphylococcal agent. If Gram-negative bacteria are suspected, an aminoglycoside should be added.

Penicillin has long been the frontline agent because of its efficacy against streptococcal and anaerobic species. However, because of β-lactamase-producing anaerobes, clindamycin may be added. Other clinicians have suggested ticarcillin or piperacillin/tazobactam. Third- and fourth-generation cephalo-sporins are also very effective. Antimicrobial regimens should include optimal coverage for *Staphylococcus aureus* (including methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus*) [1, 8, 20].

Intravenous antimicrobials are recommended for 1–3 weeks followed by oral therapy for 2–4 weeks. Anaerobic infections may require therapy for prolonged periods (≥6–12 weeks) to prevent relapse.

Healing is monitored based on clinical features, laboratory findings and chest radiographs. Healing is dependent upon several factors, such as appropriate use of antibiotics and internal drainage. Control of infection is characterized by disappearance of fever, diminished sputum production and improvement in chest radiographs. Children usually do well with only medical therapy and the requirement for other therapies is unusual. Nevertheless in neonates, immunocompromised children, and if underlying conditions are associated, medical treatment cannot be successful and more invasive procedures are necessary.

29.9.2 Invasive Treatment

If there is no improvement after 7–10 days of appropriate antibiotic therapy, external drainage by percutaneous or surgical approaches should be considered. The procedures consist of needle aspiration of the contents or placement of a pigtail catheter, and can be guided by CT or ultrasound (Fig. 29.3) [2, 64, 65] even if anteroposterior and lateral chest radiographs permit localization of the abscess and evacuation of the purulent material. Drainage leads to a rapid improvement of symptoms, thereby shortening convalescence. Failure of medical treatment associated with external drainage is rare but children who do not respond require a surgical approach.

Indications for surgical treatment are clinical

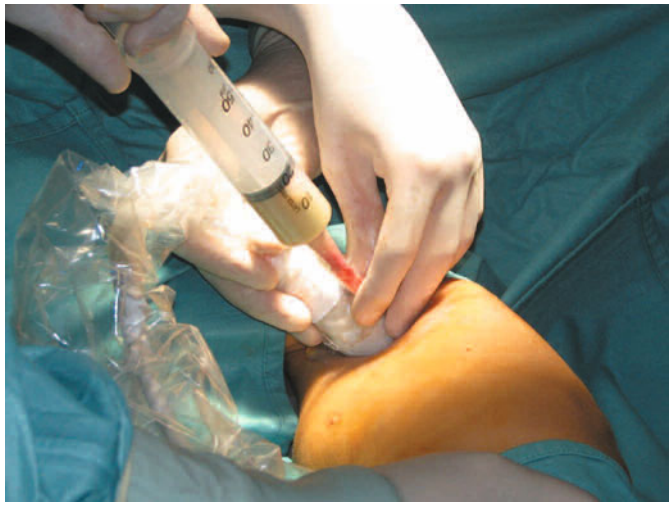

Fig. 29.3 Ultrasound-guided needle aspiration

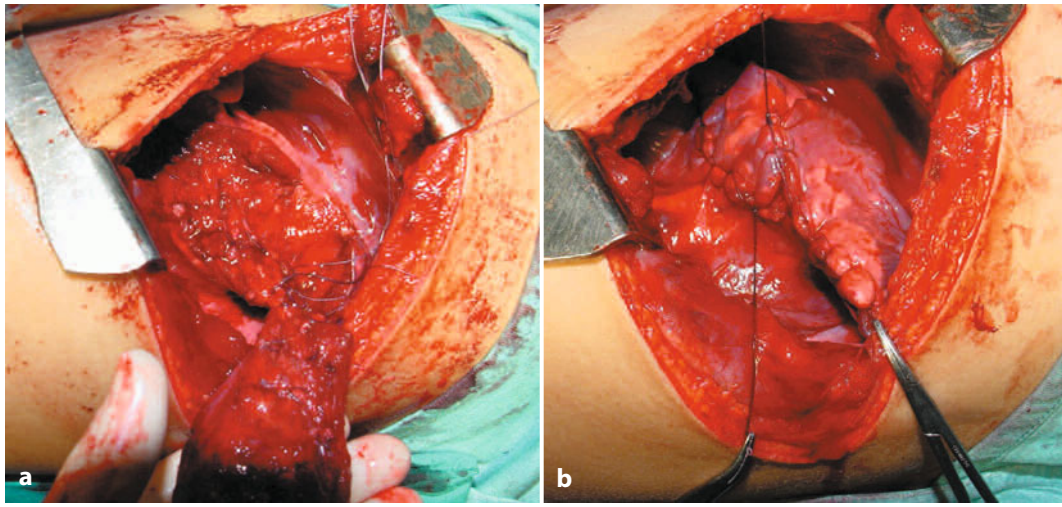

Fig. 29.4 Atypical resection of the upper left lobe by thoracotomy (**a–b**)

deterioration of the patient, an increased dimension of the abscess despite antibiotics and external drainage, and the necessity of resection due to extensive damage. After needle aspiration, a less invasive surgical procedure is placement of a closed-tube pneumonostomy into the abscess. The tube is placed trough a small skin incision without contamination of the pleural space thanks to the fusion often present between the pleura and chest wall overlying the abscess.

If the content of the abscess is not sufficiently fluid, pneumonostomy cannot be adequate and open drainage becomes necessary. A mini-thoracotomy is done and the abscess wall opened to evacuate necrotic material. At the end of the procedure, a drain is placed in the cavity.

Segmental resection or lobectomy is recommended for chronic, large and thick-walled abscesess that do not respond to intensive and prolonged therapies or percutaneous drainage. Other indications are bronchiectasis, massive necrosis and bronchial stenosis (Fig. 29.4).

In the last few years, mini-invasive surgery

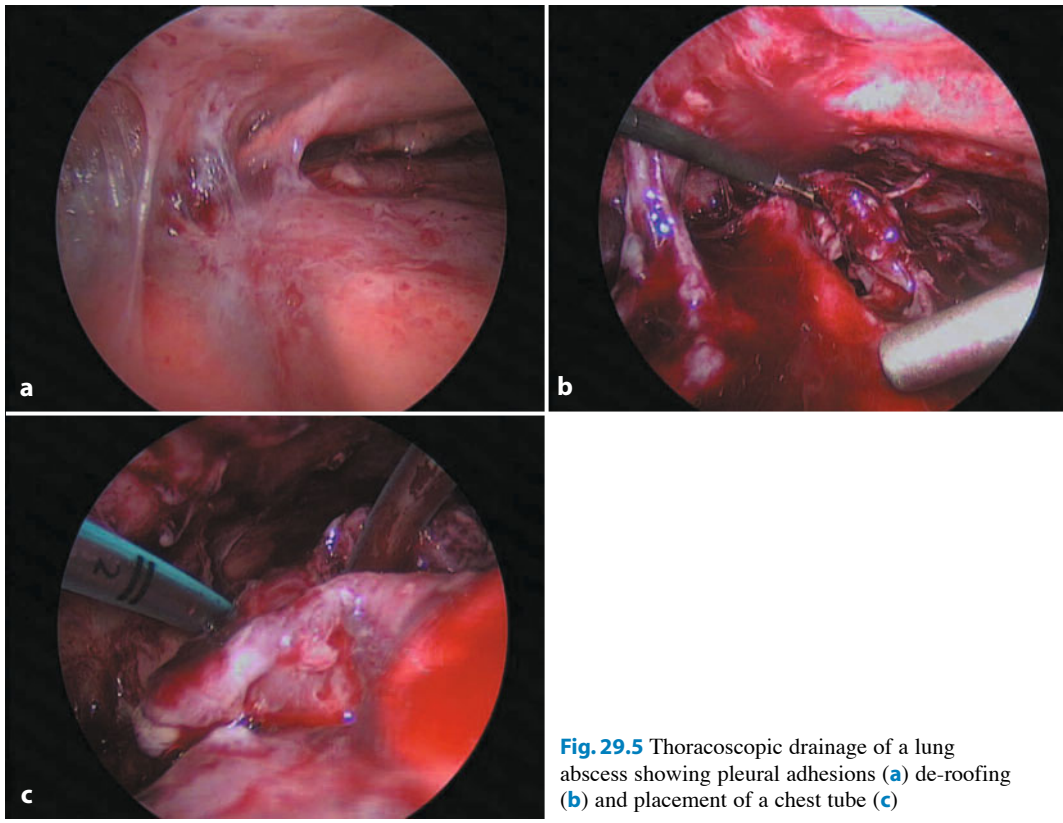

Fig. 29.5 Thoracoscopic drainage of a lung abscess showing pleural adhesions (**a**) de-roofing (**b**) and placement of a chest tube (**c**)

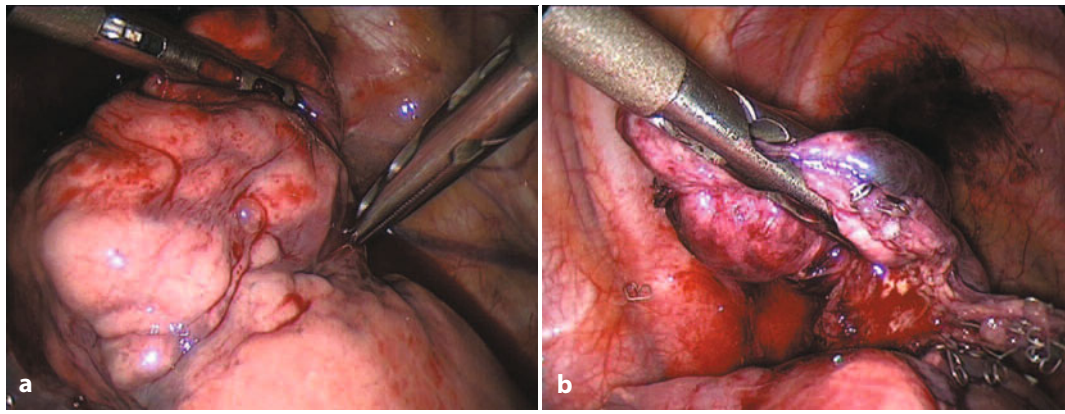

Fig. 29.6 Wedge resection in an abscess in the upper right lobe (**a–b**)

has gained a role even in the treatment of lung abscesses. Some authors have reported thoracoscopic drainage of lung abscesses (Fig. 29.5 and 29.6) [66]. This method can be used only in peripheral abscesses which are visible with the torachoscope but which permit effective drainage and copious irrigation of the cavity, thereby avoiding thoracotomy.

29.10 Complications

The complications of lung abscesses are in relation to the progression of the infection, which can lead to overexpansion of the abscess with mediastinal shift, spontaneous rupture of the abscess with formation of empyema, pyothorax or pneumothorax and bronchopleural fistulae. Hematogenous spread may also occur, so multiple abscesses may be seen [64, 67]. Diagnostic and therapeutic procedures may also lead to the same complications. Bronchoscopy can promote massive intrabronchial aspiration of purulent material whereas percutaneous drainage can be complicated by empyema, bronchopleural fistulae, small pneumothorax, lobar collapse and bacteremia.

29.11 Outcome

With appropriate antibiotic therapy, the fever resolves in approximately 1 week. Complete clinical resolution often requires 2 weeks whereas resolution based on imaging findings may occur in 1 month (but may take longer). The prognosis of children with lung abscesses is favorable. Mortality is <5% and involves children with underlying disease, and especially if they are immunocompromised [2, 18]. A worse prognosis is associated with secondary lung abscesses and higher mortality has been seen in infections caused by *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

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Pediatric Bronchiectasis

30

Giovanni Ruggeri, Dalia Gobbi, Michele Libri and Mario Lima

30.1 Introduction

The term "bronchiectasis" is derived from the Greek "bronchion", meaning windpipe, and "ektasis", meaning stretched. Bronchiectasis is characterised by the permanent dilatation of bronchi with destruction of the elastic and muscular components of their walls.

Landmarks in the history of bronchiectasis include the first, vivid description of patients with tuberculotic suppurative phlegm in the pre-antibiotic era in the writings of René Theophile Hyacinthe Laennec in the early 19th century; the introduction by Jean Athanase Sicard in 1922 of contrast bronchography (which allowed for precise images of the destructive changes in the airway); the defining studies by Lynne Reid in the 1950s linking bronchography with pathological specimens; and the subsequent decline in prevalence probably attributable to effective antituberculous therapy and immunization against pertussis and measles [1,2].

Thanks to the work of Reid the definition of the disease has remained morphologic for 50 years. Bronchiectasis is referred to as an "orphan disease" due to the limited number of studies conducted in the pediatric population. In "developing" countries, bronchiectasis is frequently met as one of the sequelae of acute infection. In the "developed" world, immunizations and antibiotics have led to a declining incidence of this disorder. In these countries, diffuse bronchiectasis is more often found in association with underlying disorders such as cystic fibrosis, immune deficiencies, primary ciliary diskinesia, and recurrent aspiration syndrome.

In spite of these assumptions, recent studies have demonstrated that bronchiectasis continues to be a problem in non-cystic-fibrosis children all over the world. It may occur in >20% of children after pulmonary infection with *Mycoplasma pneumoniae*, and generally has an incidence of approximately 1 in 6,000 children [1–3].

30.2 Epidemiology

The prevalence of bronchiectasis is higher in the developing world, where measles, adenovirus infection, pneumonia, tuberculosis, and human immunodeficiency virus (HIV) infection are on the rise. The disease is more common in patients of Polynesian and Alaskan Native ancestry. Callahan and associates reported the incidence among Alaskan Native children in the Yuskon–Kuskokwim region, to

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be about 140 cases per 10,000 population. This suggested a possible genetic predisposition in those populations in which 43% of children with bronchiectasis had parents who were first-degree or second-degree relatives but presumably without any other known underlying disorder [4]. In New Zealand, the incidence of bronchiectasis in children younger than 15 years was reported to be 3.7 cases per 100,000 population in 2001–2002. The incidence was highest among Pacific children (17.8 cases per 100,000 population). This incidence of bronchiectasis in New Zealand children seems nearly twice the rate of cystic fibrosis and seven-times that of bronchiectasis in Finland (the only other country reporting a childhood national rate). Similarly, in central Australian Aborigines, the incidence has been reported to be 14 cases per 1,000 population, compared with 0.1 cases per 1,000 in Scotland and 4.9 cases per 1,000,000 in Finnish children. Most New Zealand children with bronchiectasis developed the disease in early childhood and had a delayed diagnosis [3, 5, 6].

In the USA, current population-based estimates of occurrence are not available. The incidence of bronchiectasis associated with underlying systemic disease reflects the incidence of the particular disease. The most common congenital disease associated with bronchiectasis is cystic fibrosis. With respect to international statistics, in developed countries the frequency is similar to that in the USA, with a reported mean age at presentation of 2–10 years. In a study from the UK that started in 1949, Field studied children with bronchiectasis for almost two decades and documented a fall in the annual hospitalization rate for bronchiectasis in five British hospitals. During the study period, as broad-spectrum antibiotics became widely available, the hospitalization rate decreased from approximately 48 cases per 10,000 population to 10 cases per 10,000 population.

30.3 Etiology and Pathogenesis

Bronchiectasis may result from infection, congenital or acquired disorders, or obstruction.

Table 30.1 Common infectious causes of bronchiectasis

Severe bacterial and viral pneumonia
Bacteria *Bordetella pertussis, Mycoplasma pneumoniae, Haemophilus influenzae, Staphylococcus aureus, Pseudomonas aeruginosa, Straptococcus pneumoniae, Klebsiella penumoniae, Moraxella catarrhalis* Viruses Respiratory syncytial virus, measles, influenza, Varicella, human immunodeficiency virus
Mycobacterial and fungal infections
Tuberculosis, Mycobacterium avium, Aspergillus fumigatus
HIV infection
Children who develop lymphocytic interstitial pneumonitis seem to be at increased risk of subsequent bronchiectasis

All causes share the same pathophysiological pathway: ineffective pulmonary toilet and chronic/recurrent infection and inflammation. Effective childhood immunization strategies have led to a marked reduction in the incidence of bronchiectasis caused by pertussis or whooping cough. Conversely, in developing countries, where access to medical care is limited, infections are the most common cause of bronchiectasis [3, 4, 5]. After investigations, the etiology remains unknown in more than half of cases. Common infectious causes of bronchiectasis are: shown in Table 30.1. Congenital disorders determining deficiencies in immune function (especially in humoral immunity) cause the child to be at risk for recurrent sinopulmonary infections. Congenital disorders associated with bronchiectasis are shown in Table 30.2, and acquired disorders associated with bronchiectas are listed in Table 30.3.

Being the common outcome for various pulmonary insults, bronchiectasis is considered by many to be irreversible. Whatever the cause, carrying out mucociliary clearance is adversely affected by the compromised ability to clear the purulent material produced. Findings from mucosal biopsies and sputum of patients with proven bronchiectasis give credence to the importance of enhanced cellular and mediator responses. Chronic infection leads to the recruitment of neutrophils, T-lymphocytes, and monocyte-derived cytokines.

Table 30.2 Congenital disorders associated with bronchiectasis

Cystic fibrosis
Young syndrome
α1-antitrypsin deficiency
Primary ciliary dyskinesia
Marfan's syndrome
Bruton agammaglobulinemia
Congenital absence of bronchial muscle (Mounier–Kuhn syndrome) or cartilage (Williams–Campbell syndrome)
Deficiencies in immunoglobulin (Ig)A, IgG, and IgG subclasses (especially IgG2)
Immunosuppression of medication indices
Malignancy

Table 30.3 Acquired disorders associated with bronchiectasis

Intrinsic airway luminal obstruction (retained bronchial foreign body or extrinsic compression)
Chronic aspiration (which is associated with swallowing dysfunction, gastroesophageal reflux disease and tracheoesophageal fistulae)
Connective-tissue disorders (including rheumatoid arthritis and systemic lupus erythematosus)
Allergic bronchopulmonary aspergillosis
Tracheal stenosis with impaired mucociliary clearance
Severe tracheomalacia or bronchomalacia with impairment of mucociliary clearance
Fibrosing lung diseases associated with sarcoidosis or idiopathic pulmonary fibrosis
Persistent atelectasis

The release of inflammatory mediators (interleukin-8, tumor-necrosis-factor-alpha, myeloperoxidase, prostanoids), neutrophil elastases, and collagenases leads to inflammation and destruction of the elastic and muscular components of bronchial walls. In addition, the outward elastic recoil forces of the surrounding lung parenchyma exert traction, which causes an expansion of airway diameter. These changes may be accompanied by bronchial arterial proliferation, which predisposes to hemoptysis. Hemoptysis may also occur as a result of the dilating airways impinging on the accompanying blood vessels.

Bronchiectasis can present in two forms: (i) a local or focal obstructive process of a lobe or segment of a lung or (ii) more sporadically as a diffuse process involving much of both lungs and often accompanied by other underlying diseases (especially sinopulmonary diseases such as asthma and sinusitis). Bronchiectasis associated with bronchial obstruction may have a focal distribution distal to the site of obstruction. According to the pathological appearance of the airways, bronchiectasis can be categorized as: cylindrical or tubular when characterized by dilated airways alone (it is sometimes seen as a residual effect of pneumonia); varicose when characterized by focal constrictive areas along the dilated airways that result from defects in the bronchial wall; saccular or cystic when characterized by progressive dilatation of the airways which end in large cysts, saccules, or grape-like clusters [3, 5].

30.4 Clinical Features

Non-cystic fibrosis bronchiectasis in children presents with a wide spectrum of disease severity. The greater percentage of children on the path to develop bronchiectasis typically have recurrent (but it can occur after a single severe infection!) pulmonary infections and cough. A cough is an almost universal symptom. Some children have intermittent symptoms of cough and occasional lower respiratory tract infections, others experience daily cough and produce purulent, fetid sputum that requires frequent hospitalizations for respiratory exacerbations. Cough is frequently described as "productive" in older children and as "loose" in toddlers and infants. Because small children rarely expectorate, the clinician may observe a child with a loose-sounding cough who swallows after coughing. The sputum is variously described as "mucoid", "mucopurulent", "thick", "tenacious", or "viscous".

The diagnosis should be considered in children with a daily productive cough for >6 weeks. Bronchiectasis should also be consid-

Table 30.4 Differential diagnoses of the causes of pediatric cough

Acute (<4 weeks)
Asthma
Aspiration of a foreign body
Gastroesophageal reflux
Infections (bronchitis, bronchiolitis, upper respiratory-tract infections)
Allergic rhinitis
Sinusitis/pneumonia
Chronic (>4 weeks)
Bronchiectasis
Asthma
Aspiration of a foreign body
Gastroesophgeal reflux (induced bronchospasm or aspiration)
Allergic rhinitis with post-nasal drip
Infections: recurrent viral, bacterial, granulomatous, lung abscess
Sinusitis with post-nasal drip
Interstitial lung disease
Congenital anomalies (vascular rings, congenital heart disease with pulmonary congestion, pulmonary sequestration, tracheomalacia)
Allergic bronchopulmonary aspergillosis or mycosis
Cystic fibrosis
Inhalation of chemicals/toxic material
Psychogenic habit
Immunodeficiency with recurrent infections

ered in children with chronic or persistent cough in whom another diagnosis has been made but who are not responding to therapy. If children with cough respond to antibiotics on a recurrent basis, bronchiectasis should be considered. In some reports, cough seems more common in patients with asthma (24%), gastroesophageal reflux (15%), and viral bronchitis (11%) than in patients with bronchiectasis (4%). Common causes of pediatric cough that should be considered in the differential diagnosis are listed in Table 30.4.

Published case series have detailed other common clinical manifestations, including blood-streaked sputum or copious hemoptysis that may also result from erosive airway damage caused by acute infection. Hemoptysis has been reported to be the second most common symptom of bronchiectasis. Dyspnea and wheezing occur in »75% of patients. Pleuritic chest pain occurs in 50% of patients and reflects distended peripheral airways or distal pneumonitis adjacent to a visceral pleural surface. Acute exacerbation is a severe manifestation of bronchiectasis and is defined by symptomatic changes (including increased production of thick sputum with changes in color, shortness of breath, pleuritic chest pain and generalised malaise). Chest radiography is rarely associated with new infiltrates, and the patient may not have fever or chills [5–7].

The findings of physical examination in patients with bronchiectasis may vary from normal to variable degrees of crackles, coarse bronchi, wheezing, and clubbing. An inspiratory "honk" has been described in some children with bronchiectasis, the cause of which is unclear.

Digital clubbing has been reported in 37–51% of patients with bronchiectasis, but more recent series describe a prevalence of only 3%. Some authors found that children with digital clubbing and chest deformity showed significantly higher scores for the extent of bronchiectasis, dilatation and thickness of the bronchial wall, and overall changes based on computed tomography (CT) score. In some cases, digital clubbing has been described to clear after surgical removal of the affected part of the lung, and to improve in medically treated cases [7–9].

30.5 Diagnosis

Bronchiectasis appears to be undiagnosed before extensive disease is evident. Early recognition of children who have a chronic moist or productive cough for >6 weeks and recurrent chest infections may be critical.

Diagnostic guidelines for the evaluation of pediatric bronchiestasis are outlined in Table 30.5.

Not every patient with bronchiectasis requires each of the studies shown in Table 30.5. History-taking and physical examination should help guide the physician in the appropriate directions.

Table 30.5 Diagnostic guidelines for the evaluation of pediatric bronchiestasis

Radiology
Chest radiograph: may reveal abnormalities
High-resolution computed tomography (HRCT): gold standard
Laboratory
Complete blood count with differential counts
Sweat chloride testing to rule out cystic fibrosis
Serum levels of IgG with subtypes; IgA, IgM
Sputum culture (or deep oropharyngeal swab in younger children) or culture from bronchoalveolar fluid for bacterial, viral, fungal, and mycobacterial pathogens
Nasal scraping for evaluation of ciliary beat frequency for primary ciliary dyskinesia
Testing of neutrophil function
Antigen and mitogen stimulation (ability of B cells and T cells to proliferate)
HIV test
Evaluation of complement
α1-antitrypsin level
Specific IgE to Aspergillus (serum precipitins for Aspergillus species) and total IgE
Rheumatoid factor, erythrocyte sedimentation rate, and other autoimmune parameters if clinically indicated
Procedures
Flexible fiberoptic bronchoscopy (rule out or remove foreign body; biopsy; bronchoalveolar lavage)
Gastroenterology (barium swallow, fluoroscopic evaluation of swallow, 24-h pH probe)
Skin testing (Aspergillus skin test)
Lung function
Pulmonary function testing

Bronchiectasis is defined as an abnormal dilatation of the airways, so the diagnosis is dependent upon visualization of the typical changes based on imaging or anatomy. Therefore, it is essential to discuss in detail the imaging: 90% of chest radiographs are abnormal in patients who have bronchiectasis. Unfortunately, the findings may be non-specific in that they may include focal pneumonitis, scattered irregular opacities, linear or plate-like atelectasis, or specifically dilated and thickened airways that appear as ring-like shadows or "tramlines". In the absence of characteristic findings on chest radiography, high-resolution computed tomography (HRCT) is the diagnostic procedure of choice [10, 11].

The diagnosis of asthma or reflux-associated lung disease does not preclude bronchiectasis. In fact, bronchiectasis may be a complication of these diseases. In the same way, an underlying systemic disease or congenital anatomical malformations (e.g., tracheoesophageal fistula) or history of aspiration of foreign bodies in conjunction with respiratory symptoms should increase the suspicion for bronchiectasis. Humoral immunodeficiencies of IgG, IgM, and IgA are a risk for recurrent suppurative sino-pulmonary infections and bronchiectasis. Immunoglobulin replacement reduces the frequency of infectious episodes and prevents further destruction of the airways.

Cystic fibrosis is an autosomal recessive disease which can be diagnosed using *in utero* screening techniques or documenting elevated sodium and chloride concentrations on sweat chloride testing in a child with recurrent respiratory infections. Cystic fibrosis is associated with repeated respiratory tract infections with or without exocrine pancreatic insufficiency. Upper-lobe infiltration (apparent on imaging of the chest) and the growth of *Staphylococcus aureus* or mucoid *Pseudomonas aeruginosa* on sputum culture are clues that cystic fibrosis may be the underlying cause of illness [14].

Primary ciliary dyskinesia is an autosomal recessive disease with variable penetrance. The chief defect is an absence or shortening of the dynein arms responsible for the coordinated bending of the ciliary axons. Evaluating nasal ciliary beat frequency is the usual method to make the diagnosis.

Bronchiectasis associated with rheumatoid arthritis has been described as preceding arthritis as well as occurring during rheumatoid arthritis. The use of HRCT may reveal a prevalence of bronchiectasis as high as 30%. The diagnosis of bronchiectasis in these patients increases their morbidity [8].

Repeated respiratory tract infections and bronchiectasis have been noted in patients with inflammatory bowel disease, most often in those with chronic ulcerative colitis. This could be because of infiltration of the airway

by immune effectors cells, enhanced autoimmune activity, and complications of immune-modulating therapies [9].

Lung anatomical abnormalities are rare causes of recurrent pulmonary infections and bronchiectasis in children. Pulmonary sequestration is a non-functioning pulmonary mass of primitive tissue that does not communicate with the tracheobronchial tree. It can be complicated by recurrent infection, abscesses, and bronchiectasis if not removed surgically. Right middle lobe or lingula may be caused by an abnormal angle of the lobar bronchus at take-off in some patients, and can result in atelectasis, recurrent infections, and bronchiectasis. It is most commonly associated with asthma in young children. It often requires early and aggressive surgical strategies.

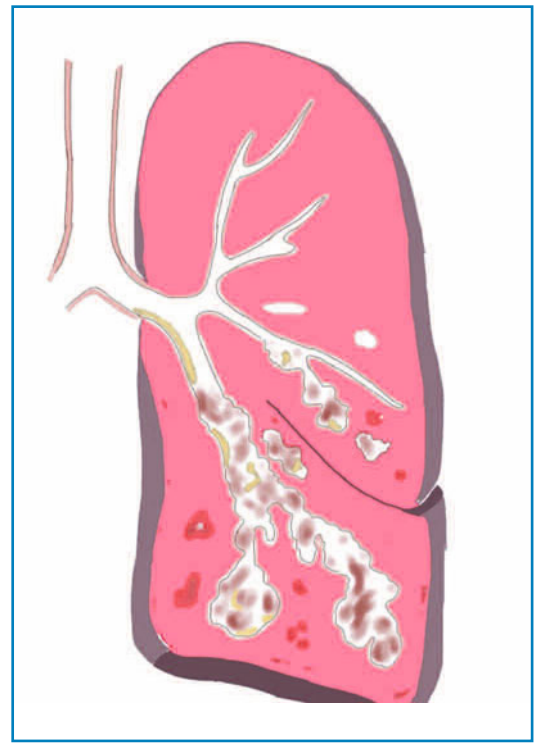

Fig. 30.1 Bronchiectasis (schematic)

30.5.1 Imaging

Aroutine posteroanterior and lateral chest radiograph should be obtained. An abnormal chest radiograph may be sufficient to make the diagnosis in the correct clinical setting, but the chest radiograph is considered to be of little diagnostic value. Bronchiectasis is primarily in the lower lobe, which is the most common distribution (Fig. 30.1). The saccular dilatations and grape-like clusters with pools of mucus are signs of severe bronchiectasis. Suspicious findings include: dilated airways with thickened walls, linear atelectasis, and irregular peripheral opacities from muco-purulent plugs. When seen laterally, the bronchiectatic airway has been described as tramlines. However, normal radiographic findings do not rule out bronchiectasis [10–12].

A chest radiograph is considered a poor method for determining bronchiectasis. The correlation between the chest radiograph completely and HRCT is poor, so significant disease may be present on HRCT in children with normal or near-normal chest radiographs.

The use of chest radiography as a diagnostic criterion explains the general statement that bronchiectasis is now rare. When HRCT is used, it is found that bronchiectasis is not that rare, with an incidence of approximately 1 in 6,000 children. The high sensitivity of HCRT (97%) clarifies the findings from chest radiography, and maps airway abnormalities that cannot be seen on plain radiographs of the chest. The appropriate CT study is a non-contrast study with the use of a 1.0–1.5-mm window every 1 cm, with acquisition times of 1 s reconstructed with the use of a high-spatial-frequency algorithm during full inspiration. Spiral CT may even elucidate additional subtle changes because it reduces motion artefacts, but it requires a larger dose of radiation. HCRT criteria for the diagnosis for bronchiectasis include the following:

- when imaged in cross-section, an enlarged internal bronchial diameter with bronchi that appear larger than the accompanying pulmonary artery (>1.5-times as wide as a nearby vessel): the is called the “signet ring sign”;

- on segmental slices, failure of the larger airways to taper while progressing to the lung periphery;
- air–fluid levels in the dilated airways due to varicose constrictions along airways;
- identification of airways in the extreme lung periphery (ballooned cysts at the end of the bronchus).

Non-specific findings include consolidation or infiltration of a lobe with dilatation of the airways, thickening of the bronchial walls, mucous plugs, enlarged lymph nodes, and a reduction in vascular markings (probably a result of the inflammatory destruction of smaller airways and vessels).

On HRCT, bronchiectasis is graded as follows: 0, absence of bronchiectasis; 1, mild and rare bronchial dilatations; and 2, severe and diffuse bronchodilatation. The "bronchiectasic spectrum" in children involves three stages. The first stage, ("prebronchiectasis") is potentially reversible. The second stage ("HCRT bronchiectasis") may persist, progress or resolve. The third stage ("established bronchiectasis") involves non-reversible bronchial wall damage. The number of abnormal airways found on HRCT seems to be correlated with the degree of impairment of pulmonary function [10–12] (Fig. 30.2).

30.5.2 Lung Function Tests

Spirometry and/or pulmonary function testing (PFT) can help determine the degree of lung damage due to bronchiectasis. Spirometry often shows a limitation of airflow, with a reduced ratio of forced expiratory volume in one second (FEV_1) to forced vital capacity (FVC); a normal or slightly reduced FVC; and a reduced FEV_1. A reduced FVC may indicate that airways are blocked by mucus, that they collapse with forced exhalation, or that there is pneumonitis in the lung.

Normal lung function may coexist with HRCT abnormalities and does not exclude lung damage. Studies in adults have shown that the presence and severity of bronchiectasis as established solely by bronchography or CT do not correlate well with alterations in ventilatory and perfusion functions. This may be an expression of functional damage which extends beyond the bronchial walls. Areas of decreased attenuation in HRCT are common findings in severe bronchiectasis. These are also found in lobes without bronchiectasis, suggesting that small-airway disease may precede the pathological changes in bronchial walls. A recent study in pediatric patients carefully examined the relationship between HRCT, ventilation and perfusion scans, and lung function in children with heterogeneous causes for bronchiectasis. The results that study demonstrated that alterations similar to those seen in adults also occur in pediatric populations, and therefore they are an early event in disease progression. The authors found a significant correlation between all the HRCT parameter scores and reduced FEV_1 [15–17].

30.6 Management

The foundations of therapy are: identification of acute exacerbations; suppression of microbial load; treatment of underlying conditions; reduction of excessive inflammatory responses; promotion of bronchial hygiene; control of bronchial hemorrhage; and surgical removal of extremely damaged segments or lobes that may be a nidus for infections and bleeding.

Treatment options are pharmacologic agents (e.g., antibiotics), non-pharmacologic measures (e.g., chest physiotherapy), and surgical procedures involving removal of the affected portions of the lung. The final goals are to control infections and improve bronchial hygiene [5]. The lack of a robust definition of "exacerbation" is a limitation in the care and research of children with non-cystic-fibrosis bronchiectasis. Early detection and treatment of pulmonary exacerbation is likely to be an important factor in preventing the decline in lung function. A recent prospective study in 69 children with non-cystic-

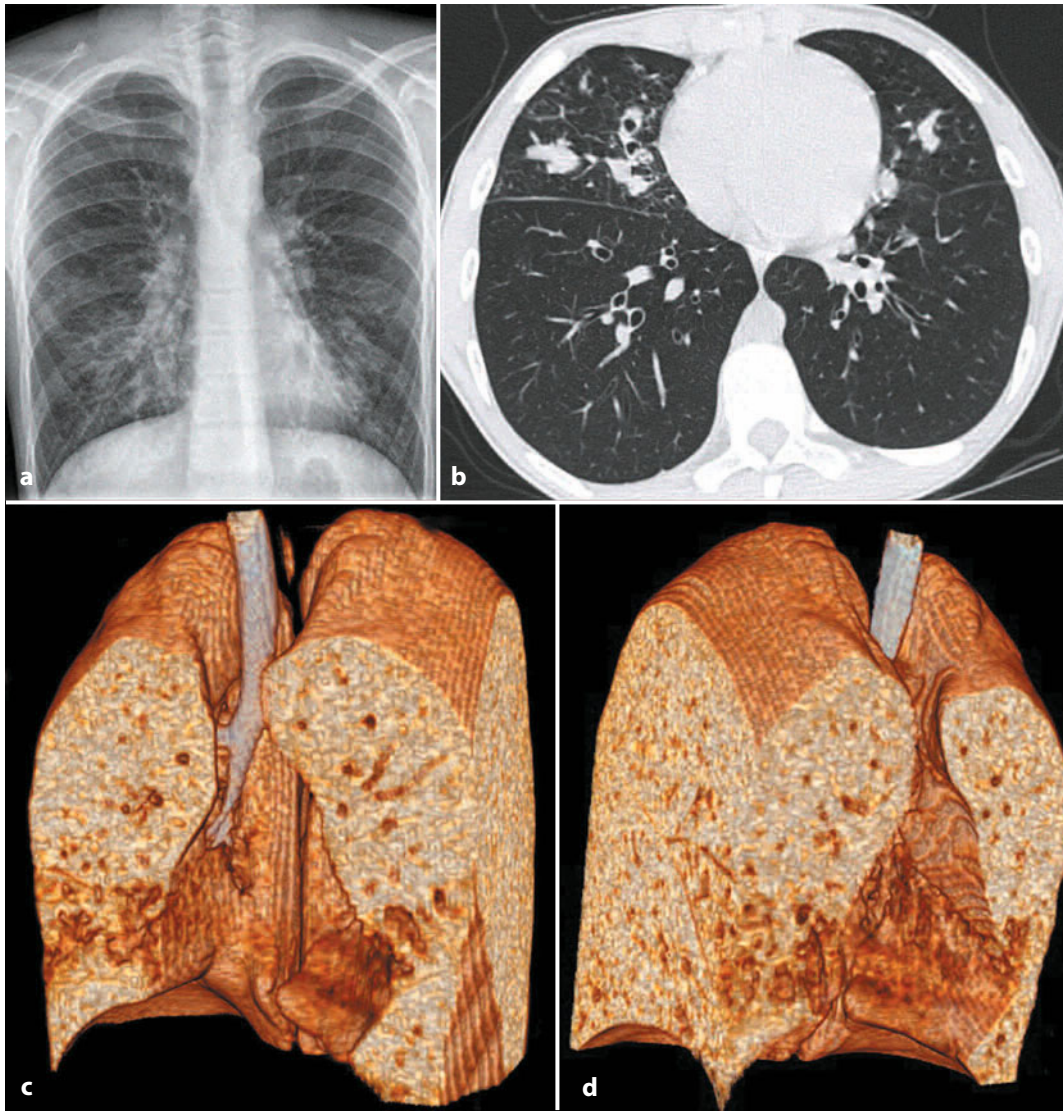

Fig. 30.2 A 14-year-old male with a history of *Mycoplasma pneumoniae* infection and H1N1 super-infection. Plain radiograph shows interstitial peribronchovascular thickening in the anterior and basal segments bilaterally (**a**). HRCT demonstrates (especially in the right middle lobe) diffuse thickening of the bronchial walls, bronchiectasis (bilateral) coexistent with bronchiectasis and associated with ground-glass areas, thickening of interlobular septa, micro-nodules and tree-in-bud opacities (**b**). Three-dimensional reconstruction better delineates involvement of the middle lobe and lingula (**c–d**)

fibrosis bronchiectasis evaluated 81 episodes of pediatric pulmonologist-defined exacerbations against lung functions and blood profiles, and formulated three combinations of signs and symptoms considered the best to define an exacerbation. The wet character of the cough and cough severity were the two strongest predictors of pulmonary exacerbations in combination with serum markers. Further studies can identify the factors associated with exacerbation frequency (Table 30.6), and thus potentially improve the overall management of a child with bronchiectasis (which continues to be a neglected condition) [16]. In

Table 30.6 Signs and symptoms frequently associated with a clinical exacerbation of pediatric bronchiestasis

Increased dyspnea (breathlessness as perceived by the parent/child)
Significant frequency of cough over 72 h; wet cough for 72 h
Increased production of thick sputum with change in color
Increased wheezing, crepitations, chest pain
Fatigue, malaise, decreased tolerance to exercise
Reduced pulmonary function (hypoxia)
Rarely: Fever >38°C; radiographic changes consistent with a new pulmonary process
Changes in chest sounds

the case of acute exacerbation, early antibiotic therapy is suggested [5, 17]. A reasonable choice includes a fluoroquinolone (levofloxacin or ciprofloxacin) for ≥7 days. Sputum culture and sensitivity testing are indicated in patients who do not have a response. A viral infection may play a direct part in acute exacerbations by increasing bacterial load. However, such bacteria probably stimulate a neutrophilic and inflammatory mediator response in the airway, having an active destructive role. Intravenous antibiotic therapy and hospitalization may be necessary for children experiencing exacerbations of endobronchial disease. Intravenous antibiotic therapy at home may be an option in some situations. Administration of aerosolized antibiotics is an intriguing alternative that would allow concentrated local therapy, reduce systemic absorption and toxic effects, and promote use of a delivery device that is already familiar to many patients with respiratory disease.

In the case of infection by the *Mycobacterium avium* complex, the American Thoracic Society recommends the use of an antibiotic regimen (including azithromycin or clarithromycin, rifampin or rifabutin, and ethambutol) until the cultures have remained negative for 1 year. As an adjunct, aerosolized interferon gamma seems to increase the effectiveness of systemic antibiotic therapy.

Along with antibiotic therapy, postural drainage, chest physiotherapy, and thinning and loosening of secretions, administration of a bronchodilator and of inhaled corticosteroids enhances bronchodilatation and mucociliary clearance to improve the removal of respiratory secretions. Secretions can be mobilized with chest physiotherapy, and mucolytic agents thereby prevent the progression of airway destruction. Traditional "chest clapping" or "chest cupping" has been replaced with the use of inflatable vests or mechanical vibrators applied to the chest. In spite of decades of experience and many uncontrolled trials, one systematic review found little justification for chest percussion and postural drainage. Maintaining adequate systemic hydration (enhanced by nebulization with saline solution) remains a necessity for patients with viscous secretions and mucous plugging [16].

Mucolytic drugs (e.g., acetylcysteine) delivered by nebulizer are given with the intent of improving tracheobronchial clearance. Aerosolized recombinant DNase breaks down the DNA released by neutrophils, which accumulates in the airways in response to bacterial infection. However, treatment with this agent has not shown significant benefit in non-cystic-fibrosis bronchiectasis. This is presumably due to a lesser component of neutrophils in the airway than in cystic fibrosis.

Randomised trials of these treatment options lack proper control groups. In children, many of the therapies have been used in cystic fibrosis. However, non-CF bronchiectasis may not always respond the same as CF. The markers used to assess therapy effectiveness have included the volume of sputum production and the clearance of a radiolabeled aerosol from the lung. More meaningful studies that focus on measures such as rate of respiratory exacerbations and quality of life and improvement in lung function and radiographic findings are needed.

Randomized placebo-controlled trials of inhaled corticosteroids in patients with non-cystic-fibrosis bronchiectasis showed no significant improvement in lung function. Inhaled corticosteroids may have a role in reg-

ulating the host response and halting inflammatory damage to the lung. In children with underlying asthma, it is important to continue inhaled corticosteroids on a long-term basis.

Bronchodilators are indicated if bronchial hyperreactivity is evident. These agents are used to improve ciliary beat frequency and thus facilitate mucus clearance. However, no randomized studies have validated their usefulness in the management of bronchiectasis. Furthermore, some patients with bronchiectasis experience paradoxic bronchoconstriction with beta-agonist therapy. This is probably secondary to a loss of airway tone due to beta-agonist relaxation of bronchial smooth muscle superimposed on already weakened bronchial cartilage. Therefore, assessing bronchodilator response before beginning such therapy is critical.

Some clinicians treat bronchiectasis with a prolonged course of antibiotics given *via* the oral route on a rotating basis. This is falling into disfavor, as it is in cystic fibrosis. A better option is to use alternating antibiotics for 7–10 days, with antibiotic-free periods of 7–10 days between each course [5, 17].

30.6.1 Surgery

The role of surgery for the treatment of bronchiectasis has declined but not disappeared. It was considered to be the only alternative method for the treatment of bronchiectasis in the early 1900s and 1950s. However, in recent decades, the indications have been limited because of the expectant results of conservative treatment.

The goals of surgical intervention in severe pediatric bronchiectasis are: elimination of the segments or lobes that are the most damaged and suspected of contributing to acute exacerbations as well as complications (lung abscess, empyema); elimination of areas that are subject to uncontrolled hemorrhage; removal of damaged lung suspected of harboring problematic organisms; preservation of as much healthy parenchyma as possible.

The indications for surgery are not fully established. The following should be considered when deciding on surgical treatment in a child: resistance to antibiotic therapy and to chest physiotherapy after a reasonable period; growth retardation caused by chronic pulmonary infections; inability to follow an educational program; and the socioeconomic status of the family.

After demonstration of gradual symptomatic improvement in some children who did not undergo surgical therapy for bronchiectasis, some pediatric surgeons in the 1990s recommended that surgery be delayed (unless symptomatically necessary) until the patient was aged 6–12 years because of the possibility for clinical improvement. Surgery should also be delayed in children with stable disease that can be controlled with medical therapy. Postoperative quality of life remains a crucial factor in decisions regarding the surgical treatment of bronchiectasis [19–21].

The aim of surgery is to excise all diseased lung areas whenever possible. It is known that 2–3 preserved segments are adequate to fill the pleural space, so segmental resection may be beneficial in cases of severe (but localized) damage. These resections can be done using thoracoscopic methods and are linked with a significant decrease in the associated morbidity (especially in terms of postoperative pain and better pulmonary toilet). Nevertheless, if the segments to be excised are the superior and inferior, the pleural space may not be filled by the expansion of a normal-sized middle lobe alone (or lingula). In this case, it is possible that the insufficient size of the remaining middle lobe could result in residual space problems (i.e., air leakage, empyema, prolonged fluid drainage), predisposing to torsion of the remaining lobe (the middle lobe is more mobile than the other lobes and more likely to twist on its narrow pedicle) [22, 23].

In unilateral bronchiectasis, total excision and pneumonectomy, as opposed to leaving residual disease, has been suggested to be well tolerated by children, who experience less functional disability than adults. If bronchiec-

tasis affects multiple lobes or segments, even in both lungs, the decision to operate is quite difficult. Even in childhood, pneumectomy has a larger negative impact on the physical aspects of health-related quality of life than lobectomy. For patients with severe progressive disease (as in subjects with other lung diseases) transplantation works well. Transplantation has been used predominantly in patients with cystic fibrosis.

30.7 Outcome and Follow-up

Children with bronchiectasis should be monitored throughout their lives by a clinician comfortable with the management of chronic lung disease. In general, children should be seen every 3–4 months when stable, and should be seen more frequently if they are not stable. Spirometry is recommended at each visit in children older than 5 years. Chest radiography need not be repeated empirically. If the clinical course changes, a radiograph should be part of the assessment. Although routine care of patients with bronchiectasis can be provided successfully by a primary care physician, a pediatric pulmonologist must be consulted to manage most of the pulmonary aspects of the bronchiectasis and the underlying disease. If recurrent aspiration is a contributing factor, a pediatric gastroenterologist should have input into the child's care. Pediatric immunologists should help manage children with HIV infection or immunoglobulin deficiencies. If the child has an underlying rheumatological disorder, a pediatric rheumatologist should be consulted on a regular basis. Physical therapists or respiratory therapists are important and helpful with regard to chest physiotherapy techniques. Whether carried out manually or with a mechanical device, the procedure needs to be thoroughly understood and periodically reviewed with the therapist.

Although developed countries have seen a decline in infection-related pediatric bronchiectasis, significant morbidity from bronchiectasis is seen, and infectious and non-infectious causes of bronchiectasis in the pediatric population remain. The importance of early evaluation and treatment in children with recurrent cough, sinusitis, potential aspiration of foreign bodies, or gastroesophageal reflux must be stressed to prevent the complications of ongoing respiratory disease and bronchiectasis. Overall, children with isolated bronchiectasis often have a good prognosis. The key to a successful outcome is determining whether the cause of the damage is ongoing and then treating the underlying problem. Growth of new pulmonary tissue in children continues rapidly until the age of 6 years and then tapers off through childhood. Injury at an early age may be compensated for by growth of normal healthy lungs without ongoing damage.

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Mediastinitis

31

Giovanni Ruggeri, Giulio Gregori, Beatrice Randi and Mario Lima

31.1 Introduction

Acute mediastinitis occurs as a result of contamination of the mediastinum secondary to perforation of the esophagus or trachea. Rarely, mediastinitis can develop from descending retropharyngeal or cervical abscesses ("descending cervical mediastinitis") or from the rupture of suppurative mediastinal lymph nodes. Mediastinitis can also be a complication after median sternotomy [1]. Due to the widespread use of diagnostic and therapeutic endoscopic procedures, the incidence of mediastinitis in children is increasing [2–8].

Esophageal perforation is the most frequent cause of mediastinitis in children (6, 8–15). Furthermore, the main interest of the pediatric surgeon with respect to esophageal diseases is the esophageal cause of mediastinitis. An anastomotic leakage from repair of esophageal atresia is analogous to an esophageal perforation. The peculiarity of this cause of mediastinitis leads us to discuss it separately at the end of the chapter.

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31.2 Pathogenesis

The esophagus, located in the posterior mediastinum, lacks a serosal layer and is surrounded by loose areolar tissue. In the case of esophageal perforation, bacteria and digestive enzymes spread readily to the mediastinum, causing mediastinitis [16].

An esophageal perforation can occur in the cervical, intrathoracic or intra-abdominal compartments. A cervical esophageal perforation is less severe than intrathoracic or intra-abdominal perforations. In fact, the esophageal attachment to the prevertebral fascia limits the spread of oro-pharyngeal flora through the retro-esophageal space. Instead, an intrathoracic perforation rapidly contaminates the mediastinum. If the integrity of the pleura is maintained, salivary organisms and gastric contents infiltrate only the mediastinum and produce mediastinal emphysema, inflammation and, eventually, cervical subcutaneous emphysema. This initial "chemical" mediastinitis is followed by bacterial invasion and severe mediastinal necrosis.

Mediastinal inflammation or initial perforation can lead to pleural rupture. As a result of the negative intrathoracic pressure, gastric fluids and bacteria are drawn farther into the pleural space, contaminating the pleural cavity and causing pleural effusion (empyema). The spread of contamination causes sequestration of fluids

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and hypovolemia, resulting in sepsis and multiple organ failure (MOF). Therefore, mediastinitis can lead to empyema, sepsis and MOF [17].

This is the reason for an overall mortality associated with esophageal perforation of 20%. Delay in treatment of >24 h after perforation can result in the doubling of this mortality [18]. However, the rarity of this condition and its non-specific presentation leads to delay in the diagnosis and treatment in >50% of patients. In the case of intra-abdominal esophageal perforation, erosion evolves into acute peritonitis [7].

31.3 Etiology

Iatrogenic injuries to the esophagus are the most common cause of esophageal perforation in pediatric patients. Others possible causes of esophageal perforation are impaction of foreign bodies and caustic burns. Rarely, perforation can occur during chemotherapy or after trauma; idiopathic esophageal perforation has also been reported [2–15, 19–23].

An anastomotic leakage after the repair of esophageal atresia can cause mediastinitis. The overall incidence of anastomotic leakage after surgical repair of esophageal atresia is around 17%, but major leakage occurs in approximately 3.5% of cases. The treatment of this type of cause of mediastinitis is peculiar because the leak is, in general, controlled by drains placed near the anastomosis intraoperatively. If a leak occurs after the drains are removed, the clinical situation is analogous to an esophageal perforation [14].

In esophageal perforations, the prevalence of mortality and morbidity is directly related to time of diagnosis. However, early diagnosis is usually possible only in iatrogenic causes, so the mortality is low only in this form [8, 21, 24]. In fact an esophageal perforation should always be suspected if a patient develops pain in cervical, thoracic, or abdominal regions or fever after esophageal endoscopy or dilatation [25].

If the esophageal perforation is diagnosed within the first 24 h, survival is reported to be as high as 92% but, after 24 h, survival rate can be as low as 67%. Other causes of esophageal perforation have high mortality because of non-specific symptoms in the first 24 h [8, 21, 24].

The main iatrogenic causes are diagnostic or therapeutic endoscopic procedures, mostly during dilatations of esophageal strictures and removal of esophageal foreign bodies [6, 8, 11, 13, 14]. Patients with benign esophageal strictures secondary to caustic ingestion have the higher risk of perforation during dilatations (4–6 perforations per 1,000 dilatations) [11]. The more common sites of iatrogenic esophageal perforation are the normal anatomical narrowings of the esophagus [26]. Other iatrogenic events that may cause perforations in children include: endoscopic sclerotherapy of esophageal varices; forced placement of nasogastric tubes; and difficult endotracheal intubation (mostly during neonatal ages) [6, 8, 11, 13, 14]. Rarely, rupture of the distal esophagus may occur during inapproriate placement and inflation of the gastric balloon of a Sengstaken–Blackmore tube to control bleeding of esophageal varices [27].

Esophageal injuries during pediatric surgery procedures occur infrequently. The surgical procedure associated with the highest risk of esophageal injuries is gastric fundoplication. When esophageal perforation is diagnosed intraoperatively, direct primary repair is almost always successful with minimal morbidity.

Ingestion of foreign bodies is a common problem in the pediatric population. Coins represent the most common type of foreign body ingested. The prevalence of esophageal perforation associated with ingestion of foreign bodies is 1% [10, 28] because esophageal perforation occurs as a result of a retained foreign body, and this is rare. In fact, a foreign body is defined as a "retained foreign body" only if it is located in esophagus for >1 week by clinical history. Although airway aspiration is, in general, considered more dangerous, delayed diagnosis of esophageal foreign bodies leads to complications that are also life-threatening [15].

The most feared complication of retained foreign bodies of the esophagus is erosion of objects into (or through) the esophageal wall. The results are acute processes (e.g., mediastinis, sepsis) but also delayed outcomes (e.g., esophageal strictures, tracheoesophageal fistulae, esophago-aortic fistulae) [9, 10, 15, 29, 30].

The esophagus anatomically has three areas of narrowing: the esophago–pharyngeal junction (C6), the aortic arch (T4) and the gastro–esophageal junction (T11). Retained foreign bodies in the esophagus most frequently lodge in the normal anatomical narrowing but also in sites of prior esophageal injury (e.g., repaired tracheoesophageal fistula) [31].

The diagnosis of a retained foreign body is often delayed, especially in those cases in which the foreign body has been present for a prolonged period of time. The delay in diagnosis is due to the particular presentation of this condition: children with esophageal foreign bodies routinely show signs and symptoms attributable to other diseases, such as respiratory or gastrointestinal diseases. Respiratory symptoms (cough, asthma and respiratory distress) are more common than gastrointestinal symptoms (nausea, vomiting, dysphagia).

Several studies have shown that patients with retained foreign bodies are commonly treated for asthma, upper respiratory tract infections or other illnesses before receiving a definitive diagnosis of esophageal foreign body. Thus, the task of differentiating between a child with a foreign body from a child with an upper respiratory tract infection, asthma or a gastrointestinal disorder is critical because prompt diagnosis of a retained esophageal foreign body generally allows for removal with minimal morbidity [9, 10, 15, 32, 33].

Most chemical-induced esophageal injuries occur due to accidental ingestion of caustic agents by children usually under 5 years of age. The severity and site of caustic esophageal injury are dependent upon the nature, amount and concentration of substance ingested and on the duration of mucosal contact [34, 35]. Because of the relative delay in transit time, the anatomical narrowings of the esophagus are most susceptible to caustic burns. There are several differences between injuries due to alkaline and acidic substances [36, 37]. Alkaline agents induce pylorospasm and spasm of the crico-pharyngeal muscle. They have prolonged and numerous contact with the esophageal mucosa and gastric mucosa. Acidic agents pass through the esophagus more quickly than alkaline agents. Hence, alkaline agents cause more esophageal injuries than gastric injuries; acidic agents are more dangerous for gastric tissue [38–39].

Classically caustic esophageal injuries are divided into three phases [36, 40]. During the initial phase (initial few days), the esophagus is characterized by inflammation, edema and necrosis (mucosal ulceration). During the second phase (3–4 weeks), the mucosa undergoes development of granulation tissue and collagen deposition. In this period, the esophageal wall is weakest and prone to perforation. During the third phase (many weeks), the destroyed esophageal submucosa and muscularis are replaced with scar tissue (cicatrisation and stricture formation) [26, 36, 40].

31.4 Clinical Aspects

The clinical picture of early esophageal injury is often vague and non-specific. Therefore, a high index of suspicion is critical to avoid delays in establishing an accurate diagnosis. Presentation depends on the cause, location of injury, size of the perforation, degree of contamination, length of time elapsed after injury, and presence of an associated injury.

In thoracic esophageal perforations, pain is the most common symptom, followed by fever, dyspnea and crepitus. Retrosternal or chest pain, lateralizing to the side of perforation, is common. Dissection of air along the subcutaneous planes or into the mediastinum is a hallmark of esophageal perforation. Occasionally, a systolic crunching sound ("Hamman's sign") can be heard over the cardiac apex and left sternal border.

The initial contamination of the visceral mediastinum is followed by subsequent perforation of the mediastinal pleura. The left pleural space is usually involved with distal esophageal perforation, whereas the right pleural space is commonly violated with proximal esophageal perforation. Influx of gastric contents into the mediastinum initiates an intense inflammatory response and cytokine activation, resulting in mediastinitis. The clinical picture is characterized by the development of tachycardia, tachypnea, fever, fluid sequestration and hypotension, leading to sepsis and shock within hours.

With cervical esophageal perforation, neck ache and stiffness are common findings, but pain is typically less severe. Subcutaneous emphysema after thoracic esophageal perforation is detected by palpation in 30% of patients. Emphysematous crepitus in the neck after cervical esophageal perforation is detected by palpation in 60% of patients.

With intra-abdominal esophageal perforation, dull epigastric pain radiating to the back may occur if the perforation is posterior and communicates with the lesser sac. More commonly, sharp, unrelenting epigastric pain is often associated with anterior perforation with subsequent widespread peritoneal contamination. The early onset of systemic signs such as tachycardia, tachypnea and fever are the usual features. Rapid deterioration with signs of systemic inflammatory response such as leukocytosis, sepsis, and shock develop within hours of presentation [26].

31.5 Diagnosis

The diagnosis of mediastinits secondary to esophageal perforation is confirmed by chest radiography, which demonstrates a pneumomediastinum, a widened mediastinum and/or bilateral pleural fluids. Computed tomography (CT) and magnetic resonance imaging (MRI) of the thorax are the "gold standard" methods to diagnose mediastinitis, and show fluid collections around the esophagus, just above the diaphragm (Fig. 31.1).

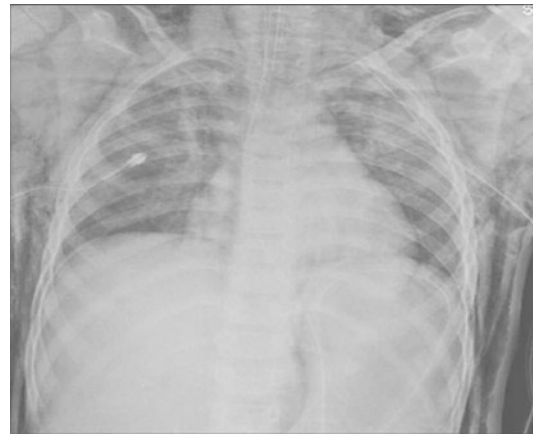

Fig. 31.1 Chest radiograph in a patient affected by traumatic tracheal rupture demonstrating a pneumomediastinum, a widened mediastinum and diffuse subcutaneous emphysema

The diagnosis of a cervical esophageal perforation is aided by a lateral radiograph of the neck, which can demonstrate air in the prevertebral fascial planes before it is detectable by radiographs of the chest or by physical examination. If a thoracic esophageal perforation is suspected, posteroanterior and lateral chest radiographs should be obtained immediately. Plain radiographs of the chest show esophageal perforation in 90% of patients, but can be normal if taken early. Radiographic evidence of mediastinal emphysema requires ≥1 h after the initial injury to become discernable, whereas pleural effusion and mediastinal widening may take several hours to evolve. Pleural effusions, pneumomediastinum, subcutaneous emphysema, hydrothorax, hydropneumothorax, or subdiaphragmatic air heighten the suspicion of esophageal perforation.

Contrast esophagography remains the standard for the diagnosis of esophageal perforation. Water-soluble isotonic contrast agents such as Gastromiro® are advocated for the first-line screening of suspected perforations.

CT is useful if perforations are difficult to locate or diagnose or if contrast esophagography cannot be carried out (Fig. 31.2). Abnormal findings suggestive of esophageal perforation include: extraluminal air in the

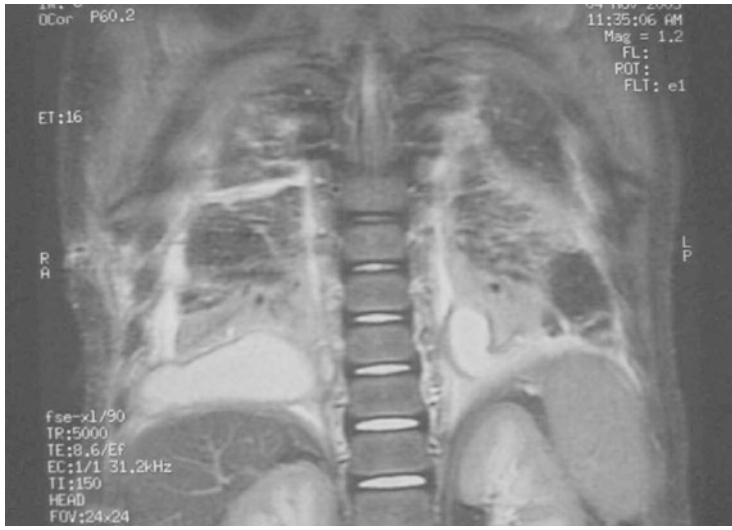

Fig. 31.2 The diagnosis of mediastinitis by MRI of the thorax. Fluid collections are seen around the esophagus just above the diaphragm. These collections are secondary to massive esophageal perforation during chemotherapy for leukemia

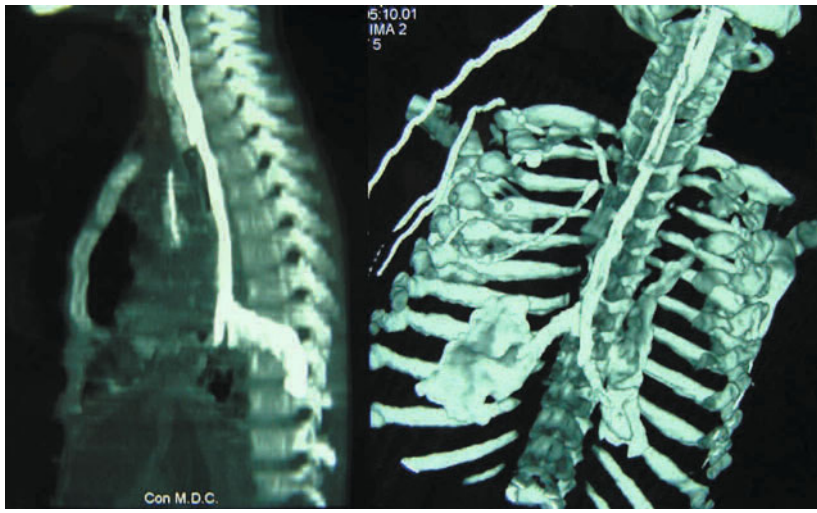

Fig. 31.3 CT with oral contrast showing the contrast spreading in the pleural cavities just above the diaphragm. The esophageal perforation was located along the posterior wall of the distal thoracic esophagus

soft tissues of the mediastinum; esophageal thickening; perceptible communication of the air-filled esophagus with a contiguous mediastinal or paramediastinal air–fluid collection; or abscess cavities adjacent to the esophagus in the pleural space or mediastinum. Left-sided pleural effusion strengthens the suspicion of perforation [6, 8, 11–14, 17].

Plain radiographs confirm or strongly suggest the presence of the foreign body in the vast majority of patients (Fig. 31.3). Imaging should include lateral soft-tissue neck and chest (posteroanterior and lateral), abdomen, and pelvis views. A radiopaque foreign body lodged in a bronchus or the esophagus is a straightforward diagnosis (Fig. 31.4), but many aspirated or ingested foreign bodies are radiolucent or too small to be seen on a radiograph. Esophageal foreign bodies may cause mediastinal inflammation and significant extrinsic tracheal compression, both of which should be evident on chest radiographs. Barium and water-soluble contrast materials are thought in some cases to obscure the for-

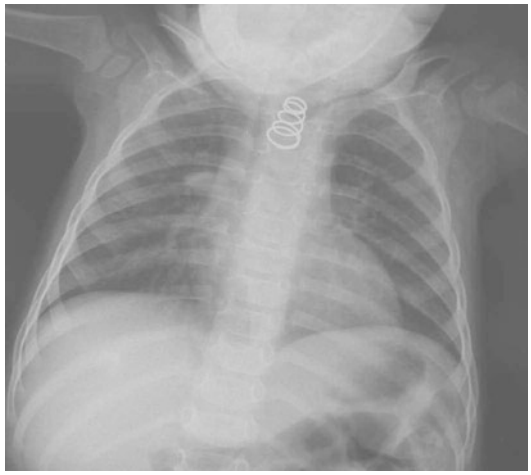

Fig. 31.4 Chest radiograph demonstrating a radiopaque object (spring) in the proximal portion of the esophagus

eign body and complicate subsequent endoscopic examination [9, 10, 15, 31].

31.6 Management

Conservative management is the treatment of choice in esophageal perforation in children [6, 8, 9, 11–15, 24, 41, 42]. Historically, the management of esophageal perforations in infants and children has been based on adult reports, which have favored surgical management. In general, most surgeons who operate in adults believe that direct surgical repair is associated with less morbidity and mortality than conservative management. However, adult perforations often occur with underlying esophageal disease, such as cancer and achalasia, which may affect management decisions [13]. Pediatric surgeons realize that children have different causes and a greater propensity to heal, and therefore require different treatment.

A retrospective study in 1988 from the Netherlands reported 12 children with iatrogenic esophageal perforations treated with conservative management (nutrition, antibiotics, thoracic and esophageal drainage). Eleven of these patients were healed with this therapy, with the exception of one patient who did not improve and required a thoracotomy [24]. Conservative management has also recently been documented with success in selected adult cases [17].

The overall goal of conservative management is to promote healing with control of infection and nutritional support. This attitude is based on the particular anatomy of the esophagus, i.e., separated from each pleural space only by thin pleura. This pleura is in close contact with the oesophagus, so any leak of air or fluid tends to drain spontaneously into the pleural space (from where it can be removed by adequately positioned tubes). Once drainage is established, the esophageal perforation can be treated as an esophago-cutaneous fistula which, like other gastrointestinal fistulae, heals spontaneously if downstream patency is preserved and as long as adequate treatment of sepsis and nutritional support are provided.

Therefore the standard of care involves endoscopic removal of the foreign body (if present) (Fig. 31.5), a combination of wide-spectrum antibiotics, total parenteral nutrition or enteral nutrition (eventually by gastrostomy), and prompt drainage of pleural effusions or mediastinal abscesses (if necessary). Only if these measures fail is it justified to approach the esophagus directly, bearing in mind that repair might imply loss of the organ. Direct surgery on the esophagus is indicated only if it is unavoidable.

Controlling contaminations is another component of conservative management. The patient should be nil-by-mouth, and nutritional support is started in the from of total parenteral nutrition, a nasogastric feeding tube or surgical gastrostomy [14]. Several methods of safely placing a feeding tube past the perforation have been suggested. It may be placed under direct vision *via* endoscopy or laryngoscopy or *via* fluoroscopy [13].

Pleural effusion, pneumothorax or mediastinal abscess should be managed by drains to control the leak. The collected specimens are cultured for aerobic and anaerobic pathogens to

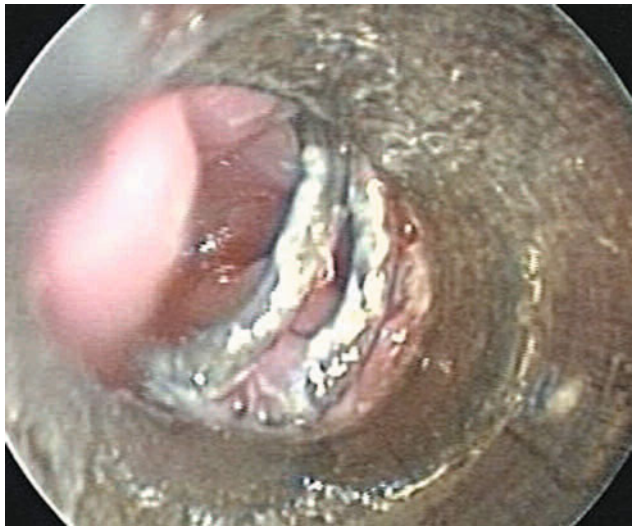

Fig. 31.5 Endoscopic view of a foreign body (spring) during removal

guide antibiotic therapy. The goal of conservative management is shown by the clinical status of the patient and improvement in laboratory and imaging indices. Oral feeds can be resumed after an esophagogram shows no further leak, and timing is determined on an individual basis. If conservative management fails (clinical picture progresses to severe sepsis), a direct surgical approach to the esophagus is essential. Early diagnosis and treatment, iatrogenic origin, young age, and the absence of underlying disease are the best prognostic predictors for conservative management.

The surgical approach requires primary repair if possible. There is often a combination of extensive scarring, inflammation or friability of tissues (Fig. 31.6). Hence, construction of a cervical esophagostomy, exclusion of the perforated area, and a gastrostomy for feeding are recommended. After some time, the patient should be considered for esophageal replacement (removing the native esophagus) [6, 8, 9, 11–15, 24, 41, 42].

Recently, a type of minimally invasive surgery has been employed in esophageal perforation which respects the aims of conservative management. Eight children with esophageal perforation were treated with thoracoscopic drainage of the mediastinum. In this series, a diagnosis of mediastinitis secondary to esophageal perforation was made. The fluid collection around the esophagus was treated thoracoscopically. After the right mediastinal pleura was opened longitudinally with blunt dissection around the periesophageal spaces, abscess pockets were drained and necrotic materials debrided. At the end of the procedure, a chest tube was placed in the mediastinum through an opening in the mediastinal pleura for drainage of mediastinal pus under direct vision, and another chest tube was placed in the pleural cavity [12].

31.7 Anastomotic Dehiscence After Repair of Esophageal Atresia

Anastomotic dehiscence is one of the most common and serious complications of the surgical repair of esophageal atresia. In most cases, there is minor leakage (17%) that can be managed with conservative treatment, but more serious defects (3.5%) may require surgical correction [43].

The most common causes of dehiscence are excessive tension at the anastomosis and poor blood supply. Long-segment repairs are at particularly high risk for developing anasto-

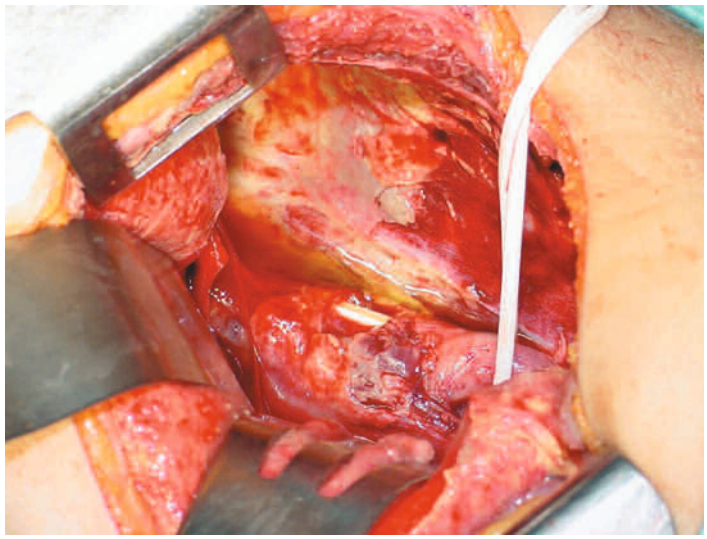

Fig. 31.6 Intraoperative image of an esophageal perforation during chemotherapy for leukemia

motic leaks because of the tension between limbs [43–45]. Minor anastomotic leaks are often asymptomatic and discovered incidentally on routine postoperative esophagography. Major anastomotic leaks (15–85% of the anastomosis) are diagnosed by esophagography prompted by salivary drainage from the chest tube.

Complete disruption of the anastomosis is a rare complication occurring in <2% of cases, and presents with a tension pneumothorax and significant salivary drainage from the chest tube. Most minor leaks seal within 1–2 weeks with conservative management, including withholding oral feeds, intravenous antibiotics, parenteral nutrition, and chest-tube drainage. Conservative treatment with prolonged chest drainage is now widely used for minor anastomotic dehiscence.

The classic approach for major leakage used to be cervical esophagostomy and gastrostomy. The distal esophageal pouch is temporarily closed until the continuity of the organ can be restored with colon, gastric or jejunal interposition. Today, the goal of most approaches is to salvage the native esophagus (except in cases of complete anastomotic disruption, which are quite rare). When major anastomotic dehiscence occurs, the choice between surgical and conservative management can be difficult. It depends largely on the dimensions of the dehiscence and the physical condition of the child. The decision to abandon the "wait-and-see" approach and re-operate is always complex.

In 1996 Chavin et al. reported 11 cases of anastomotic leaks, 7 of which were considered to be major. All 7 patients underwent surgical revision (re-anastomosis or repair with pleural or intercostal muscle patches). In 3 of these cases, the second procudure was ineffective, and the problem was resolved definitively only after prolonged (39–50 days) postoperative chest drainage. This series underlines the risk of failure associated with surgical repair of anastomotic dehiscence and the importance of orienting all efforts toward conservation of the native esophagus [46].

Another case of major esophageal dehiscence treated with re-operation has been reported. The anastomosis was partially intact, so the authors opted for repair of the primary anastomosis. Immediately, a second dehiscence occurred. The clinical and imaging characteristics of the second leak were quite similar to the first. Conservative management of this second dehiscence was chosen and the leak resolved.

These cases illustrate that prolonged chest-tube drainage can lead to spontaneous closure even in cases of major anastomotic leaks [47]. In the case of pleural empyema, mediastinitis or tension pneumothorax (which are generally related to complete dehiscence), an early thoracotomy is required. It is essential to carry out the revision of the anastomosis (if possible) or cervical esophagostomy and gastrostomy for feeding with subsequent esophageal replacement [46, 47].

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Chylothorax

32

Olivier Reinberg

32.1 Introduction

Chylothorax is a rare condition characterized by chyle in the pleura. In children, it can be a potential life-threatening disorder that may induce respiratory distress and nutritional (hypoalbuminemia), electrolyte (hyponatremia), and immunological (lymphopenia, hypogammaglobulinemia, T-cell depletion) consequences [1]. It was first described by Virchow in 1856 [2].

32.2 Etiology and Pathogenesis

Chylothorax can be primary (congenital) or acquired. Primary chylothorax is an anomaly of the lymphatic and/or thoracic ducts and appears in neonates [3]. It can be associated with syndromes (Noonan's, Down, Turner's [4, 5] or with lymphangiomatosis [4, 6, 7]. Congenital chylothorax can be diagnosed prenatally (prenatal procedures have improved considerably during the last 15 years). Fetal and per-partum thoracocentesis with pleuro-amniotic drainage are increasingly carried out [3, 8–12].

Acquired chylothorax may be a consequence of thoracic trauma (blunt, penetrating, baro) [13], but most often is iatrogenic and follows thoracic surgery. It is a possible complication of: repair of esophageal atresia; closure of a congenital diaphragmatic hernia [14, 15]; cardiac surgery [16–18]; insertion of a central venous catheter [13, 20]. Injury to the thoracic duct may occur during surgery to the mediastinum or in the left lower neck. The incidence of chylothorax after repair of a congenital diaphragmatic hernia is probably under-estimated. Chylothorax related to insertion of a central venous catheter can be the consequence of thrombotic occlusion of the superior vena cava as well as direct trauma to the thoracic duct. Some cases of neonatal chylothorax are acquired as a result of birth trauma. Some acquired forms can also be a consequence of extrinsic compression of the thoracic duct by thoracic tumors or due to inflammatory diseases [21, 22].

32.3 Clinical Features

Chylothorax appears as a non-infectious pleural effusion causing non-specific symptoms such as cough, asthenia, abdominal pain, and respiratory distress [23]. Congenital chylothorax may present as acute respiratory distress at birth or develop progressively during the first weeks of life. It is the most common type of

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pleural effusion seen during the neonatal period [24]. Acquired chylothorax appears as a pleural effusion a few days after thoracic surgery or trauma. Beghetti et al. [18] recorded a mean interval of 7 (range, 1–25) days between the surgical procedure and detection of chylous effusions.

32.4 Diagnosis

Once the effusion has been revealed by conventional thoracic roentgenography, it usually has to be punctured under ultrasound guidance. The two major findings that can be used to diagnose chylothorax are lymphocytic pleocytosis and elevated levels of triglycerides.

Chyle is a lymphatic fluid enriched with lipids secreted by intestinal cells. It is collected and then transported *via* the thoracic duct into the venous stream. Measuring lipid content and demonstrating the predominance of lymphocytes in the pleural effusion serves to prove that chylothorax is present. Chylothorax is confirmed by a milky appearance, sterile bacterial cultures and triglycerides >1.1 mmol/L after normal feeding (including fat) and an absolute cell count >1,000/mL (>70% lymphocytes) [18, 19, 23]. Without enteral intake of lipids, differentiating between chylous and non-chylous effusions may be difficult. Chyle becomes milky with a fatty diet and light-yellow if the patient is not fed. Positive red Sudan III (fat-soluble dye) staining of the fluid confirms the diagnosis if doubt persists.

32.5 Management

Management of congenital chylothorax in the neonatal period differs from that resulting from a tear in the thoracic duct in older children. The optimal therapeutic strategy (i.e., conservative *versus* surgical) is controversial because there is no clear evidence of when to operate.

32.5.1 Initial Conservative Treatment

Once the diagnosis of chylothorax has been confirmed, conservative treatment is undertaken with drainage of pleural fluid, supportive ventilation, supplementation of fluid loss, and elemental enteral feeding using fat-free formulas or medium-chain triglycerides (MCTs) and/or total parenteral nutrition (TPN) [18, 23]. MCTs enter the portal circulation directly, bypassing the lymphatics. Therefore, they do not increase the flow in the thoracic duct [19]. Conservative treatment using an MCT-rich enteral diet and/or TPN, drainage using a chest tube, and assisted ventilation leads to successful resolution of chylothorax (defined as drainage of <10 mL (kg/day) after 4 weeks of medical treatment) in 80% of cases [16, 19, 24].

The use of somatostatin has been shown to be useful in some cases of chylothorax, but the mechanism of action is unclear. Somatostatin has recently been replaced by its analog octreotide. Octreotide has a comparatively longer half-life with greater potency, is synthetic, and can be given via the intravenous or subcutaneous route [25]. At least 20 regimens of dose, route and duration for octreotide therapy have been described. They have been reviewed by Helin et al. [19]:

- somatostatin or octreotide should be started after 4 weeks if conservative treatment (i.e., drainage >10 mL (kg/day) has failed;
- the recommended dose is continuous infusion of 5 μg/kg/d;
- the recommended mean duration is 10–14 days.

Despite the lack evidence, the use of octreotide seems safe and leads to a reduction in chyle production, but side effects include: cholelithiasis, liver impairment (including cholestasis); renal impairment; transient intolerance to glucose [26, 27]; hypothyroidism [28]; and necrotizing enterocolitis [25].

Several techniques of chemical pleurodesis have been suggested. These include the use of adhesive substances such as sirolimus (ra-

pamycin), povidone-iodine elemene, streptococcal derivative OK432 (or equivalent preparations of streptococci) and talc. In accordance with le Nué et al., we are strongly against the injection of povidone-iodine because of its ineffectiveness and associated effects. These effects include increased respiratory distress, acidosis, hemodynamic instabilities, acute renal failures evolving into severe and chronic failure, as well as its effects on the thyroid glands of neonates and infants [5, 29, 30].

32.5.2 Surgical Treatments

Opinions and recommendations about the length of conservative management vary considerably. Most reports focusing on pediatric subjects state that conservative treatment should be of long duration. However, some reports on surgical treatment have shown benefit if surgery is carried out after 10 days of conservative treatment [31, 32], even in neonates and infants with congenital forms of chylothorax [29]. The delay before surgical treatment is dependent upon the amount of drainage (>50 mL/kg/d) and the tolerance to the pleural effusion without impairment in ventilation [33]. Hence, the best timing for surgery should be debated between the pediatricians, pediatric gastroenterologists and pediatric surgeons involved.

Several surgical options are possible through different approaches. That is: drainage; pleural abrasion; pleurectomy; or ligation or repair of the thoracic duct (which can be done by thoracotomy, video-assisted surgery (VAS) or thoracoscopy). The "ideal" treatment would be to close the wound on the thoracic duct by repairing it, or by carrying out resection and an anastomosis to restore its permeability. This procedure cannot be carried out on a small thoracic duct in a child. Attempts to reanastomose the thoracic duct in the azygos vein have been attempted in the pediatric population, but with a high incidence of failure due to occlusions [34]. The major challenge is to localize precisely the site of the leak to repair or close the duct. This is rarely done, so the remaining options are either to close the thoracic duct just above the diaphragm or to perform a pleurodesis.

32.5.2.1 Drainage

A drain can be pleuroperioneal (with or without a valve) or external. Drains can remain *in situ* for 1–3 months [35–38]. In the pediatric population, external drains are usually employed and carry a risk of infection. Hence, external drains should be removed as soon as drainage is complete. Internal drains are not indicated for small children because an appropriate device is not available, and because the smallest drain may occlude or break, leading to recurrent surgical procedures for replacements [29]. Internal drains could be an option for older children.

32.5.2.2 Pleurodesis

Creating adhesions between the lung and thoracic wall and thereby reducing the size of the cavity in which a pleural effusion may collect is the purpose of pleurodesis. Chemical adhesions are not recommended for the reasons outlined above. Any aggressive surface (e.g., tip cleaner) can be used to scratch the pleura ("pleural abrasion"). Surgical pleurodesis can be achieved through thoracotomy or thoracoscopy by injuring or removing the parietal pleura ("pleurectomy"). Pleurectomy is usually done by removing several bands of pleura between two adjacent ribs. Mediastinal and diaphragmatic pleura must also be treated with special care to avoid injuries to the phrenic nerve. The problem with pleurodesis is that the chyle effusion prevents the lung from adhering to the pleura. Good drainage is crucial, and can sometimes involve several drains. However, recurrence is common [29, 34, 39].

The long-term side effects of surgical pleurodesis have not been evaluated, but such side effects should be expected. A firm scarring process all around a growing lung will affect pulmonary function and effect the development of the thorax, leading to orthopedic complications [29, 34].

Technically, pleurodesis can be achieved by thoracoscopy but, to be effective, long bands of pleura must be removed. The problem for the surgeon is being able to move in the thorax facing backward, upward and down to the diaphragm as well as far forward to reach the internal mammary artery. Patient positioning is of major importance. The arms must be left free so that they are not hit when facing down to the diaphragm. The surgeon must be able to work on either side of the table. For pleurectomies, our team uses a 30° × 5 mm telescope so that we can exchange the port site with the other 5-mm instrumental ports.

32.5.2.3 Repair or Ligature of the Thoracic Duct

Repair or ligature of the thoracic duct is the most effective way to cure chylothorax as long as the leak point has been identified. This can be done by thoracotomy or thoracoscopy. Thoracotomy is usually undertaken in the fifth intercostal space and gives a good view of the middle mediastinum. However, a leak in the upper or lower mediastinum can be difficult to identify and to reach for closure. The advantage of thoracoscopy is that the surgeon can go anywhere in the thorax to search for the leak (even in the very narrow posteroinferior diaphragmatic sinus or up to the confluent of the thoracic duct in the left subclavian vein). Developments in thoracoscopy (even in neonates) permit a minimally invasive approach [40–43]. To help identification of the leak, a high-fat meal (oil or full-fat cream) is given 3 hours preoperatively.

Thoracoscopy should be done through the side where the pleural effusion is located. This enables the tear to be repaired and, in case of failure, to identify the leak. The thoracic duct can be occluded from either side. The patient is placed in the lateral prone position. The operating side is elevated by 35–40°. The arm must be left free to allow the surgeon to adopt any position around the child if pleurectomy is indicated. The surgeon faces the spine. The chest drain must be removed preoperatively.

Selective intubation in the opposite bronchus is not essential but can be useful. The ipsilateral lung is collapsed gently with a low-pressure pneumothorax (5–6 mmHg). A first port is inserted for the telescope (30° × 5 mm) at the tip of the scapula. Our team avoids placing a port in the drainage hole because of the underlying adhesions. Another 5-mm instrumental port is inserted in triangulation away from it. The pleural adhesions are divided, then the drainage hole can be used subsequently as a port hole. Exploration for the leak can now begin. The phreno-pulmonary ligament must be divided to give a better view of the posterior pleural sinus.

If the site of the chyle leak is identified, attempts to close it are made. No single method can secure it reliably. Sutures, ligatures, clips and monopolar/bipolar cautery have been used. New sealing tools such as harmonic scalpels or Ligasure® seem promising but few studies have been reported [40–43].

Ligature or closure of the thoracic duct above the diaphragm should be done if there is no obvious site of leak. The thoracic duct lies posterior behind the aorta then between the esophagus and aorta. This area can be reached from either side by thoracoscopy. If the duct is not clearly identified, mass coagulation is carried out with a sealing device (e.g., Ligasure) after securing the posterior vagus nerve and esophageal wall.

The tension pneumothorax must be relieved because the pressure it produces can lead to misinterpretation regarding efficient closure of the thoracic duct. Careful inspection should then be done to search for a persistent leak (which may appear as a collection of liquid along the spine). If in doubt, additional procedures should be considered, such as the use of sealing glue (Tisseel®) or pleurodesis.

At the end of the procedure, at least one chest drain is left in the most posterior port hole, laid along the spine and placed under low suction (10 mmHg) to avoid overdrainage. Patients are left nil-by-mouth postoperatively with TPN.

32.6 Outcome and Follow-up

Chylothorax in children is not common so reliable outcome data are lacking. Conservative treatment should be the first resort, with surgery undertaken in cases of long-lasting or serious chyle effusion. The few surgeons using minimally invasive procedures have reported good outcomes in small series, shortening the previously reported delay for healing [29, 40]. Patients with definitive closure of the thoracic duct must have long-term follow-up for malabsoption at 3 months and 6 months, with dosage of α-1-antitrypsin in the stools.

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Part VIII

Trauma

Thoracic Trauma

33

Marcello Dòmini, Veronica Carlini and Mario Lima

33.1 Introduction

Thoracic injuries are uncommon in children but, if they occur, they are suggestive of a significant mechanism of injury. The child must undergo a thorough examination to exclude or detect concomitant injuries to the head, abdomen and spine. These concomitant injuries often result in appreciable morbidity and mortality.

33.2 Epidemiology

Males are affected 2–3-times more often than females because boys are more prone to undertake dangerous activities or to involve themselves in risky situations. International studies have reported thoracic trauma to comprise 0.2–7.0% of all cases of pediatric trauma. The ratio of penetrating to blunt injuries varies between countries.

A study of war history reflects the progression of the management of thoracic injuries. In World War I, chest wounds accounted for 2–5% of all injuries with a prevalence of mortality of 25%. This prevalence of mortality rate was more than halved in World War II. Though the prevalence of thoracic injuries remained at 8%, the prevalence of mortality dropped to only 12%. This improvement in survival can be attributed to implementation of rapid evacuations to appropriate field hospitals (a concept originally recommended by Napoleon's surgeon, Larry). Children were rarely the victims of these wars. However, the lessons learned from these injuries were applied to injuries caused by civilian road traffic accidents and penetrating injuries suffered by children through other means. Nowadays the prevalence of mortality in children who have had thoracic trauma is 26%.

Studies comparing patients who have suffered isolated thoracic trauma to those who have associated injuries demonstrate that the prevalence of mortality differs significantly between two groups: (i) children who do not sustain associated injuries have a prevalence of mortality of ≈5%; and (ii) children who have the involvement of other body regions have a prevalence of mortality of 25%. Pediatric death may occur before reaching the hospital. It is predominantly secondary to hemorrhagic shock or cardiopulmonary arrest related to a tension pneumothorax.

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33.3 Etiology and Pathogenesis

There are several functional compartments in the thoracic cavity (air spaces, intrapleural spaces, vasculature and the mediastinum), each of which requires a specific pressure range to function normally. These pressures influence cardiac load, lung expansion, and ventilation–perfusion relationships. Hence, a change in pressure in any of these compartments will affect the others, and may result in major physiological impairment. The care of patients who have sustained a chest injury should be based on the understanding of this anatomical and physiological interplay. Intrapleural pressure combined with contraction of inspiratory muscles (predominantly the diaphragm) allows effective inspiration, alveolar ventilation and subsequent oxygenation of blood.

A disturbance in the mechanism of ventilation along with ventilation–perfusion mismatch and cardiovascular injury can occur in chest trauma. These factors can then lead to respiratory impairment and hypoxemia. This disorder can result from: lung collapse; blood or air within the pleural cavity; herniation of the abdominal contents due to diaphragmatic rupture; intraparenchymal injury as a result of an extensive contusion; hemorrhage; or inhalation of gastric contents. In these types of injuries, cardiogenic shock and hemorrhagic shock have an important role:

- hemorrhagic shock means that the circulating volume passing through the lungs for oxygenation is reduced, and this can occur as a result of bleeding within the chest;
- cardiogenic shock is secondary to ventricular dysfunction caused by myocardial contusion, a tension pneumothorax or a pericardial tamponade that impair oxygenation.

Thus, effective delivery of oxygen is the central focus in the management of any type of chest trauma.

In children, the thorax differs structurally from that of the adult. In young children, the greater flexibility of the thoracic cage permits the anterior ribs to be compressed to reach the posterior ribs. As a consequence, pulmonary contusions are more common, whereas rib fractures occur less frequently than in adults. As the bony rib cage ossifies, fractures and flail segments become more common. Similarly, bony thoracic spine injuries are uncommon in infancy through to pre-adolescence. Because the bones are incompletely ossified, the ligamentous attachments are more flexible and the supportive musculature not fully developed. Hence, younger patients are more likely to experience injuries without these abnormalities being seen on plain radiographs.

In children, the internal thoracic organs are smaller and exhibit different physiological characteristics than those seen in adults. Early in life, the trachea is narrow, short, more compressible and narrowest at the level of the cricoid cartilage. Therefore, small changes in airway diameter, small foreign bodies or seemingly inconsequential wounds in the thoracic cage may lead to rapid respiratory distress. In addition, children have a diminished functional residual capacity coupled with higher oxygen consumption per unit body mass. For these reasons, young children are more prone to the rapid evolution of hypoxemia. Metabolic rate and functional lung volume migrate toward adult values by 8–10 years of life. Thus, airway management requires adequate pre-oxygenation, expeditious intubation, and minute ventilation adjusted to age, weight and metabolic rate.

Great vessel and mediastinal injuries are far less frequently encountered in the pediatric population than in adults. This difference is because: the mediastinum in children is relatively mobile and less susceptible to the rapid acceleration and deceleration forces commonly experienced in traumas; vascular disease in children is rare; atherosclerosis and other vascular diseases commonly seen in adults reduce the muscular elasticity of the vessel walls and so they are susceptible to tearing or rupture in the case of trauma. Children have also far greater cardiovascular and pulmonary reserves than adults, so they are less likely to demonstrate compensatory responses.

Together with the anatomical and physiological considerations mentioned above, physicians that take care for children with thoracic injury must also know the most common causes of chest trauma:

- infants and toddlers are often the passive victims of blunt trauma such as motor-vehicle collisions and non-accidental injury;
- school-age children are more often subject to transport-related mechanisms of injury from skateboards, roller-skates and bicycles;
- teenagers are more likely to be involved in sports injuries, personal violence and suicide. Their risk is amplified by the potential coincident use of illegal drugs and alcohol.

Geographic variations such as proximity of mountains, water or deserts may be associated with different injury patterns in the adolescent group. Moreover, the evolution of "extreme" sports may carry a greater risk of profound injury. These activities are characterized by increased physical risk due to the potential for high-energy impacts, lack of appropriate safety precautions, and remoteness from immediate medical attention.

33.4 Clinical Features

The mechanisms of chest trauma differ according to whether it is a blunt or penetrating injury. As a general rule, blunt injuries are more common than penetrating injuries in the pediatric population. In fact, with few exceptions, stab wounds or gunshots occur only in teenagers involved in fights, riots or wars. In regions in which firearm use is controlled (as in most European countries), penetrating thoracic trauma during peacetime is practically unheard of.

More than half of blunt thoracic injuries in children are secondary to accidents involving motor vehicles. The remainder of these are in due to falls, other transport accidents or, rarely, as a result of non-accidental injuries. The lesions caused by blunt mechanisms may present diagnostic difficulties if external signs of trauma are absent.

Penetrating injuries (although infrequent) raise the prevalence of mortality up to 33%. The nature and depth of injury depends upon the etiology, anatomical location, and direction of the agent of force. All penetrating chest trauma should undergo to rapid initial assessment to verify that the airways are adequate and to identify respiratory impairments.

The spectrum of childhood traumatic injuries ranges from simple pulmonary contusions (>50% of all pediatric thoracic injuries) to more complex lesions such as fractures of the ribs or sternum, pneumothorax or, rarely, exanguinating vascular injuries.

33.4.1 Blunt Thoracic Trauma

The spectrum of blunt traumatic chest injuries in children is wide.

33.4.1.1 Fractures of the Ribs and Sternum

Fractures of the ribs and sternum are uncommon in pediatric thoracic trauma because the elasticity and flexibility of the thoracic cage protects children from sustaining injuries to the chest wall (including flail segments). An isolated broken rib is usually a self-limiting condition, but it must be considered an indicator of significant energy transfer. Rib fractures should draw attention to the risk of severe associated injuries. In addition to pneumothorax and hemothorax (which will be addressed separately), children with first rib fractures have been noted to have clavicular fractures, injuries to the central nervous system, facial fractures, pelvic fractures, extremity injuries and major vascular trauma.

33.4.1.2 Flail Chest

Fortunately, a flail chest is a very rare event in children. It is likely to be the most common serious injury to the thorax seen by clinicians. A flail chest may result when multiple adjacent ribs are broken in multiple

places along the midlateral or anterior chest wall, separating a segment, so that a part of the chest wall moves independently. The number of ribs that must be broken to have a flail chest varies according to different definitions: some sources say at ≥2 adjacent ribs must be broken in ≥2 places; others require ≥3 ribs in ≥2 places. The flail segment moves in the opposite direction as the rest of the chest wall because of the ambient pressure in comparison with the pressure inside the lungs: it goes in while the rest of the chest is moving out, and *vice versa*. This "paradoxical motion" can increase the work and pain involved in breathing. When it occurs, it results in significant ventilatory compromise and reduces venous return due to mobile mediastinum, which shifts secondary to altered pleural pressure.

Most often a flail chest is diagnosed by chest radiography carried out during the initial evaluation. Computed tomography (CT) of the chest should be undertaken if further information regarding the extent of any injuries is required.

Direct examination of the chest wall reveals it to be bruised or abraded; rarely, respiratory distress is present. It may be possible to palpate subcutaneous emphysema. Percussion of the thorax may be hyper-resonant. In this case, normal ventilation is appreciated upon auscultation.

Management of rib fractures revolves around supportive measures. The first priority is the prevention of atelectasis and pneumonia. These goals are best achieved with the judicious use of pain medication and, when the child is old enough to participate, with incentive spirometry and deep-breathing measures. Even small children may have objective estimation of their pain by use of validated scales for facial expression or visual analog scales.

33.4.1.3 Pulmonary Contusion and Laceration

Pulmonary contusion and lacerations are the most frequently encountered thoracic injuries in children. There are two main mechanism of injury:

- direct compression of the parenchyma by the traumatic agent;
- violent displacement of the lung, tracheobronchial tree and mediastinal structures during deceleration during the accident and particularly in vehicular accidents with or without body restriction.

After the contusion, the lung parenchyma undergoes several anatomical changes. Hemorrhage, edema and consolidation reduce the compliance of extensive parts of the lungs, leading to ventilation–perfusion mismatch, hypoventilation and hypoxia. Laceration is often seen in the mid-lung and results from sudden compression of the thorax, causing rupture of the lung. The parenchymal tear may extend through the visceral pleura, thereby causing pneumothorax.

Initially, children who sustain lung lesions may appear well. This condition can deteriorate within the first 24–72 h from trauma, and the diagnosis can be made by chest radiography. Suspicion must be high for children who have experienced a major mechanism of injury if they complain of chest plain or chest-wall tenderness, or if the chest wall is bruited or abraded. These injuries are commonly associated with hemothorax or pneumothorax. In a small number of cases, a traumatic pneumatocele may develop. An infectious disease may develop in the edematous, fluid-filled alveoli or collapsed air spaces surrounding the injury.

Upon clinical examination the chest wall is usually bruised or abraded and tender. Reduced breath sounds over the affected lung field may be heard upon auscultation. Chest radiography is diagnostic but, because of the progressive nature of pulmonary contusions and lacerations, it is not uncommon for it to be negative during the first 48–72 h after trauma. Therefore, repeating chest radiography after 48 h if it is initially negative is important. High-resolution CT allows better depiction of associated lesions. These patients require close monitoring with supplemental oxygen and supportive care. Minimal-access surgery has been proposed for the assessment of some intrathoracic injuries.

Occasionally, it may be difficult to differentiate aspiration from contusion. Aspiration may occur at the time of injury during intubation or with vomiting while being restrained in the supine position during evaluation. The right lower lobe of the lung is the most frequently affected, although diffuse infiltrates are sometimes seen. Radiographic abnormalities from aspiration occur in a delayed fashion unlike the immediate findings seen with contusions. Although aspiration may predispose to the development of pneumonia, no benefit has been shown by empirical administration of antibiotics or corticosteroids.

33.4.1.4 Pulmonary Contusion Hematoma

A pulmonary contusion hematoma is due to a collection of blood within the pulmonary parenchyma, and it presents immediately after blunt chest trauma. It continues to evolve over the first 24–72 h after injury and usually does not impair respiratory function. Pulmonary hematomas may become infected and progress into abscess cavities. These patients present with a bruised chest wall and mild reduced breath sounds over the affected lung field. Radiographs show patchy areas of opacity. These will evolve over 2–3 days to become nodular and develop more distinct margins.

33.4.1.5 Pneumothorax

Pneumothorax occurs if pleura are breached and inspired air leaks into the intrapleural space. Air accumulates in this space due to negative pressure during inspiration. This results in lung collapse and compromised ventilation. Tension pneumothorax is an immediate life-threatening condition that must be recognized and treated rapidly; it occurs if the accumulation of air in the pleural space is massive and rapidly increasing.

Pneumothorax can be asymptomatic or can manifest as tachypnea and respiratory distress. There may be chest-wall tenderness and subcutaneous emphysema. Decreased air entry on the affected side can be felt upon auscultation.

Radiography is the most appropriate investigation and reveals free air around the periphery of the lung field and decreased lung volume. CT of the chest may provide further information regarding the extent of injury (e.g., location of extrapulmonary air).

In the case of tension pneumothorax, the clinical examination is different. There will be severe respiratory distress with tachypnea and decreased oxygen saturation, tachycardia, hyper-resonant percussion on the ipsilateral side and tracheal shift to the controlateral side. Absent breath sounds on the ipsilateral side with reduced air entry on the controlateral side will also be noted. Chest radiography demonstrates a lack of lung markings on the ipsilateral side with evident lung collapse. The mediastinum is pushed toward the controlateral side.

A tension pneumothorax must be drained as soon as possible by a needle thoracocentesis. This procedure should be closely followed by insertion of an intercostal drain. The drain must be connected to an underwater seal to allow air to exit from the pleural space while avoiding entrance of external air into it. Patients receive supplemental oxygen, are monitored closely in a pediatric center, and receive ventilatory support if necessary. Chest physiotherapy has a significant role in these children.

33.4.1.6 Hemothorax

Hemothorax is a rare injury in children. Large amounts of blood accumulate in the pleural space. The source of blood is variable: it could be the result of pulmonary or cardiac contusion or a rapid, massive accumulation secondary to injury to a great vessel or the heart. Tachypnea, respiratory distress decreased oxygen saturation, tachycardia, slow capillary refill, decreased chest expansion and reduced or absent air entry upon auscultation are the most features of clinical examination.

Chest radiography is the investigation of choice. It may depict extravasated liquid. If the patient is clinically stable and the diagnosis of hemothorax has been made, chest CT may be carried out to detect the cause of bleeding.

When the patient is hemodynamically unstable, insertion of an intercostal catheter to drain the fluid and to assess the magnitude of the blood loss must be carried out. A potential complication of this procedure is hypovolemic shock, which may lead to renal failure, profound acidosis, cardiac arrhythmias and cardiac ischemia. Therefore, a good venous catheter for infusion to restore the loss of liquid is crucial.

The optimal timing of surgical intervention in hemothorax is not known. Urgent thoracotomy may be required if there is ongoing massive blood loss (>1–2 mL/kg/min) and hemodynamic stability cannot be achieved. Hemothorax may also occur due to blunt or penetrating injury.

33.4.1.7 Traumatic Asphyxiation

Traumatic asphyxiation is a very rare and potentially immediately life-threatening injury. It occurs if there has been severe and sudden compression of the chest and upper abdomen. The clinical features include subconjuntival and upper-body cutaneous petechial hemorrhages, cyanosis, facial edema and a variable degree of pulmonary and central nervous system (CNS) abnormalities. Radiography and CT of the chest should be carried out to evaluate the underlying parenchymal and vascular injuries. These patients will require ventilatory support, oxygen administration, insertion of a nasogastric tube, analgesia, and chest physiotherapy.

33.4.1.8 Pericardial Tamponade

Pericardial tamponade involves accumulation of blood in the pericardial space. It can be seen in blunt and penetrating injuries. Pericardial tamponade may originate from a cardiac chamber, one of the great vessels or from the myocardium. The normal volume of pericardial fluid is ≈25 mL; if this volume is acutely increased by as little as 5–10 mL, it can result in significant hemodynamic compromise. This type of injury is poorly tolerated in children. The classic symptoms are distended neck veins, raised central venous pressure and pulsus paradoxus. Often the tamponade is not so evident.

The diagnosis is usually made from clinical examination alone. A soft heart sound is heard upon auscultation. It may be complicated by myocardial ischemia or infarction causing impaired cardiac function. This condition is therefore imminently life-threatening and requires urgent intervention.

All patients require close monitoring, including electrocardiography (ECG). The goal of management is a reduction in the volume of pericardial fluid. Pericardiocentesis is a potentially lifesaving procedure but provides only temporary relief. It should be carried out if the patient is acutely hemodynamically unstable or if surgical intervention is not immediately available.

33.4.1.9 Myocardial Contusion

A myocardial contusion is a myocardial bruise and it is generally secondary to blunt trauma to the anterior chest. The most common cause for this type of injury in the pediatric population is road-traffic accidents. This injury tends to evolve over the first 24–48 h after the trauma, and thus the patient's condition may deteriorate over this time.

The clinical examination may show bruising to the anterior chest wall, tachypnea, tachycardia and arrhythmias. In this case, early examination may be unremarkable and it is very important to monitor troponin I levels as well as to carry out serial ECG and close cardiac monitoring. Echocardiography is also useful to determine impairment of myocardial function.

33.4.1.10 Injury to Great Vessels

Injury to great vessels often results in rapid death by exsanguination. The thoracic vessels at risk of injury are the aorta, vena cava, innominate artery and vein, left subclavian artery and left common carotid artery. The patient has tachypnea, an altered level of consciousness, respiratory distress, tachycardia.

Muffled heart sounds, decreased air entry and a possible bruit over the anterior chest are observed upon auscultation.

The diagnosis of aortic injuries in children may be difficult due to their rarity. Chest radiography may demonstrate mediastinal widening, loss of a defined aortic stripe, deviation of the esophagus or mainstem bronchus, apical cap hemothorax and first- or second-rib fractures. CT may reveal a mediastinal hematoma and can delineate the thymic outline. The arteroius phase of the CT or arteriography are the "gold standard" investigations.

Many of these patients cannot be stabilized and thus require immediate surgical intervention to repair the damaged vessel with direct suturing or, in some cases, an interposition graft. These type of injuries necessitate aggressive fluid resuscitation blood trasfusions.

33.4.1.11 Diaphragmatic Rupture

Diaphragmatic rupture is a rare injury in children. It is the result of a significant blunt force to the lower chest or abdomen. A sudden, severe rise in intra-abdominal pressure is the most common cause of diaphragm rupture. This condition is usually leftsided and, if the defect is large, abdominal contents may become displaced into the thoracic cavity and cause respiratory compromise.

Bruising to the abdomen and the mechanism of injury should increase the suspicion of diaphragmatic injury. Upon clinical examination patients show increased respiratory effort, tachypnea, and decreased chest-wall movements. Upon palpation, a tender abdomen and an ipsilateral thorax that is dull to percussion due to the displacement of abdominal contents may be observed. Decreased breath sounds on the affected side are noted upon auscultation.

The definitive diagnosis can be made with oral contrast studies, which clearly demonstrate the bowel in the chest. These patients require oxygen supplementation, surgical repair of the diaphragm and reduction of abdominal contents out of the chest. If the diagnosis is delayed there is a risk of ischemic injury to the bowel or omentum, as well as contusion or perforation of the bowel.

33.4.2 Penetrating Thoracic Trauma

33.4.2.1 Open Pneumothorax

Open pneumothorax occurs if a penetrating injury creates an opening between the intrapleural space and the external enviroment. Air is "sucked" into the pleural space from the outside; this communication is a response to the negative pressure. The overall result of these physiological events is significantly impaired ventilation and hypoxia. Open pneumothoraces require immediate intervention before investigation.

These patients show respiratory distress, decreased chest-wall movement, a tender chest wall and decreased expansion of the chest wall. Percussion is hyper-resonant on the ipsilateral side. Decreased air entry on the affected side is noted upon auscultation. The clinical status of patient may dictate if rapid intervention is necessary before investigations. Imaging investigations are undertaken after insertion of an intercostal drain. Radiography is the gold standard modality and chest CT may be carried out to obtain more information regarding the injury if the patient is stable.

Management involves assessment of the airway and providing supplemental oxygen. Analgesia is important to reduce the effects of splinting of the chest wall secondary to pain. An intercostal catheter should then be inserted into the affected side (preferably at a site distant from the original injury).

Open pneumothorax may be complicated by a concurrent hemothorax or progression of pneumothorax into a tension pneumothorax. An important potential complication is infection, so these patients should be treated empirically with intravenous antibiotics.

33.4.2.2 Tracheobronchial Injuries

Cervical trauma or violent compression/displacement of the thorax may injure the main

airways. These lesions can be grouped into two categories: intrapleural and within the mediastinum. In the former, a large pneumothorax result and persists in the presence of an intercostal catheter. In the latter category, inhaled air accumulates in the mediastinal space, causing a pneumomediastinum. It is also possible for air to be lost directly outside *via* the wound created by the injury. In this situation, little or no air will pass along the tracheobronchial tree into the lungs. Infection is a risk in this group of patients. It is also possible that an associated esophageal injury may have occurred and a fistula may develop between two organs.

Patients may have respiratory distress and hemoptysis. Upon palpation, a decreased chest expansion may be noted. Subcutaneous emphysema may be observed over the neck or in the upper thorax. Upon auscultation, decreased air entry will be evident bilaterally if the injury is to the larynx or trachea or unilaterally if injury is further along the tree.

Plain radiography of the thorax shows pneumomediastinum and eventually pneumothorax that may be bilateral. Segments or lobes of the lung may be atelectatic beyond the level of the rupture. CT of the neck or chest may allow better visualization of this complete or major disruption. Tracheo-bronchoscopy is usually recommended to locate and assess the extent of the lesions.

Management involves establishing a definitive airway. Bronchoscopy is needed to insert an airway stent or to intubate the controlateral main bronchus. Passing the tube beyond the tear may allow appropriate ventilation and even healing. Sometimes, separate bronchial intubation and selective ventilation have permitted healing of the tear or survival until surgical repair. A direct approach to the injured airway may be necessary if the air leak is not controlled by the intercostal tubes, or as a delayed procedure in some cases. The trachea can be approached through the neck in high lesions and sternotomy is rarely necessary. Lower bronchial disruption is approached by thoracotomy for closing the defect by direct suture or, if this is not possible, for segmental or lobal resection.

33.4.2.3 Esophageal Injuries

Esophageal injuries are rare and almost always due to penetrating trauma. Injuries to the esophagus and trachea commonly occur in tandem. These patients have respiratory distress, retrosternal chest pain, dysphagia, cough or stridor, subcutaneous emphysema, tachycardia, and decreased chest-wall expansion. Decreased air entry is noted upon auscultation.

Chest radiography will demonstrate air and/or fluid in the pleural space, pneumomediastinum and subcutaneous emphysema. CT of the chest will provide a definitive diagnosis as well as the site of the rupture.

Many of these injuries can be managed conservatively with good analgesia and close monitoring. Children should all have a nasogastric tube and receive regular chest physiotherapy and intravenous antibiotics to reduce the risk of infection. If the esophageal laceration is large or is not responding to conservative management, surgical repair of the injury may be required.

33.4.2.4 Cardiac Laceration

Cardiac laceration may be due to the ingestion of a sharp object that has pierced the heart posteriorly from the esophagus. Rarely, penetrating cardiac injuries may result in transection of a coronary vessel, damage to a valve, or rupture of chordae tendineae.

Upon clinical examination, tachypnea, distended neck veins, tachycardia, decreased chest expansion, muffled heart sounds and decreased air entry will be noted. The diagnosis of penetrating cardiac injury should be possible by clinical assessment alone.

These patients require supplemental oxygen with ventilatory support, aggressive and rapid fluid resuscitation, close monitoring, ECG as well as central venous and arterial catheters.

Pericardiocentesis may relieve the immediate threat to life temporarily but the keystone of management is surgical intervention. Cardiac laceration may be complicated by pericardial tamponade, myocardial infraction, mediastinitis and ischemic injuries to other organs due to profound shock.

33.4.2.5 Injury to the Thoracic Duct

Injury to the thoracic duct may result in significant morbidity if not recognized early. An untreated leak in the thoracic duct may result in profound malnutrition. The thoracic duct lies on the posterior wall of the thorax and so is more likely to be damaged from a penetrating injury to the back rather than to the anterior chest wall. The thoracic duct crosses the thorax from right to left at the T5 level. Therefore, injuries inferior to T5 will result in right pleural effusion whereas those above this level will produce left-sided disease.

Clinical examination detects tachypnea, decreased chest-wall expansion and decreased air entry on the ipsilateral side. Chest radiography demonstrates an air or fluid level in the pleural space on the affected side. This condition is usually diagnosed by identification of chylous fluid draining from an intercostal drain placed to treat pleural effusions. Occasionally, the diagnosis may not be made until nutritional abnormalities are noted upon blood investigations. This condition may be complicated by ongoing leaks or recurrence of fistulas.

Patients usually recover with conservative management: total parenteral nutrition and fasting. Surgical management may involve repair of the duct or closing of the fistula. This process may be assisted by meals high in triglycerides several hours preoperatively to induce chyle production and thus making the defect in duct more evident. These patients require intravenous antibiotics.

33.5 Conclusions

Thoracic trauma is due to high-energy accidents with multi-organ involvement that cause most of the relatively frequent fatalities. The lung is the organ more frequently affected together with the ribs and pleural space, whereas tracheobronchial disruption is extremely rare.

Trauma often inflicts several injuries. The clinician must diagnose, prioritize and treat these injuries. Therefore, any consideration of thoracic trauma must include a discussion of the complex, multiply injured child. Priority should be given to airway and breathing problems and bleeding. Recognition and treatment depends heavily on a high index of suspicion combined with the appropriate diagnostic test and a multidisciplinary approach.

Diagnostic imaging remains a significant source of radiation exposure in all patients. Recent medical literature and the media have heightened concerns regarding the long-term risks of radiation exposure (especially in children). However, imaging studies are important adjuncts in the diagnosis of injuries in the traumatized patient, and radiography should be the first imaging modality in the chest. CT of the chest rarely results in management changes, and may be limited to those children with mediastinal abnormalities identified on screening chest radiography and/or findings of physical examination suggestive of vascular injury rather than those based on first-rib or sternum fractures.

Thoracic injuries should be managed initially by following the generally accepted emergency and resuscitation procedures that ensure step-by-step attention to airway patency, effective breathing and cardiovascular support (ABS).

Adequate oxygenation should be ensured by face masks. If gas exchange is insufficient because of restriction of lung parenchyma, intubation and ventilation (often with positive end-expiratory pressure) help to maintain patent as many alveoli as possible while reducing interstitial edema. Sophisticated respiratory assistance methods such as high-frequency oscillatory ventilation or inhaled nitric oxide are rarely used.

After these measures have been taken, most injuries can be treated conservatively or only with intercostal tubes. Urgent surgical treatment is imperative in a small proportion of cases in whom blood loss is massive because of lung hilar, aortic or cardiac injuries. Lifesaving emergency thoracotomy at the scene of the accident is seldom required in children.

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Part IX

Tumors

Anterior Mediastinal Tumors

34

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34.1 Introduction and Epidemiology

The mediastinum is the most common site of chest masses in children. Mediastinal masses are placed in one of three mediastinal compartments (anterior, middle, posterior) on the basis of a lateral chest radiograph [1] They comprise a wide spectrum of disease, and around 40% occur in children aged <2 years of age. Mediastinal masses are usually assigned to a single mediastinal compartment to limit the differential diagnosis. Large mediastinal masses can cause compression of adjacent structures. Patients may have airway compression or cardiovascular compromise. A total of 39% of mediastinal masses are benign and 61% are malignant, with more than half of these being lymphoma [2]. A total of 44% of all mediastical lesions are anterior mediastinal tumors [3], which are relatively rare in the pediatric population. Most are due to hematogenous malignancy and about half of these patients are asymptomatic. Anterior mediastinal masses represent a heterogeneous group of congenital and neoplastic lesions, many of which are malignant [4, 5].

The purpose of this chapter is review the features, diagnosis and management of the different types of lesions. Children with anterior mediastinal masses are at risk of life-threatening airway compromise during anesthesia, and can present a diagnostic and management challenge for pediatric surgeons.

34.2 Etiology and Pathogenesis

To understand the classification and differential diagnosis of mediastinal masses, it is useful to have an understanding of the embryologic development and anatomical features of the anterior mediastinum.

The mediastinum develops after the craniocaudad migration of organs, the creation of the celomic pleura and pericardial cavities, and separation from the abdomen by means of the diaphragm. Early in embryologic development, germinal blastomeres undergo early differentiation near the region of the primitive cephalic pole and migrate toward the lumbar region. During this migration, these elements may stop prematurely and become homoplastic or heteroplastic teratomas. The upper anterior midline is one of the pathways by which embryonal germ cells migrate toward their final settlement in the gonads. For this reason, germ cell tumors may be in this location. The thymus is derived from paired primordia located in the

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third branchial pouches that, after migration into the anterior mediastinum, fuse to form the ultimate single organ. For this reason, lesions related to this organ can be cervical and/or mediastinal.

The mediastinum is the portion of the thorax between the pleural sacs. It is bound superiorly by the thoracic inlet, inferiorly by the diaphragm, posteriorly by the vertebral bodies, and anteriorly by the sternum. The anterior mediastinum is considered to be the area between the posterior surface of the sternum and behind the pericardial sac, the anterior surface of the great vessels and the trachea. It is surrounded on each side by the pleura and lungs. It contains lymphoid structures, the thymus gland, and numerous nerves and vessels.

34.3 Classification and Clinical Features

Anterior mediastinal masses in children can be classified into three categories: solid; cystic; and fatty or other lesions (Table 34.1). As in adults, malignant lymphoma and germ cell tumors are the most common. In contrast with adults, primary malignant thymic tumors are uncommon.

Anterior mediastinal masses are usually discovered incidentally on chest radiographs undertaken due to non-specific symptoms. Tumors in the anterior mediastinum may become large before they elicit symptoms. Over one-half of children with mediastinal masses are symptomatic. Malignant lesions have a greater chance of being symptomatic than benign lesions [6]. Symptomatic children may have different degrees of respiratory impairment or cardiovascular compromise (e.g., superior vena cava syndrome). Respiratory symptoms related to local airway compression are respiratory distress, cough, orthopnea, stridor or wheezing. Rarely, the sternum is bulging (mainly seen in infants or newborns with large teratomas). Systemic symptoms may be present in patients with lymphoproliferative disease (including malaise, fever, weight loss and night sweats).

34.4 Diagnosis

Diagnostic evaluation of the mediastinum has advanced significantly in the last two decades. In particular, anterior mediastinal tumors (principally teratomas) have been diagnosed prenatally by ultrasonography [7]. In cases of malignant or immature teratomas, serum levels of alfa-fetoprotein and gonadotrophins (that can induce precocious puberty, especially in Klinefelter syndrome) may be elevated [8]. The posteroanterior and lateral chest radiograph is the first imaging test (Fig. 34.1). Ninety percent of mediastinal masses can be seen on posteroanterior and lateral chest radiographs. In the asymptomatic patient, the mediastinal mass is often an incidental finding on a chest radiograph obtained for other reasons.

Computed tomography (CT) of the chest is the second imaging test. CT establishes the site of the mediastinal mass, the consistency and architecture of the mass, the relationship to adjacent structures, and other details [9]. CT is highly effective at differentiating between fatty tissue, cystic or calcification components, vascular components and soft tissues. Teratomas may have calcified areas, like other tumors such as hemolymphangiomas [10]. Spiral CT is better than conventional CT for evaluating enteric and bronchogenic masses. CT is also important for estimating the patency of the airway.

Ultrasonography may be used to investigate the cystic or solid nature of the masses [11]. Magnetic resonance imaging (MRI) may have some advantages over CT for defining the relationship of tumors to the spine and possible invasion into adjacent structures. MRI better defines a vascular origin of the masses [12]. MRI also has the advantage of avoiding ionizing radiation, but is limited by the protracted duration of the study and the need for control of ventilation.

Barium esophagography and bronchography is carried out infrequently for evaluation of mediastinal masses. However, barium esophagography may be useful for suspected enterogenic cysts or other esophageal lesions.

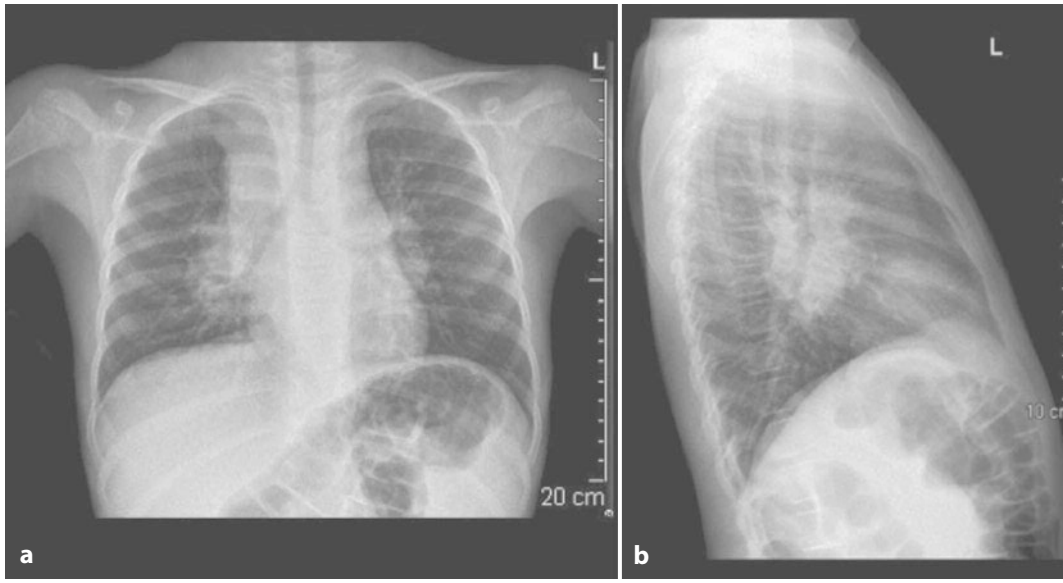

Fig. 34.1 Plain radiographs of an anterior mediastinal Hodgkin's lymphoma

In tumors for which surgery is not the primary treatment, biopsy of the lesions is fundamental using cell markers and molecular biologic features to ensure the most appropriate therapy is chosen. Histological correlation of fine-needle aspiration guided by ultrasonography or CT provides a diagnostic sensitivity and specificity of 87% and 88%, respectively, for the detection of tumors, and 82% and 83%, respectively, for the determination of malignancy [13]. In such cases, cells can be obtained by distant lymph-node biopsy or by pleural/pericardial fluid aspiration [14]. If this is not possible and mediastinal tissue is necessary, thoracoscopic [15] or anterior mini-thoracotomy biopsy using the Chamberlain incision (second interspace anterior thoracotomy) is a valuable tool. Mediastinoscopy is rarely indicated in the pediatric patient [16].

34.5 Management

Most mediastinal masses, regardless of whether they are malignant or benign, require surgical intervention for the diagnosis or definitive treatment. The basic principles involved in the treatment of mediastinal masses are protection of the airway from compression, an accurate diagnosis, and complete resection with minimal morbidity.

The decision for anesthesia must involve consideration of the risk of respiratory collapse during the induction of general anesthesia. Ventilation may become seriously difficult due to the reduction in vital capacity of the resting lung, changes in pulmonary compliance, and the loss of negative inspiratory pressure [17]. Anesthetic risks are best assessed using a mixture of clinical, functional and radiological evaluations [18]. Only clinical signs and symptoms do not correlate well with anesthetic complications [19]. Orthopnea is the only symptom powerfully associated with respiratory collapse [20, 21]. If the cross-sectional area of the tracheal lumen is decreased by ≥50%, the anesthetic risk is high. These patients often require particular anesthetic procedures such as laryngeal masks or spontaneous ventilation.

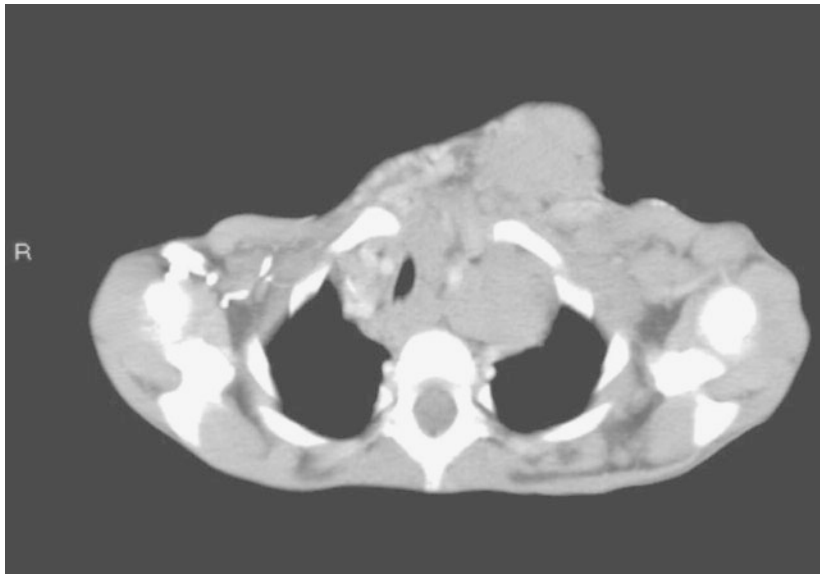

Fig. 34.2 CT of an anterior mediastinal Hodgkin's lymphoma showing compression and deviation of the trachea

34.5.1 Lymphoid Tissue Tumors

34.5.1.1 Hodgkin's Lymphoma (HL)

Lymphoma is the third most common malignancy in children, but is the most common malignancy of the mediastinum in children, representing approximately one-half of all mediastinal malignancies. Approximately one-third of lymphomas are HL and two-thirds are non-Hodgkin's lymphoma (NHL).

Lymphomas may involve all compartments in the mediastinum. In the pediatric population, lymphoma occurs most frequently in the anterior and middle compartments. HL more often affects pre-adolescents, adolescents and young adults. Children with HL are more likely to experience the systemic symptoms of weight loss, night sweats and malaise, and less likely to have pleural effusions. The Reed–Sternberg cell is the main cell component. These cells are implanted in lymph nodes in which the proportions of fibrous stroma, lymphocytes and plasma cells vary: lymphocyte-predominant, lymphocyte-depleted, mixed cellularity and nodular sclerosis. Nodular sclerosing is the most common cell type, representing approximately 75% of cases. [22]. In most patients, the diagnosis can be made by lymph-node biopsy because most children have coexistent cervical or supraclavicular lymphadenopathy that is readily accessible to biopsy. Infrequently, tissue must be obtained by direct biopsy of the mediastinal mass or bone-marrow aspirate. Nodular HL starts in one group of lymph nodes and then extends to contiguous or distant ones by following lymphatic pathways. The stage of the disease determines the treatment. The Ann Arbor classification subdivides HL into four stages with subgroups according to the presence or absence of systemic disease. Positron emission tomography-computed tomography (PET-CT) seems to be a promising modality for non-invasive staging.

HL may be located primarily in the anterior and mid-mediastinum in children and may cause compressive effects (Fig. 34.2). If biopsies are not possible in extrathoracic nodes, the Chamberlain procedure or thoracoscopy can be useful to find tissue for the diagnosis. In HL, surgery is not the primary treatment, except in very localized cases [23]. In very rare situations in which a child presents with so bulky a tumor that airway compression is life-threatening, surgical debulking may be indicated.

34.5.1.2 NHL

NHL represents approximately two-thirds of mediastinal lymphomas. NHL is a systemic disease in which several lymph nodes and structures are affected by massive proliferation of lymphoblasts. NHL is frequently extended beyond the original site, involving the regional nodes and distant organs such as the pleura, pericardium or bone marrow. Abdominal organs and the central nervous system may be affected in rare cases. NHL is typically synonymous with lymphoblastic lymphoma in children, although non-lymphoblastic (large cells) may occur rarely [24].

Children with NHL often present with symptoms related to local compression in the respiratory system or obstruction of the superior vena cava. Generalized symptoms are often present, and include fever, night sweats and weight loss. Pleural effusions and cervical adenopathy are also common. Involvement of the bone marrow occurs in more than one-third of patients. Like HL, patients with NHL require biopsy before treatment initiation, but resection should not be attempted. The tumor has an excellent response to chemotherapy and radiotherapy and disseminated disease is often present [25]. An open procedure provides the best and safest approach to tissue diagnosis [26]. However, the risk of anesthetic complications from the mass effect of the large mediastinal mass should to be assessed carefully prior to any procedure.

CT may is used to define better the extent of the disease and attachments of the airway. An opportunity for the diagnosis is often offered by cytologic and marker analyses of pleural or pericardial fluids. If peripheral lymph nodes or fluids are not available for biopsy or puncture and the bone marrow has not been invaded, cytologic analyses is by fine-needle aspiration under ultrasonography or CT guidance [27]; biopsy by thoracoscopy or by the Chamberlain procedure may be necessary [16]. As in HL, the anesthetic risks should be emphasized [28], and surgery is not the primary option in the treatment of mediastinal NHL. These neoplasms are particularly responsive to chemotherapy. The main role of the surgeon should be to provide adequate biopsy while preserving airway patency.

34.5.2 Germ Cell Tumors

Germ cell tumors of the mediastinum account for 6–18% of pediatric mediastinal neoplasms [29]. They are the second most common tumor of the anterior mediastinum. Primary germ cell neoplasms arise from collections of primitive germ cells present in the anterior mediastinum while on their migration to the gonads during embryologic development. Because they are histologically indistinguishable from germ cell tumors arising in the testes and ovaries, the diagnosis of a primary malignant mediastinal germ cell neoplasm requires exclusion of a primary gonadal tumor as a source of mediastinal metastases.

34.5.2.1 Teratomas

Teratomas account for about 60% of all germ cell tumors in the mediastinum. Most are asymptomatic (unless when large). Children may present with respiratory symptoms such as severe respiratory distress, especially while lying supine due to airway compromise because the tracheal cartilages are less rigid and may be compressed. Resection is indicated not only to relieve symptoms, but also to rule out malignant elements.

Teratomas are classified in two main types: immature malignant and mature benign. On chest radiography, immature and mature teratomas usually present as round and sharply marginated anterior mediastinal masses. Calcification, which occurs in »25% of teratomas, may be central, peripheral, or curvilinear. The hallmarks of immature and mature teratomas are fat, fluid and calcified components on CT or MRI. Mature benign teratomas tend to displace rather than invade adjacent structures and have an excellent prognosis after complete excision. Immature malignant teratomas must be treated with chemotherapy and radiotherapy in addition to surgery. Resection of anterior

mediastinal teratomas is best achieved by a median sternotomy; posterior mediastinal teratomas can be excised by thoracotomy. Care must be taken during the induction of anesthesia because loss of muscle tone may result in complete collapse of the airway.

34.5.2.2 Non-Teratomatous Germ Cell Tumors

Non-teratoumatous germ cell tumors (e.g., yolk-sac tumor, dysgerminoma, seminoma, embryonal carcinoma, choriocarcinoma) are very rare [30]. They are malignant; patients require complete removal of non-teratoumatous germ cell tumors and chemotherapy [31].

34.5.3 Lesions of the Thymus Gland

The thymus gland is a bilobed encapsulated organ located anterior to the great vessels and pericardium. Its primary function is enabling the maturation of T-lymphocytes. In infancy and childhood until 5 years of age, the thymus gland has a quadrilateral shape with convex margins. After this time, the thymus gradually becomes more triangular and the margins straighten. By the age of 15 years, the margins of the thymus should be straight or concave.

34.5.3.1 Prominent Thymus (Pseudomass)

On chest radiographs, the normal thymus gland is not visible in adolescents and adults. In infants and children, however, the thymus gland may be very prominent and mistaken for a true mass. A retrocaval thymus is a normal variant in which there is posterior extension of the thymus between the superior vena cava and great arteries. On chest radiography, a retrocaval thymus may produce a confusing appearance that mimics a true mediastinal mass or collapse of the right upper lobe.

34.5.3.2 Thymic Hyperplasia

Hyperplasia of the thymus is the most common process to involve the thymus gland in infants and children. The hyperplastic gland usually maintains the radiographic characteristics of the normal thymus. Thymic enlargement rarely causes neonatal respiratory distress but should be considered in the differential diagnosis of marked tachypnea in the neonatal period [32]. True thymic hyperplasia is a very rare entity in which the thymus is enlarged without disruption of the normal architecture of the gland or any pattern of abnormal cellular proliferation [33, 34]. In such cases, the hyperplastic thymus can cause a mass effect on adjacent structures without invasion. Thymic hyperplasia may be associated with Graves' disease [35]. In some cases, thymic hyperplasia is a thymic rebound after atrophy from severe illness or drugs (e.g., chemotherapy or corticosteroid treatment). After chemotherapy, the thymus atrophies in approximately 90% of cases. The thymic gland grows back over the subsequent several months, and the volume of the rebounding thymus may exceed the baseline value.

34.5.3.3 Thymic Cysts

A thymic cyst is a rare, fluid-filled mass that represents a cystic remnant of the thymopharyngeal duct. Although typically found in the lateral infrahyoid neck and intimately associated with the carotid sheath, a thymic cyst may occur anywhere along the thymopharyngeal duct from the pyriform sinus to the anterior mediastinum. It may also be connected to the mediastinal thymus directly or by a fibrous cord. The pathological visualization of Hassall corpuscles in the cyst wall confirms the diagnosis. Often asymptomatic, when sufficiently large a thymic cyst may cause dysphagia, respiratory distress, or vocal-cord paralysis. Most affected patients present between 2–15 years of age, although thymic cysts may present in adults rarely. Thymic cysts require surgical excision through cervical or trans-sternal approaches. The prognosis is excellent if the lesion is completely resected.

34.5.3.4 Thymomas

Thymomas are epithelial neoplasms containing a variable amount of lymphocytes. Al-

though representing approximately 20% of mediastinal tumors, thymomas are rare in the pediatric population, accounting for only 1–2% of mediastinal tumors. Thymomas may be discovered incidentally, although about one-third of patients have symptoms related to local compression or invasion. About 40% of patients with thymomas present with a paraneoplastic syndrome such as hypogammaglobulinemia, red cell aplasia or myasthenia gravis. Thymomas are classified as non-invasive or invasive. Non-invasive thymomas tend to have well-defined margins because they do not extend beyond their fibrous capsules. Invasive thymomas extend beyond their fibrous capsule, tending to spread locally to invade adjacent mediastinal structures and the chest wall. An invasive thymoma also may spread contiguously along the pleural surface (usually unilaterally) and often recurs after surgical removal.

34.5.3.5 Thymic Carcinomas

Thymic carcinomas are exceedingly rare in children. However, some instances of malignant thymoma with or without myasthenia gravis have been reported [36].

34.5.4 Fatty Lesions

34.5.4.1 Lipomas

Lipomas are encapsulated masses with a composition identical to subcutaneous fat. They may occur anywhere in the body, including the mediastinum. Because lipomas are soft and pliable, patients are usually asymptomatic and the lesion is found incidentally on a chest radiograph or CT. Depending on the size and location of the lipoma, chest radiographs may show a mass that is relatively radiolucent compared with adjacent soft tissues. CT and MRI can confirm the fatty nature of the mass.

34.5.4.2 Thymolipomas

A thymolipoma is an uncommon benign anterior mediastinal mass that consists of normal thymic tissue interspersed with fat. Because these are pliable fatty masses, patients are usually asymptomatic. No treatment is necessary unless this benign tumor becomes massive and exerts a mass effect on adjacent structures.

34.5.5 Vascular Tumors

Vascular tumors are rare and may be found in the anterior mediastinum, posing difficult therapeutic problems. Vascular tumors have very diverse clinical behaviors and need an individualized approach.

Vascular tumors can be congenital hemangiomas, hemangiomas and kaposiform hemangioendotheliomas. Congenital hemangioma is classified into two forms: non-involuting and rapidly involuting. Mainly hemangiomas are in continuity with cervicofascial components. Like the other anterior mediastinal masses, they may be asymptomatic or cause respiratory symptoms. The asymptomatic masses should not be treated because they tend to regress over time. Nevertheless, if respiratory symptoms are present, active anti-angiogenic treatment with corticosteroids and/or interferon-2α or -2β must be administered promptly [37].

Kaposiform hemangioendothelioma is usually accompanied by a Kassabach–Merritt's syndrome in which there is massive platelet trapping. This is very dangerous because the risk of hemorrhage is high, with a mortality near to 20% without aggressive treatment [37]. Kaposiform hemangioendothelioma needs full anti-angiogenic therapy and hematologic monitoring and, eventually, surgery.

34.5.6 Vascular Malformations

Vascular malformations are rare and may be found in the anterior mediastinum, posing difficult therapeutic problems. Vascular malformations have very diverse clinical behaviors and need an individualized approach.

These malformations are capillary, venous, arteriovenous, or lymphatic alterations. Lymphati-

Table 34.1 Classification of anterior mediastinal masses

Solid Lesions	Lymphoma	Hodgkin's lymphoma Non-Hodgkin's lymphoma
	Germ cells tumors	Teratoma Yolk sac tumor Dysgerminoma Seminoma Choriocarcinoma
	Normal thymus	Prominent thymus (pseudomass) Ectopic thymus (pseudomass)
	Thymic hyperplasia	
	Thymoma	Non-invasive thymoma Invasive thymoma
	Thymic carcinoma	
Cystic Lesions	Thymic cyst Lymphatic malformation	
Fatty Lesions	Lipoma Lipoblastoma/liposarcoma Thymolipoma	
Other	Hemangioma Lymphangioma Histiocytoses	

covenous masses are located mainly near the confluences of large venous and lymphatic collectors. The anterior mediastinum is one location [38, 39]. The tumor may expand into the hemithorax and ultimately to the neck and base of the mouth.

Lymphangiomas are multicystic and infiltrate the anatomy. The tissue is like other lymphatic structures, and reacts in the case of local infections with increments of the volume of the mass and eventually suppurates. Respiratory symptoms may occur in cases with airway compromise [40]. These masses do not have a propensity to involute spontaneously [41]. Treatment must take into account that: it is a benign mass; total removal is often not possible; too-radical surgery may endanger nervous trunks or other structures [42]. An alternative or complementary treatment is sclerosis with OK-432 [37]. Only in cases of single cysts are the results of sclerosing procedures adequate. For masses with multiple infiltrating cysts of small size, partial debulking may be sufficient [41].

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Posterior Mediastinal Tumors

35

Philip J. Hammond and Robert Carachi

35.1 Introduction

The posterior mediastinum lies behind the fibrous pericardium and is traversed by the esophagus, descending thoracic aorta, and thoracic ducts. The sympathetic trunks, associated with spinal ganglia, run alongside the thoracic vertebral bodies. Posterior mediastinal masses account for around 36% of all mediastinal tumors [1, 17], and usually arise from the paravertebral neurogenic structures. These neoplasms include neuroblastoma, ganglioneuroma, and more rarely, neurofibroma, Schwannoma (nerve-sheath tumors), paraganglioma (pheochromocytoma), primitive neuroectodermal tumors (PNET), and sarcomas. Accordingly, most of this chapter will be concerned with neuroblastoma, although the rarer conditions will be addressed more briefly. A wide differential diagnosis should be considered when caring for a child with a posterior mediastinal mass because some lesions, such as extra-lobar sequestrations, foregut duplications, or rarely lateral thoracic meningocele, may have similar presentations to neoplasms (Table 35.1) [19].

Table 35.1 Classification of posterior mediastinal tumors [19]

Neurogenic tumors
Ganglion cell tumors
Neuroblastoma
Ganglioneuroblastoma
Ganglioneuroma
Paraganglioma
Nerve-sheath tumors
Benign
Neurofibroma, Schwannoma
Malignant
Neurofibrosarcoma, Malignant peripheral nerve-sheath tumor
Non-neurogenic tumors
Peripheral primitive neuroectodermal tumor (PNET/Ewing's sarcoma)
Rhabdomyosarcoma, osseo-cartilagenous tumors
Germ cell tumor
Metastasis
Non-neoplastic
Foregut duplication cyst
Extra-lobar pulmonary sequestration
Vascular malformations/haemangiomas
Lipomatosis
Histiocytosis
Lymphadenopathy – infectious, sarcoidosis,
Castleman's disease
Juvenile fibromatosis
Desmoid tumor
Thoracic duct cyst

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35.2 Neuroblastoma and Ganglioneuroma

35.2.1 Introduction

Neuroblastoma is derived from neural crest cells, which may arise in the adrenal medulla or anywhere along the sympathetic ganglion chain from the neck to the pelvis. Approximately 15–20% are thoracic [20, 28]. It is the most common malignancy diagnosed in infancy and is remarkable for its broad spectrum of clinical behavior. Some tumors progress despite intensive multimodal therapy (poorly differentiated malignant neuroblastoma) whereas others mature or regress spontaneously (completely differentiated benign ganglioneuroma or partially differentiated ganglioneuroblastoma). Because of this heterogeneity the treatment and study of neuroblastoma is challenging. This diversity in behavior correlates closely with several clinical and biological features, and these are used for risk-group assignment and treatment stratification. A thoracic site tends to confer a more favorable prognosis.

35.2.2 Epidemiology

In the UK, the incidence of neuroblastoma was 9.2 per million children per year between 1991 and 2000 and similar incidences are reflected worldwide. Some reports have suggested that the incidence has increased in recent decades even accounting for age and spontaneous regression [2]. More than half the patients are <2 years of age at diagnosis [3] and it is the most common cause of a mediastinal mass in this age group [4]. Nonetheless, neuroblastoma is also the commonest extracranial solid tumor of childhood, accounting for around 10% of all childhood tumors and 15% of all cancer deaths.

Antenatal ultrasound of the adrenal glands has identified neuroblastoma in numerous reports. Neuroblastoma cells are found in the adrenal gland in about 1 in every 260 neonates who die of congenital heart disease; yet clinical neuroblastoma presents in only approximately 1 in 8,000 to 11,000 children [20]. In an attempt to identify early cases of neuroblastoma amenable to cure, mass screening has been attempted in several countries, including Japan, by evaluating urinary catecholamine metabolites in infants at 6 months of age. During this Japanese screening, the incidence of neuroblastoma among those <1 year of age doubled, but there was no decrease in the number of cases diagnosed in older children and there was no improvement in the survival of children over 1 year of age [18]. Other screening studies have added to the body of evidence, suggesting that most tumors detected by screening would have regressed spontaneously and may have been treated unnecessarily. As a result, screening studies have been discontinued since 2004. It is unclear whether thoracic neuroblastoma has a similar propensity to mature or regress, although Saenz et al. found that out of 63 posterior mediastinal masses, 32 (51%) were neuroblastoma and 14 (22%) were ganglioneuroma, suggesting that a significant minority had matured [1]. A more recent series showed that of 43 thoracic neurogenic tumors, 20 (47%) were neuroblastoma, 13 (30%) were ganglioneuroblastoma, and 10 (23%) were ganglioneuroma [21]. The incidence of ganglioneuroblastoma is higher in thoracic compared with non-thoracic neurogenic tumors [28].

Some authors have advocated expectant management with serial imaging for abdominal neuroblastoma detected incidentally or by screening, with resection reserved for cases which fail to reduce in size. However, most clinicians recommend resection of posterior mediastinal neuroblastoma [20].

35.2.3 Etiology and Pathogenesis

Most cases of neuroblastoma are sporadic with <1% having a familial predisposition (likely to represent autosomal dominant inheritance with incomplete penetrance). Familial cases tend to have a mean age at diagnosis of 9

months, compared with »18 months in sporadic cases, and frequently involve multiple tumors. Patients with neuroblastoma rarely have associated congenital anomalies but there may be an association with other neurocristopathies, including Hirschsprung's disease, neurofibromatosis type 1 (von Recklinghausen's disease), multiple endocrine neoplasia type 2A, congenital central hypoventilation syndrome (Ondine's curse), and hypomelanosis of Ito. Other syndromes observed in association with neuroblastoma include Beckwith–Wiedemann syndrome, congenital hemihypertrophy, and Sotos syndrome. These observed associations have aided the search for genetic mutations linked to tumorigenesis (*vide infra*). Although these associations have been noted with all neuroblastomas, it is unclear from the literature whether tumors at thoracic sites specifically share such associations. There is limited evidence to suggest environmental factors predispose to the development of neuroblastoma, although some studies have implicated maternal alcohol, phenytoin, or medical treatment for vaginal infections or even a possible protective effect of breastfeeding and supplementation with folic acid [18].

Neuroblast cells are derived from primordial neural crest cells which migrate from the mantle layer of the embryonic spinal cord. They populate tissues such as the adrenal medulla and sympathetic ganglion chain. Neuroblastoma may occur at any site where neural crest cells are found, including the neck, posterior mediastinum, retroperitoneal paraspinal ganglia, adrenal medulla, and pelvic organ of Zuckerkandl. These progenitor neural crest cells are believed to have phases of proliferation and differentiation with subsequent maturation to form normal ganglion cells when the proliferative phase of the cell-cycle is exited. The fate of these neuroblasts may be to regress spontaneously, mature by differentiation to benign ganglioneuroma, or progress to malignant neuroblastoma. The cell pathway is determined by complex molecular signalling mechanisms determined by genetic abnormalities. Certain abnormalities confer a poor prognosis, including gene amplifications (N-myc), allelic losses (including 1p and 11q), allelic gains (such as unbalanced 17q), cytogenetic abnormalities (diploid DNA karyotype) and overexpression of certain proteins (such as yrosine-kinase TRK-B).

N-myc is a transcription factor related to a proto-oncogene found at the chromosome 2p24 locus, which has become one of the most important biological factors for the prognosis. When there are ≥10 copies of N-myc, as detected by fluorescent *in situ* hybridization (FISH), it is considered to represent genomic amplification which confers a poor prognosis, independent of age or disease stage. N-myc amplification promotes proliferation of neuroblasts and their transformation to neuroblastoma by preventing terminal differentiation and successful exit from the cell cycle. Approximately 30% of all neuroblastoma cases are found to be N-myc-amplified, but only 0% to 6% of thoracic primaries are found to be N-myc-amplified [19, 21]. About 25% of those with primary thoracic neuroblastomas present with stage-4 disease compared to approximately 44% of all other neuroblastomas [14, 28]. The Pediatric Oncology Group reported survival of 24% for N-myc-amplified tumors compared with 76% for non-amplified tumors [4]. Sonic hedgehog (Shh) is a mitogenic glycoprotein signal pathway involved in the development of several cancers (e.g., medulloblastoma). Although the role of Shh in neuroblastoma development has not yet been fully investigated, it appears to increase the transcription and stabilization of N-myc, thereby potentiating its expression [5].

35.2.4 Clinical Features

Clinical presentation is variable, depending on the age of the patient, site of primary tumor, and metastases. Between 14% and 30% of thoracic neuroblastomas are asymptomatic at presentation; often with apparently unrelated symptoms such as upper respiratory tract infection resulting in an incidental observa-

tion of a mediastinal mass on chest radiography [18, 21].

Alternatively, mediastinal tumors may be associated with a cough (in up to 30%), dyspnea (21%), or wheeze (12%) related to a mass effect on lung expansion [21], or dysphagia due to extrinsic compression of the esophagus. Tumor extension through the intervertebral foramina may cause extradural compression of the spinal cord and manifest as paraplegia, back pain urinary incontinence or retention. Symptomatic-cord compression occurs in approximately 7% of children with neuroblastoma, nearly half of whom have thoracic primaries [21]. Most have complete neurological recovery after treatment, though up to 44% may have permanent sequelae [15]. Neoplasms arising in the neck or upper mediastinum may involve the stellate ganglion and result in Horner's syndrome (ipsilateral miosis, ptosis, facial anhydrosis, iris heterochromia, and enophthalmos) in 7% [21]. Occasionally, the tumor may extend to involve the chest wall, thoracic inlet, or traverse the diaphragm.

Rarely, paraneoplastic syndromes such as acute cerebellar ataxia, presenting with opsomyoclonus and nystagmus ("dancing eye syndrome" in 7% [21]), or intractable watery diarrhea with hypokalemia (related to tumor production of vasoactive intestinal peptide) occur in association with neuroblastoma. Although rare, approximately half of children who present with opsomyoclonus will have neuroblastoma and two-thirds of these will have localized thoracic disease with favorable outcome. Unfortunately, these neurological symptoms tend to be difficult to treat despite removal of the tumor. A study is ongoing to evaluate the effectiveness of immunosuppression and cyclophosphamide.

Pleural effusion may be present at the time of diagnosis in approximately10% of children with neuroblastoma, and tends to be associated with metastatic high-risk disease but may uncommonly be related to a primary thoracic tumor [6]. The diagnosis may be feasible by identifying malignant cells or rosettes in the pleural aspirate.

Metastatic neuroblastoma may involve the bone marrow, bone cortex, lymph nodes, liver, skin or, occasionally, the lungs or brain. Bone-marrow invasion may result in anemia or thrombocytopenia. Bone metastases often involve the metaphyseal areas of long bones, skull, vertebral column, pelvis, ribs and sternum. Patients with bone-cortex metastases have an ominous prognosis and may present with extreme pain or refusal to use the relevant limb. Metastases to the bony orbits may produce proptosis or bilateral orbital bruising ("panda eyes"). Generalized symptoms may include weight loss, failure to thrive or fever. Hypertension is found in 25% of cases and is related to the production of catecholamines by the tumor [7].

35.2.5 Diagnosis

The diagnosis of a posterior mediastinal tumor in a child is made by correlating the clinical features with laboratory and imaging studies and subsequent biopsy. The minimum criteria for establishing a diagnosis of neuroblastoma are a tissue biopsy with histological confirmation or unequivocal tumor cells within a bone-marrow aspirate/trephine along with increased levels of urinary catecholamines.

35.2.5.1 Laboratory Studies

More than 90% of children with neuroblastoma have tumors that produce elevated levels of catecholamines or their metabolites. The most commonly elevated metabolites are vanillylmandelic acid (VMA) and homovanillic acid (HVA); these are the metabolites of dopamine and norepinephrine, respectively [18]. Levels of these metabolites can vary with age, renal function or even excessive dietary intake of amines (bananas). Random urine samples are adequate for monitoring response to treatment as well as the diagnosis because they are often expressed as a fraction of the concentration of creatinine, thereby accounting for renal function or urinary dilution; timed samples are not necessary. In a

recent study of 114 cases of neuroblastoma (including 20 thoracic primaries) the diagnostic sensitivities of urinary VMA, HVA and dopamine were 81%, 72% and 61% respectively [8]. Some authors have suggested that more undifferentiated tumors tend to excrete higher levels of certain metabolites (e.g. HVA) [9].

Baseline full blood count, urea, electrolyte and liver function tests are carried out. Although elevated levels of serum lactate dehydrogenase (LDH) and ferritin are not independent prognostic factors and do not affect treatment, they may reflect increased tumor burden.

35.2.5.2 Imaging: Diagnosis and Staging

Plain radiographs of the chest obtained for investigation of respiratory symptoms may demonstrate an apical or paravertebral soft tissue mass; nearly half of which show finely stippled calcification (Figs 35.1a and 35.2a). More subtle signs may include splaying or erosion of posterior ribs or widened intervertebral foramina suggestive of intraspinal extension. Occasionally, fluoroscopic contrast swallow assessments may indicate esophageal distortion, particularly related to foregut duplications [19].

Cross-sectional imaging studies are employed for baseline assessment of tumor volume, resectability, and evaluation for metastatic disease within the chest or abdomen. The presenting tumor may be a metastatic lesion from a neuroblastoma of primary intra-abdominal origin. In recent years, there has been an increasing reliance on image-defined risk factors (IDRFs) of resection to inform treatment decisions. Computed tomography (CT) and/or magnetic resonance imaging (MRI) with three-dimensional measurements and of sufficient quality to address IDRFs is essential for imaging the primary tumor [10].

CT is the preferred modality for evaluation of chest tumors although adjacent areas of the neck and abdomen should be included in the study to evaluate for tumor extension or metastasis. In the presence of pleural effusion, CT is useful for identifying underlying pulmonary or mediastinal lesions. Pre-contrast images frequently demonstrate heterogeneity with areas of calcification, hemorrhage or necrosis within the mass. Intravenous contrast (and oral contrast for abdominal scans) is given to aid with clarifying anatomical details, including visualization of adjacent vascular structures with arterial and venous phases of the scan (Fig. 35.2b). Spiral CT scanners can produce sufficiently good-quality images within a fraction of a second so that, even in young children, many such studies may be done without general anesthesia.

MRI is particularly useful for the evaluation of intraspinal extension and the anatomical relations of the tumor to vascular structures (Fig 35.1b and 35.2c). Neuroblastoma produces a low signal on T1-weighted and high signal on T2-weighted sequences, although calcification is not appreciated. Gadolinium contrast may aid in the differentiation of residual or recurrent tumor from scar tissue resulting from multi-modal therapies. Unfortunately, a longer scanning time for MRI often dictates that general anesthesia is required in pre-school children to limit movement artefact. Whole-body MRI is increasingly employed for staging to evaluate the treatment response of metastases, as well as follow-up imaging in the long-term because there is no ionizing radiation.

Iodine-123 metaiodobenzylguanidine (MIBG) scintigraphy is essential, and it is recommended that it is done before tumor excision. This whole-body scan uses a labelled isotope derivative of norepinephrine to identify areas of increased uptake and activity, and has high accuracy and specificity for the detection of metastatic (particularly bone marrow) disease (Fig. 35.2f). A single unequivocal MIBG-positive lesion at a distant site is sufficient to define metatastic disease whereas, if the lesion is equivocal, it requires confirmation by another imaging modality (e.g., plain radiograph or MRI) and/or biopsy [10]. Technetium-99 bone scintigraphy may be helpful in rare cases with a negative MIBG scan, where it may differen-

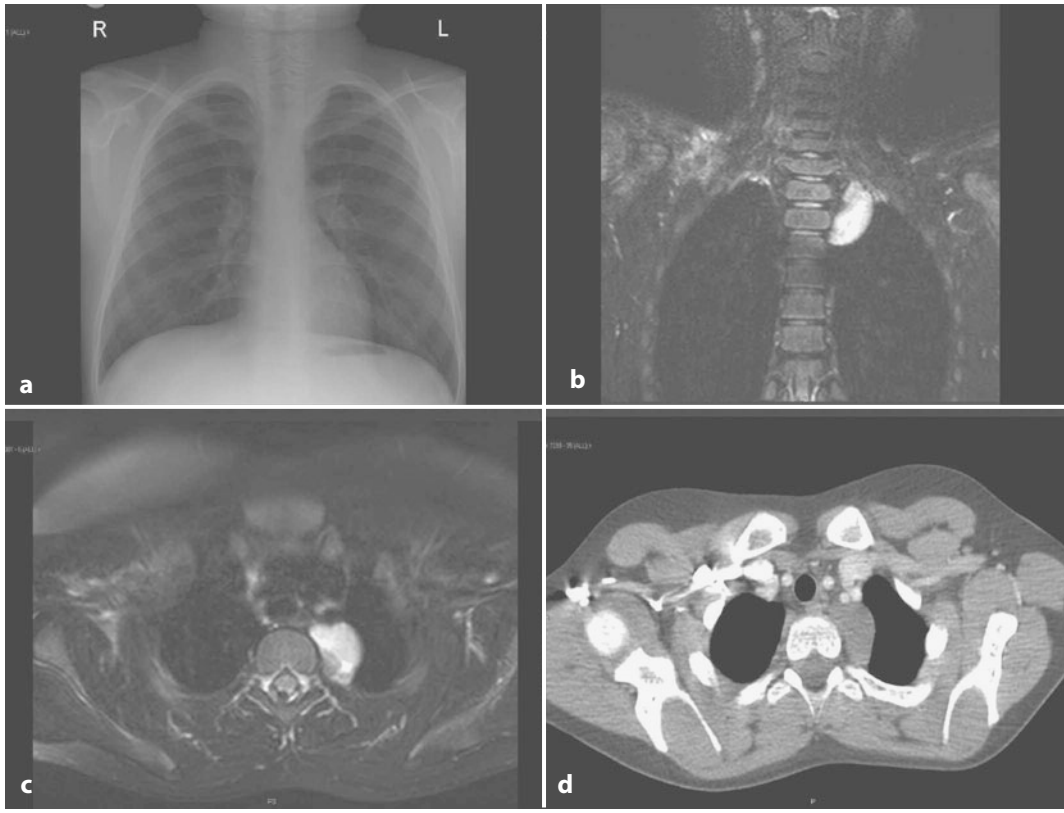

Fig.35.1 a Chest X-ray showing subtle left apical posterior mediastinal mass which was identified incidentally. This patient with inflammatory bowel disease had a chest X-ray performed prior to starting methotrexate therapy. **b** MRI shows left apical posterior mediastinal mass clearly and excludes involvement of the intervertebral foramina. Proximity to major vessels and brachial plexus may also be assessed. **c** MRI. **d** CT scan with intravenous contrast is helpful for staging and assessing proximity to major vessels

tiate between bone cortical metastases and bone-marrow involvement. Most new patients with neuroblastoma have metastases at presentation, so bilateral bone-marrow aspirates and trephines are done to determine the extent of disease.

The International Neuroblastoma Staging System (INSS) was widely adopted following its development in 1986 to allow a consensus in the staging and evaluation of therapeutic response [16]. This system requires an assessment of postoperative resection which has resulted in some anomalies. For instance, a certain tumor could be categorized as stage 1 or 3 by different clinicians depending on the extent of resection. Similarly, an evaluation of lymph-node involvement (as required for INSS staging) is dependent on the surgeons sampling of lymph nodes, which is difficult to apply uniformly. Alternatively, localized tumors which are observed with the expectation of regression cannot be staged using INSS criteria. Because of these difficulties, since 2005 the International Neuroblastoma Risk Group (INRG) task force has adopted a system of staging based on preoperative, diagnostic imaging to make an assessment of resectability of locoregional tumors. The presence or absence of IDRFs of surgical excision are determined with the anticipation that an assessment of imaging will allow a more reproducible evaluation than one based on surgical findings and approach [10]. These IDRFs allow categorization of patients as having

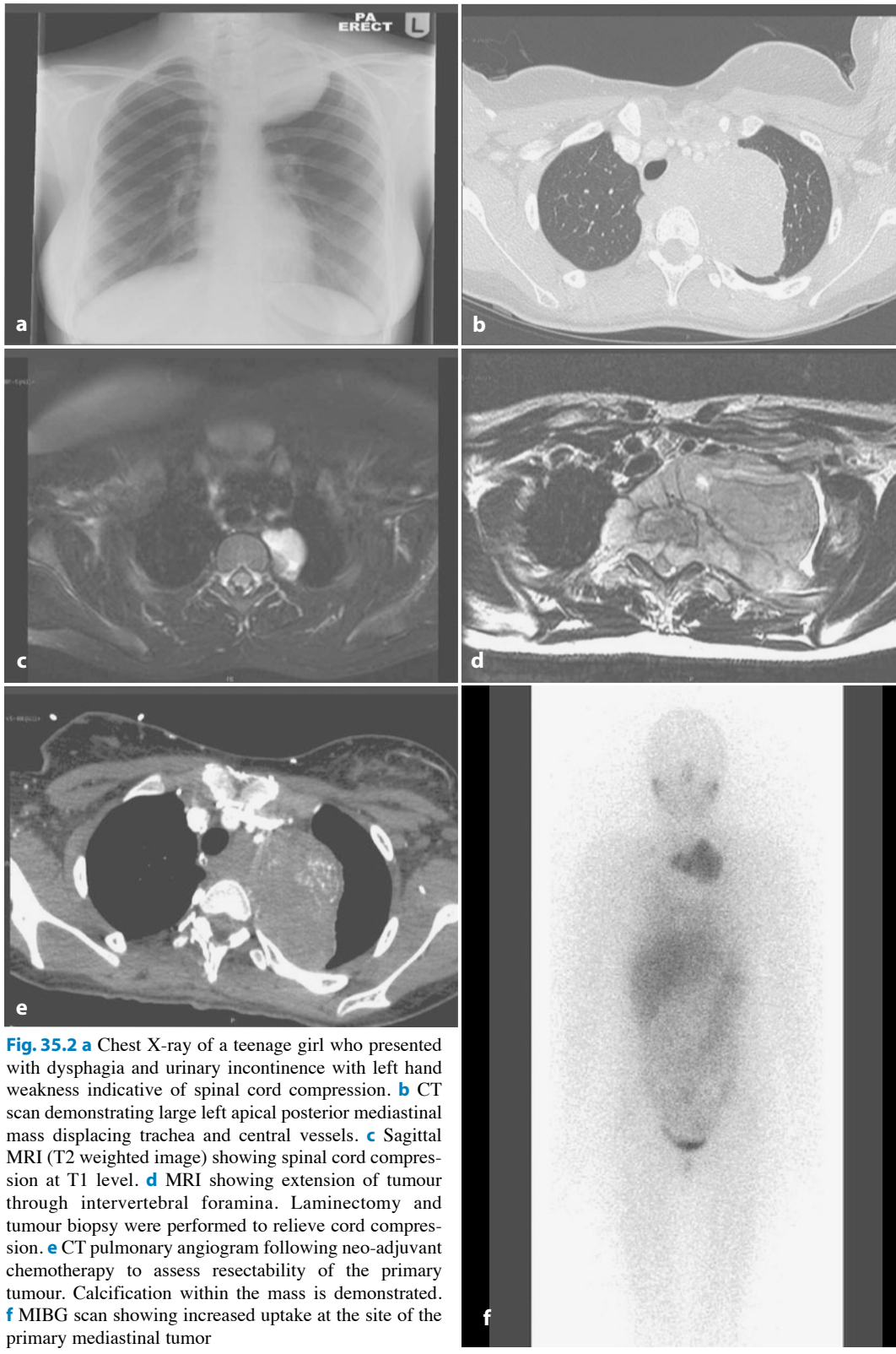

Fig. 35.2 a Chest X-ray of a teenage girl who presented with dysphagia and urinary incontinence with left hand weakness indicative of spinal cord compression. **b** CT scan demonstrating large left apical posterior mediastinal mass displacing trachea and central vessels. **c** Sagittal MRI (T2 weighted image) showing spinal cord compression at T1 level. **d** MRI showing extension of tumour through intervertebral foramina. Laminectomy and tumour biopsy were performed to relieve cord compression. **e** CT pulmonary angiogram following neo-adjuvant chemotherapy to assess resectability of the primary tumour. Calcification within the mass is demonstrated. **f** MIBG scan showing increased uptake at the site of the primary mediastinal tumor

locoregional (L1 or L2 – analogous to INSS stage 1–3), metastatic (M – analogous to INSS stage 4), or MS disease (similiar to INSS stage 4s but for patients younger than 18 months) [10]. It is anticipated that the IDRF status of tumors may be reassessed during treatment and will allow prospective evaluation of the impact of IDRFs on resection, complications, and outcome.

Excisional biopsy may be achieved when imaging suggests that primary resection is feasible or an incisional or Tru-Cut needle biopsy may be required to establish a histological diagnosis for more complex lesions. The biopsy should be sited so that the tract can be excised with any future resection [19]. The pseudocapsule is opened and a blade is used to carefully remove the specimen without crush or diathermy artefact. Hemostatic sutures or agents such as Surgicel® may be required. Central areas of the tumor may be necrotic and hence some surgeons favor intraoperative frozen section to confirm that an adequate diagnostic sample has been taken. If inadequate, further samples can be taken under the same anesthetic. This requires close liaison with the pathologist, who will be able to give advice about how the specimen should be transported. Usually, the fresh specimen is immediately sent to the pathologist. When imaging studies indicate that a posterior mediastinal tumor is intimately associated with major vascular structures, thoracoscopy may help clarify whether the tumor simply abuts these structures or invades their walls, thereby making resection unfeasible. Thoracoscopic biopsy of such lesions may avoid the morbidity of a large thoracotomy wound, potentially allowing neoadjuvant chemotherapy to be initiated sooner. Although the biopsy is usually taken from the primary tumor if the site of a metastasis is more accessible, such as a skin nodule in an infant with MS disease, then this may be excised instead. If laminotomy or laminectomy is required at the time of a presentation with spinal-cord compression, a tumor sample may be adequate to confirm the diagnosis. Adequate tissue for diagnostic histological and molecular analyses (as well as tissue banking for ongoing research) may require open biopsy although multiple cores from an automatic-firing 16 G Tru-Cut® needle biopsy (usually with radiological guidance) are now considered sufficient. Fine-needle aspirates are not considered appropriate because they are unlikely to provide adequate tissue for histological analyses [13]. The local oncology multidisciplinary team (MDT) will decide the most appropriate approach to gain adequate tissue for establishing the diagnosis.

The gross pathology of neuroblastoma may reveal a vascular and friable pseudocapsule. Histologically, neuroblastoma cells are typically small, round blue cells with hyperchromatic nuclei and little cytoplasm. Formation of Homer–Wright pseudo-rosettes is classical, and may be evident in bone-marrow aspirates or pleural effusion fluid samples. The tumor must be differentiated from similar small, round blue cell tumors of childhood, such as Ewing's sarcoma, lymphoma, PNET, and rhabdomyosarcoma. Large-cell neuroblastoma has been identified as a distinct phenotype with aggressive clinical behaviour [12]. The International Neuroblastoma Pathology Classification (INPC) is an adaptation of the Shimada Classification with some minor modifications. This divides neuroblastic tumors into age-related favorable and unfavorable histological categories based on whether the tumor exhibits a stroma-rich or stroma-poor appearance. All patients older than 5 years are categorized as having unfavorable histology. This histological category and N-myc-amplification provide prognostic information independent of staging [11].

35.2.6 Management

Treatment protocols individualize patient management using risk factors as predictors of outcome in an effort to maximize survival, minimize long-term morbidity, and optimize quality of life. Traditionally, the North American COG and the European SIOP have stratified the in-

tensity of therapy by creating three risk groups [16, 18]. Different collaborations worldwide have used different criteria to assign patients to these groups, making outcome comparisons with varied treatment protocols difficult. Recently, the INRG have established a consensus approach for pretreatment risk stratification to allow more meaningful comparisons. In the INRG classification, 16 statistically and/or clinically different pretreatment groups of patients are identified using the criteria of INRG stage (with IDRFs), age, histological category, grade of tumor differentiation, MYCN status, presence/absence of 11q aberrations, and tumor cell ploidy [13]. These categories place patients in pretreatment very low-, low-, intermediate-, or high- risk groups with 5-year event free survival (EFS) of >85%, 75–85%, 50–75% or <50%, respectively [13]. It is hoped that reporting of the outcome of patients assigned to the 16 pretreatment groups will facilitate the comparison of risk-based clinical trials conducted in different regions of the world and specifically provide an opportunity to address randomized surgical questions [13]. Currently, therapeutic strategies for an individual patient are established with MDT consultation. Precise chemotherapy and radiotherapy management and the timing of surgery depends on local protocols which may be part of multicenter trials and are frequently updated, thereby requiring close cooperation with other specialists within the MDT to optimize outcome.

In most regions of the world, patients assigned to a high-risk group are treated with intensive, multimodality therapy, whereas those predicted to be very low-risk receive minimal therapy. Patients in low- and very low-risk groups are often treated with surgical excision alone as long as unnecessary surgical morbidity can be avoided. Primary resection is the treatment of choice in INSS stage-1 and -2 disease [23]. Patients with INSS stage-1 disease can be treated with surgery alone without the requirement for adjuvant chemotherapy. Relapse after excision can be successfully treated with chemotherapy to induce remission [18]. INSS stage-2A/2B low-risk tumors are also treated with initial surgery without the need for preoperative chemotherapy. Chemotherapy or radiotherapy may be considered if spinal-cord compression or life-threatening symptoms develop. If there is rapid neurological deterioration from cord compression then neurosurgical decompression with laminectomy or laminotomy may provide relief. Equal efficacy has been demonstrated between laminectomy, radiation and chemotherapy to relieve neurological deficits [15, 52]. However, patients treated with chemotherapy seldom require additional treatment and have less orthopedic sequelae. For dumbbell tumors in which the intraspinal component is not causing neurological compression then it can be left *in situ* when the extraspinal tumor is resected without compromising outcome or risking paraplegia or cerebrospinal fluid (CSF) leakage [15]. Supportive management is usually sufficient in cases of MS disease, although chemotherapy or radiotherapy may be given consideration. Resection of the primary tumor in infants with stage-4s disease does not alter outcome [22]. If abdominal compartment syndrome is problematic despite the measures outlined above, fashioning of a temporary abdominal silo has been described but the authors' experience with this technique has been disappointing.

After biopsy, intermediate-risk patients are treated with standard chemotherapy regimens of 12–24 weeks consisting of carboplatin, cyclophosphomide, doxorubicin, and etoposide, followed by surgery. The aim of surgery is to resect as much tumor as possible without damaging vital structures, obtain adequate tissue for analysis, and undertake lymph-node sampling for staging. Postoperative chemotherapy regimens will then depend on the extent of residual disease and histological assessment of viable tumor and biological analyses. Completely resected INSS stage-3 disease has a significantly better survival (77%) than when incompletely resected (28%) [24, 25].

After biopsy to establish the diagnosis, high-risk patients receive induction chemotherapy to attempt to induce remission, improve tumor resectability, and clear the bone

marrow of tumor cells, thereby allowing for safer harvesting of cells for autologous transplantation. Resection is then attempted followed by myeloablative therapy with peripheral blood stem-cell rescue. Surgery is to remove the macroscopic disease to reduce the number of viable tumor cells capable of developing resistance to myeloablation. Controversy exists as to the extent of resection required in INSS stage-4 neuroblastoma. Some authors have shown no survival advantage of complete *versus* incomplete resection whereas others have demonstrated that survival and local control rates are improved after gross local resection [26, 27]. Thoracic neuroblastoma appears to have a better prognosis even when resection is incomplete. Horiuchi et al. found that infants and children with thoracic neuroblastoma all survived 4–14 years of follow-up despite 13 of the 20 patients having had positive resection margins even when 6 patients had INSS stage-3 or -4 disease [28]. Although thoracic radiotherapy may be considered in the therapeutic armamentarium, the long-term consequences on pulmonary fibrosis and skeletal growth should not be underestimated.

35.2.6.1 Resection

With MDT consultation and an assessment of IDRFs suitability for resection can be judged, although this can ultimately be determined only at the time of surgery. The procedure should be done when the platelet and white cell count have returned to normal after the bone-marrow suppression of chemotherapy – usually about 2 weeks after the last course of chemotherapy. Careful preparation with the surgical and anesthetic teams is required. A possible requirement for an arterial catheter, central venous access, and blood transfusion should be anticipated. Postoperative analgesia should be planned with consideration given to thoracic epidural catheter placement depending on local anesthetic expertise [19].

In locoregional (INRGSS L1 and L2) disease a thoracoscopic approach is gaining increasing acceptance. No difference in complications, recurrence, and disease-free survival has been found with thoracoscopic compared with open thoracotomy, but the thoracoscopic approach has the advantages of improved visualization, less postoperative pain, decreased blood loss, and shorter hospital stay [29, 30]. With the child under general anesthetic, ventilation is established with an endobronchial tube for older children and intubation of the contralateral main bronchus with an uncuffed tube or a bronchial blocker for younger children. The child is placed in the lateral position and three 5-mm ports (larger children having a 10-mm port) introduced between the anterior and posterior axillary lines to optimize visualization. Intrathoracic CO_2 insufflation ($\leq$5 mmHg) is given for ipsilateral pulmonary collapse. The pleura overlying the tumor is incised around the edge of the lesion, and the dissection progressed with endoscissors and diathermy (Fig. 35.3). The intercostal vessels supplying the tumor can be divided with diathermy, ultrasonic scalpels, or endoscissors between clips. The tumor can then be retrieved within an endocatch plastic bag through an enlarged port-site incision. A chest drain is usually left *in situ* at the end of the procedure [21]. Thoracoscopic resection is most frequently used for small tumors (diameter, <6 cm).

Conventionally, a posterolateral thoracotomy in the intercostal space above or below the mass is appropriate to avoid entering directly into the tumor. Even access to tumors at the apex of the hemithorax or extending through the diaphragm can be achieved with a suitably planned incision. A thoraco-abdominal approach or separate laparotomy may be required for lesions traversing the diaphragm. For tumors extending to the contralateral paravertebral space, bilateral thoracotomies may be appropriate. Cervicothoracic tumors may be particularly challenging with regard to access. Modifications of a trap-door incision (in which the medial third of the clavicle is divided to allow reflection) have been described which give good exposure for tumors in the thoracic inlet [19]. Neuroblastoma frequently

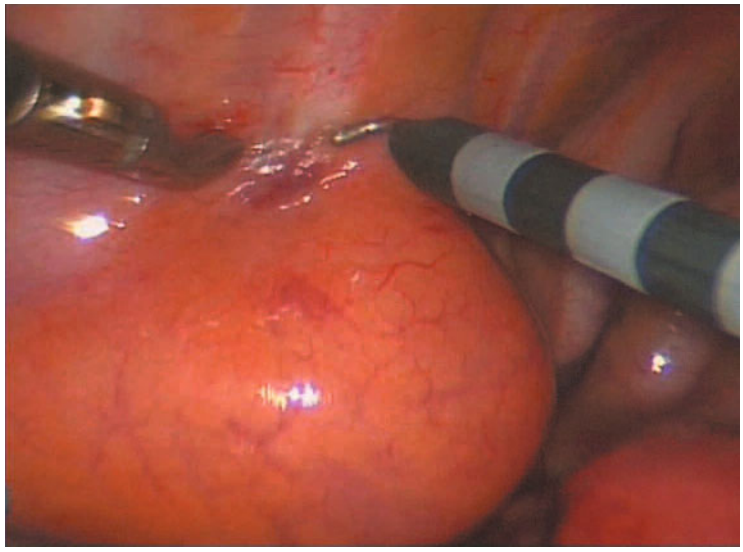

Fig. 35.3 Thoracoscopic view of apical ganglioneuroma

encases major blood vessels, though subadventitial dissection usually allows piecemeal resection. These tumors are frequently intimately associated with the brachiocephalic veins and carotid and subclavian arteries. Sharp dissection should be employed to separate the tumor from the sympathetic chain to avoid diathermy injury to the stellate ganglion or intercostal nerves. Injury to the thoracic ducts should be avoided and vagus and phrenic nerves should be identified and protected. Appropriate lymph-node sampling should also be undertaken. In view of incomplete resection of thoracic neuroblastoma not worsening the outcome, excessive surgical risks should be avoided.

35.2.7 Outcome and Follow-up

Studies have demonstrated no difference in the incidence of complications, recurrences or outcomes between thoracoscopic and open approaches [31]. The most common complications are Horner's syndrome and chylothorax [21]. Horner's syndrome occurs in 3–29% of resections [30]. The incidence of Horner's syndrome is more likely to be related to the location of the tumor in the superior cervical sympathetic ganglion rather than the mode of resection [30]. It may be transient due to postoperative edema of the stellate ganglion. One study noted chylothorax in 4 patients after 104 thoracic tumor resections [14]. Chylothorax usually settles with a chest drain and a medium-chain triglyceride diet, but total parenteral nutrition may be required. It may be that lymphatic obstruction from the tumor itself may also result in chylothorax. Chest wall-related complications after posterolateral thoracotomy in children are common with scoliosis, shoulder elevation, asymmetric nipples, and winged scapula occurring in up to one-third of patients, with some protection being achieved with a muscle-sparing thoracotomy (through the bed of the rib) and even lower incidences after thoracoscopy [30, 32].

Thoracic neurogenic tumors present as low-stage disease and have better outcomes compared with those in the abdomen. Survival has been reported to be between 77% and 100% despite incomplete resection, thereby making thoracoscopic resection increasingly attractive [14, 28].

35.3 Neurofibroma

Neurofibromatosis type-1 (NF1) is an inherited disorder in which neurological and benign cutaneous lesions are associated [33]. It has a spectrum of localized and systemic manifestations, including *café-au-lait* patches, axillary and inguinal freckling, peripheral neurofibromas, plexiform neurofibromas, optic gliomas and pheochromocytoma. Plexiform neurofibromas are the most common benign tumors in NF1 (von Recklinghausen's disease) with a prevalence of 25–50% [34]. These tumors necessitate surgical excision because of a tendency towards local growth causing pressure effects on adjacent tissues resulting in cough or dysphagia, the potential for malignant transformation, and occasionally for cosmetic reasons [3].

NF1 is a common neurogenetic disease affecting children and adults with a reported incidence of 1 in 3,500–4,000 individuals [34]. It is an autosomal dominant disease related to a gene on chromosome 17 with spontaneous mutation in 50%. NF1 can affect several tissues, including the nervous system (central and peripheral), skin, bone, gastrointestinal tract, and vascular systems. Neurofibromatas are the most common benign pediatric peripheral nerve sheath tumors, and have diverse cellular compositions [34]. Histologically, they are composed of neoplastic Schwann cells, neurites and fibroblasts in a matrix of collagen fibres and mucosubstances. They tend to grow slowly along the nerve fiber and can remain silent for many years. They may present at birth but are typically seen in the fifth and sixth decades in 25–30% of patients with NF1 [34]. Functional abnormalities may result from continued tumor growth, the rich vascular network even predisposing to hemorrhage.

Neurofibromatas occurs most commonly on the trunk and extremities [35] and pediatric thoracic neurofibroma is rare [37]. One report was of a 5-year-old male presenting initially with a neck mass and who was subsequently found to have much more extensive diffuse retroperitoneal and intrathoracic infiltration with liver extension [37]. In the mediastinum they may involve the sympathetic trunk or the vagus or phrenic nerves. On computed tomography (CT) neurofibromatosis may mimic other diagnoses such as lymphadenopathy (Fig. 35.4). However, multiplanar T2-weighted MRI allows more accurate diagnosis in neurofibromatosis [33].

Surgical excision is the mainstay of therapy. Because of the infiltrative nature of the tu-

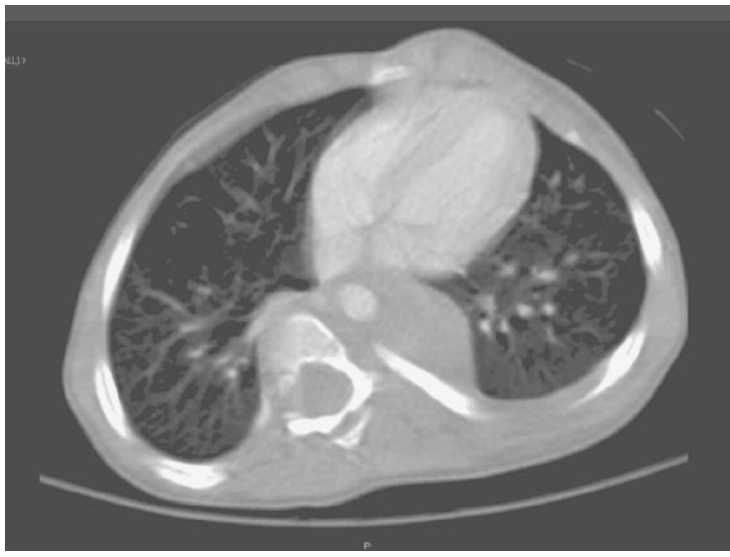

Fig. 35.4 CT scan of a 4-year-old male with scoliosis. Café-au-lait patches led to a clinical diagnosis of NF1 and imaging studies alerted clinicians to a posterior mediastinal neurofibroma

mor, complete excision is rarely achieved but debulking may relieve symptoms as well as provide a histological diagnosis. Neurosurgical collaboration is often required if there is intraspinal disease because without excision continued expansion results in cord compression. Factors associated with postoperative progression of disease include younger age at diagnosis, incomplete excision, and tumors arising from sites other than the extremities (such as the posterior mediastinum). It has been suggested that growth in the pubertal period results in a higher incidence of recurrence in younger patients [39]. Frequently, multiple debulking procedures are required. Other treatment modalities include maturation agents, anti-angiogenic agents, anti-histamines and antimetabolites [38]. More recently, biological therapies targeting the molecular genetics of neurofibromatosis have been investigated but such treatments remain experimental [33].

One large series of 68 patients with NF1 demonstrated that 44% of patients developed plexiform neurofibromata by the age of 5 years [35]. Most were located on the trunk and extremities, and 2 patients developed malignant peripheral nerve sheath tumors in a preexisting plexiform neurofibromata. There were no specific clinical features associated with transformation of plexiform neurofibromata, and the authors stressed the importance of serial follow-up. At present, surgical excision will continue to be the mainstay of treatment.

Patients with NF1 have a 3–10% lifetime risk of neurofibromata undergoing malignant sarcomatous transformation [34–36]. These rare mediastinal neurofibrosarcomas respond poorly to adjuvant therapy and hence require surgical excision. A prevalence of recurrence of 70% has been reported, with poor survival resulting from local recurrence or distal metastases.

Malignant triton tumor (MTT) is a rare type of malignant peripheral nerve-sheath tumor usually arising in patients with NF1. The prognosis is poor even if complete excision is feasible. Piecemeal excision of lesions involving the brachial plexus or intervertebral foramina may be required. Some authors have suggested that they should be treated as high-grade soft-tissue sarcomas [40].

35.4 Schwannoma (Neurilemmoma)

Schwannoma is usually associated with neurofibromatosis type-2 (NF2) and is a benign encapsulated neoplasm composed of Schwann cells within a background of loose reticular tissue. NF2 is an autosomal dominant condition related to a gene on chromosome 22, though half are *de novo* mutations. Vestibular Schwannomas (acoustic neuromas) are classical tumors related to NF2, though lesions may also present in the central nervous system, skin and eyes. They arise from the nerve sheath and extrinsically compress the nerve fibers [41]. These benign lesions present with pain and loss of function of the adjacent nerves (including the spinal cord) with intervertebral extension or loss of function of the phrenic nerve [19, 42]. Surgical excision is the treatment of choice [43]. Rarely, this tumor may be associated with the Carney complex; a multiple neoplasia syndrome characterized by myxomas, Schwannomas, mucocutaneous pigmentations and endocrine tumors [44].

35.5 Paraganglioma (Extra-adrenal Pheochromocytoma)

Although pheochromocytoma and paraganglioma are derived from neural crest-derived catecholamine-secreting cells, pheochromocytomas arise from the adrenal medulla whereas those originating in extra-adrenal (usually paravertebral) locations are termed paragangliomas. Paraganglioma may rarely present in childhood along the sympathetic chain in the neck and mediastinum, and produce symptoms of compression as well as flushing, sweating, palpitations, headache, hypertension, and even result in cerebrovascular accidents [45]. These features result from

the secretion of catecholamines from the tumor. Urinary levels of catcholamine metabolites are elevated in most children with paraganglioma (particularly free normetadrenaline, noradrenaline, and VMA). Once a biochemical diagnosis has been made the tumor must be localized with cross-sectional imaging and ^{131}I-labelled MIBG imaging, which accumulates where noradrenaline is taken up [20].

The treatment of paraganglioma is surgical excision, but medical management with endocrinological consultation is an essential part of the preoperative preparation. Preoperative use of α-adrenergic blockers such as phenoxybenzamine minimizes the effects of catecholamines, thereby limiting the perioperative blood pressure lability. β-blockers and careful fluid balance may also be required once α-blockade is achieved.

Increasingly in the adult population (in which most of these tumors arise from an adrenal source) a laparoscopic (or retroperitoneoscopic) approach is favored to limit the stress response to surgery and the release of vasoactive catecholamines from handling the tumor [46, 47]. This may be more difficult in the pediatric population, however, because there is a higher likelihood of the tumor being extra-adrenal and retroperitoneal, although if preoperative imaging studies indicate a mediastinal location, a thoracoscopic approach may be most appropriate [48, 49].

It may be difficult to assess the biological malignant potential of such tumors on histological criteria alone. Features normally typical of malignancy may not be borne out by clinical progression. Because of the rarity of such tumors in childhood, there is little evidence-based literature on the subject of adjuvant therapy [50]. Nonetheless, if histological features of malignacy or incomplete excision are present (particularly if MIBG imaging is suggestive of residual increased uptake) we advocate consideration of therapeutic radiolabelled-MIBG to help in eliminating occult foci of disease [45]. Resection remains the treatment of choice for pheochromocytoma and paraganglioma, with MIBG therapy for patients with features suggestive of incomplete resection or malignancy.

In childhood, paragangliomas are usually associated with an underlying predisposing condition such as von Hippel–Lindau syndrome, familial pheochromocytoma-succinate dehydrogenase gene (SDH B/D), MEN 2A or 2B, or rarely NF1 [45]. Genetic counseling is advocated for all families of children diagnosed with paraganglioma. Patients and family members with mutations identified should undergo lifelong surveillance tailored to the underling syndrome due to the increased risk of synchronous and metachronous tumors associated with these genetic syndromes [45].

35.6 Primitive Neuroectodermal Tumors (PNET, Askin's Tumor)

PNETs are a rare, rapidly progressive, small, round-cell tumors with a poor prognosis despite multimodal therapy, usually affecting adolescents [51]. Patients usually present with pain or symptoms relating to the mass. After imaging, a biopsy is taken which reveals the diagnosis [19]. Induction chemotherapy leads to a greater complete prevalence of resection, which involves removal of the rib from which the mass is arising. Involvement of the costovertebral junction indicates poorer survival [51].

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Lung Tumors

36

Riccardo Masetti, Luca Bertelli, Daniele Zama, Tamara Belotti and Andrea Pession

36.1 Introduction

In children, primary lung tumors are rare, but metastases are much more common. Lung masses in children are ten-times more likely to be a developmental or reactive lesion than a tumor. The ratio of primary tumors to metastatic tumors to non-neoplastic lesions is estimated to be 1:5:60.1 [1]. On the basis of the rarity of primary lung tumors in children, the diagnosis remains a challenge. Several cases are asymptomatic or present with non-specific symptoms, and they are discovered incidentally. Non-specific respiratory symptoms such as wheezing, persistent cough, hemoptysis, or recurrent episodes of pneumonia may be attributed initially to other diseases (e.g., asthma, inflammatory processes), so diagnosis can be delayed. Even if a mass is found, it may not be possible to differentiate endobronchial lesions and cystic parenchymal lesions from reactive processes or lung malformations on imaging studies. It may also be difficult to distinguish between benign and malignant lesions without histological examination. Thus, all lung lesions in children should be removed to clearly ascertain the true origin.

36.2 Epidemiology

Most primary lung tumors in children are malignant, with a ratio of malignancies to benign neoplasms of approximately 3:1 [2–3]. The most common primary malignant tumors are carcinoid tumors and pleuropulmonary blastomas; the most common benign tumor is inflammatory myofibroblastic tumor (52%) [3]. Malignant tumors of the trachea, bronchus, and lungs correspond to 0.2% of all neoplasms in children [4]. The mortality for primary benign lung tumors in children is 8.7%, and for primary malignant tumors is around 30% [3].

36.3 Etiology, Pathogenesis and Management

36.3.1 Tracheobronchial Masses in Children

36.3.1.1 Pleomorphic Mixed Adenoma

Pleomorphic mixed adenoma should be considered to be malignant on the basis of local recurrence if resection is incomplete. It is typically found in the large airways and can be polypoid or sessile. Histological features include epithelial tubules and stromal ele-

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ments. Rarely, children can present with acute, severe airway obstruction [5]. The treatment for this tumor is based on wide local surgical excision [6].

36.3.1.2 Juvenile Respiratory Papillomatosis

Juvenile Respiratory Papillomatosis is due to infection by human papillomavirus, most often acquired during birth. Multiple recurrent squamous papillomas are typically found in the larynx but in approximately 5% also involve the distal bronchial tree and lung [7]. Children can present with breathlessness, hoarseness of the voice, stridor, and hemoptysis. Treatment can include surgical excision and/or CO_2 laser vaporization [8].

Malignant degeneration to squamous cell carcinoma has been described and may be related to prior radiation therapy. Parenchymal involvement is usually fatal as a result of respiratory failure.

36.3.1.3 Mucous Gland Adenoma

Mucous gland adenoma is extremely rare: only 2 cases have been described up to 1983 [9]. Histological features include tubules lined by a single layer of columnar goblet cells and distended, mucus-filled cysts. Tumors are, in general, solitary and cause partial bronchial obstruction. Children can present inhaled foreign body-like symptoms. Biopsy is crucial for the differential diagnosis and complete resection is curative.

36.3.1.4 Carcinoid Tumor

Carcinoid tumors are defined as low-grade neuroendocrine neoplasms on the basis of their locally aggressive growth and low potential for metastasis. They represent »80% of endobronchial lesions in children [10–11], and may be found in the lobar bronchi (75%), mainstem bronchi (10%) or within the lung parenchyma (15%) [12]. Neuroendocrine tumors of the lung are distinguished into “typical” and “atypical” carcinoid tumors on the basis of mitotic activity, cellularity, and the presence of areas of necrosis [13–14]. Children (in general, older children and adolescents) can present with wheezing, cough, hemoptysis or pneumonia due to bronchial obstruction (or chronic distal infection and bronchiectasis in the case of advanced tumors). The carcinoid syndrome is very rare with no metastases. Diagnostic investigations of choice are computed tomography (CT) and bronchoscopy. Biopsy should be considered carefully given the high risk of bleeding into the airway.

Treatment is primarily surgical. On the basis of location and size, complete excision and removal of involved lymphatics may be obtained by bronchial sleeve resection, lobectomy, or even pneumonectomy [15]. Survival rates range from 90% for typical carcinoid tumors, to 25–69% for atypical carcinoid tumors [15-16].

36.3.1.5 Bronchogenic Carcinoma

Bronchogenic carcinomas are rare and predominantly affect adolescents. Undifferentiated adenocarcinoma represents approximately 80% of bronchogenic carcinomas and squamous cell carcinomas, with a smaller percentage of lung carcinoma cases in children (12%) [2]. Presentation may range from cough, chest pain, pneumonia and hemoptysis (due to local effects) to bone pain, weight loss or anemia (in cases of metastatic disease). Delay in the diagnosis (because the imaging and clinical features often lead to a misdiagnosis of pneumonia) and the presence of metastasis lead to a poor prevalence of survival [17]. These tumors can develop as a second malignancy after Hodgkin’s disease, Ewing’s sarcoma, and testicular germ cell tumors, or in association with congenital pulmonary airway malformations (CPAMs) [18–20]. Resection of asymptomatic CPAMs remains controversial even though it is considered to be safe by many surgeons [20–21]. Complete resection of a bronchioalveolar carcinoma elicits good results [22]. Squamous cell carcinomas are not frequently discovered as primary carcinomas in children: they are usually secondary to respiratory papillomatosis. Management is not easy because squamous carcinomas, due to respiratory papillomatosis, can often be unresectable.

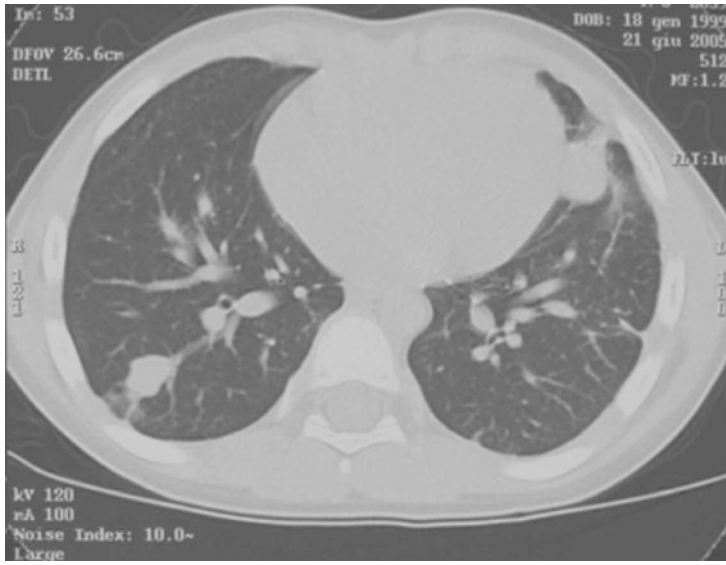

Fig. 36.1 CT showing several lung nodules in a child with fibrosarcoma

36.3.1.6 Fibrosarcoma of the Lung

Fibrosarcoma of the lung (Fig. 36.1) is a rare, chemoresistant malignancy in children; 26 cases have been reported up to 1989 [1]. Children can present with non-resolving pneumonia due to distal obstruction [23]. Diagnostic investigations of choice are bronchoscopy, bronchoscopic biopsy, bronchioalveolar lavage, or brush biopsy. Surgical treatment consists of lung-preserving sleeve resection or, for distal lesions, resection with lobectomy. In case of complete resection, the prognosis is excellent [24].

36.3.2 Parenchymal Lung Masses in Children

36.3.2.1 Hemangiopericytoma

Hemangiopericytomas arise from capillary pericytes. Multiple tumors are usually found and children can present with wheezing, cough, hemoptysis, breathlessness or chest pain due to bronchial obstruction. Histological features include vascular channels surrounded by sheets of spindle or round cells containing pale cytoplasm and large vesicular nuclei and a central area of necrosis. Surgical treatment is complete excision because these tumors have variable behaviors.

36.3.2.2 Inflammatory Myofibroblastic Tumor

Inflammatory myofibroblastic tumors frequently occur as a single pulmonary nodule in children. They comprise up to 80% of all benign lung cancers in children [2–10]. The pathogenesis is not clear; a history of infection or trauma should be a risk factor but often these lesions are found incidentally on chest radiography. Children are usually asymptomatic, but can present with fever, cough, chest pain and haemoptysis. Usually these lesions are confined to a small area and have a benign course. The tumor infrequently invades near structures or recurs after complete resection [25–26]. Histological features include proliferating spindle cells consisting mainly of myofibroblasts. First-line treatment for localized tumors is complete resection with clear margins and preservation of lung parenchyma [27].

36.3.2.3 Sclerosing Hemangioma

Sclerosing hemangioma is an unusual benign lung tumor, discovered mainly in adolescent

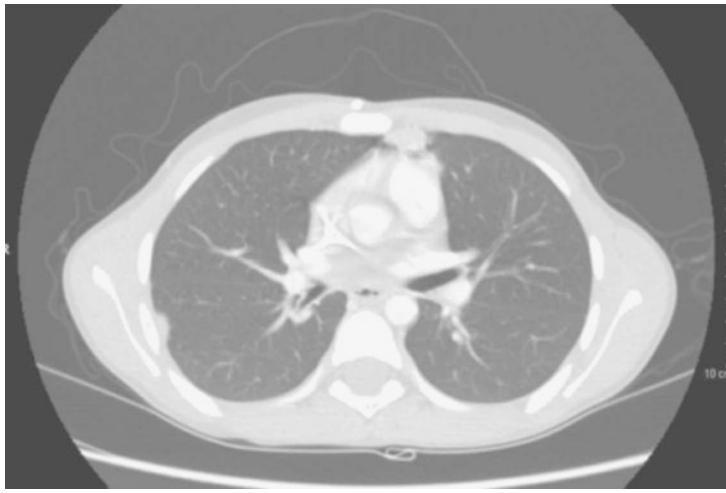

Fig. 36.2 CT showing two lesions in the left upper lobe and one in the right lower lobe in a child with rhabdomyosarcoma

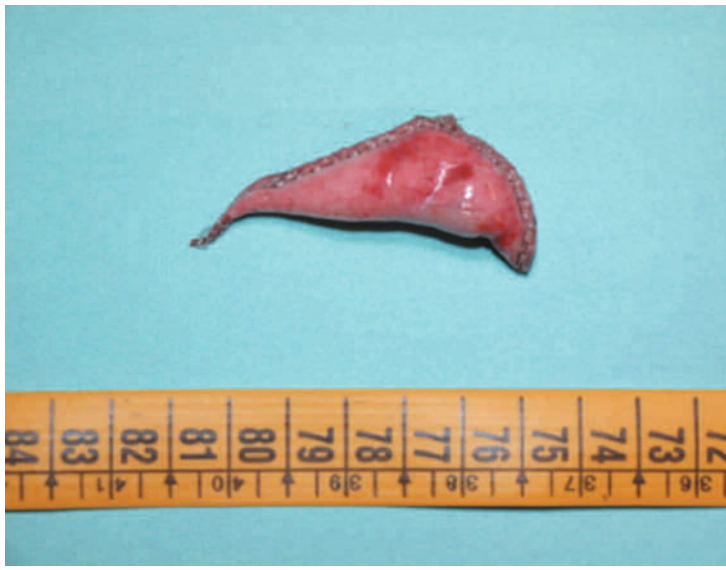

Fig. 36.3 Rhabdomyosarcoma removed through resection

girls. Multiple lesions have a malignant tendency. The pathogenesis is not clear; it seems to be derived from a primitive respiratory epithelial cell. Resection is curative.

36.3.2.4 Hamartoma

Hamartoma is one of the most common benign single lung lesions in adults and children [28]. Large lesions may cause respiratory distress, especially in early life. Histological investigations undertaken after resection can lead to the diagnosis. Hamartomas are frequently discovered in the periphery of the lung and rarely near the hilum or endo-bronchially. CT findings include calcification and fat within the lesion [29]. First-line treatment for localized tumors is complete resection, with lobectomy for large or centrally placed lesions.

36.3.2.5 Rhabdomyosarcoma

Rhabdomyosarcoma is a rare tumor (Fig. 36.2 and 36.3). It may be endobronchial, mediasti-

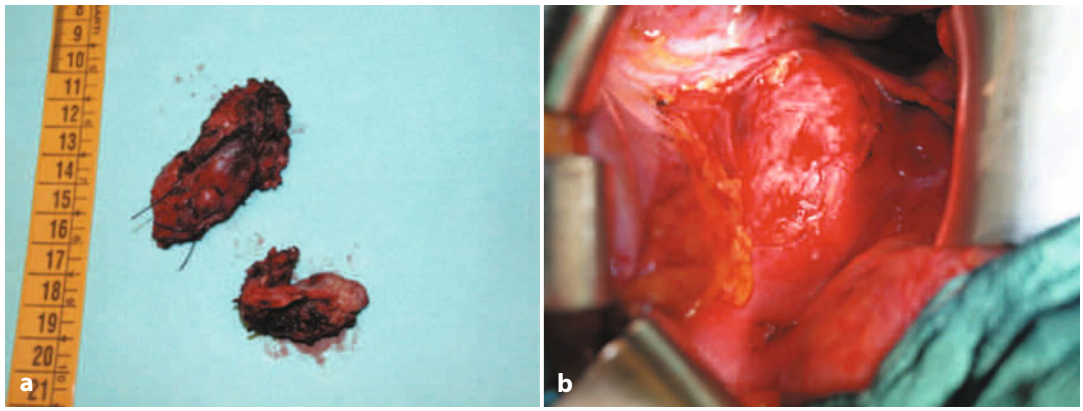

Fig. 36.4 Synovial sarcoma (a) and its resection (b)

nal, pulmonary or pleural [30]. Pulmonary rhabdomyosarcoma represents approximately 0.5% of all rhabdomyosarcomas in children [3].

36.3.2.6 Synovial Sarcoma

Synovial sarcoma is a rare tumor (Fig. 36.4a and b) but is one of the more common lung sarcomas in children. Typical markers are epithelial membrane antigen, cytokeratin, BCL2 and CD99. Cytogenetic and/or molecular investigations help to find the t(X;18) translocation, forming an SSX-SYT fusion transcript, which is specific for this tumor.

36.3.2.7 Pleuropulmonary Blastoma (PPB)

PPB is a rare malignant embryonal mesenchymal lung tumor found mainly in infants and toddlers, and rarely in those aged >12 years. Different tumors, such as undifferentiated sarcomas, blastomas, cystic mesenchymal hamartomas, pulmonary rhabdomyosarcoma, are part of PPB [31]. Three types of PPB have been described [32]. Type 1 is a cystic form found in very young children. Type 2 is characterized by a solid form associated to the cystic form. Type 3 is a mainly solid form usually seen in older children. Cystic cancers have been discovered in pre-existing congenital cystic lung lesions and may degenerate into malignant cancers [33–34], In particular, congenital cystic adenomatoid malformations (CCAMs) and PPB are clearly related, but the transformation process is poorly understood. Histological features include diffuse proliferation of undifferentiated blastemal cells associated with areas of chondroblastic foci with alveolar patterns and lipoblastic differentiation. The immunohistochemical markers are S100, vimentin, α1-antichymotrypsin, desmin, lysozyme, α1-antitrypsin and KP1 [35]. Children can present with cough, fever, and chest pain [31], and imaging findings are pneumonia, pleural effusion or pneumothoraces. Complete resection with chemotherapy may elicit good long-term results. Adverse prognostic factors are mediastinal or pleural involvement and distant metastasis, more frequently found in the central nervous system and bone.

36.3.2.8 Neurogenic Tumors

Neurogenic lung tumors are mucosal neuromas, neurofibromas, Schwannomas and malignant peripheral nerve-sheath tumors. One of the most important tumors is neurofibroma, which can be associated with neurofibromatosis. Hence, neurofibromatosis must be excluded in a children with a pulmonary neurofibroma.

36.3.2.9 Other Malignant Parenchymal Tumors

Malignant fibrous histiocytomas, leiomyosarcomas, lymphomas, post-transplant lymphoproliferative disorders and Langerhans' cell histiocytosis are rare tumors which can be found in children.

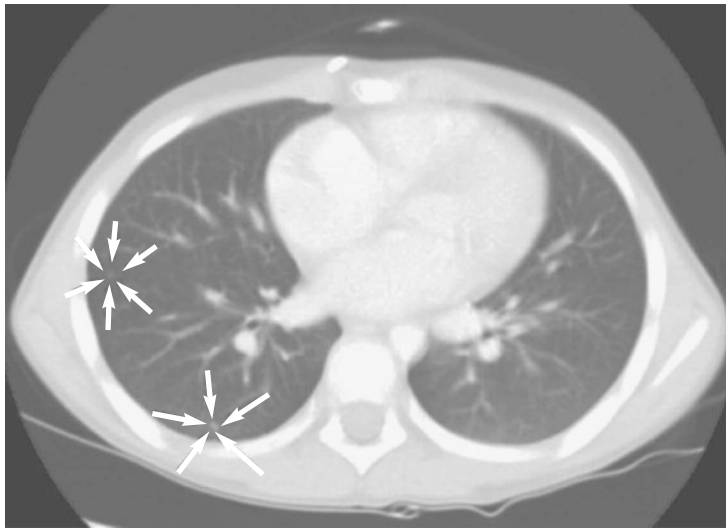

Fig 36.5 CT showing two nodules (*arrows*)

36.3.3 Metastatic Tumors

Osteogenic sarcoma, Wilm's tumor, malignant germ cell tumors and soft-tissue sarcomas are the most common tumors that can cause pulmonary metastases. The most important imaging for metastatic tumors is CT because it can be used to find lesions that are too small to be found by routine chest radiography. Management of pulmonary metastases includes treatment of the primary tumor and metastasectomy. Total removal of metastases significantly increases the chance of survival [36–38]. Surgical procedures based on bilateral metastatectomy are sequential posterolateral thoracotomy or median sternotomy [39–40]. Children can tolerate sequential bilateral thoracotomy with an interval of 2 weeks between procedures. The role of video-assisted thoracoscopic surgery (VATS) in the treatment of metastatic tumors is controversial. VATS is entirely reliant on CT for the detection of metastases. However, additional lesions not previously identified on CT can be detected by palpation. Recurrences after VATS have been described [41].

36.4 Clinical Features

In most cases, patients with lung cancer are asymptomatic. Children can present with cough, recurrent episodes of pneumonia, fever, symptoms similar to those seen after the inhalation of foreign bodies, or haemoptysis. Respiratory failure is rare and occurs in cases of generalized infiltration, secondary infection, or collapse of the lung distal to an obstruction. Chest pain may show pleural or chest-wall involvement. Dysphagia and superior vena caval obstruction could signify expression of large lesions.

36.5 Diagnosis

The complete diagnostic evaluation of lung tumors is based on chest radiography (the first investigation), CT, magnetic resonance imaging (MRI), angiography, bone scintigraphy, bronchoscopy and biopsy.

CT describes lung lesions in detail. Contrast-enhanced CT can also provide information about the vascularity of the tumor. In particular, Contrast-enhanced CT can allow the distinction between lung tumors from other pulmonary lesions which present in a similar way (e.g., empyema). Thus, CT is important for defining pulmonary lesions because it permits the detailed description of nodules, and often aids in the detection of other deeper and smaller lesions (Fig. 36.5).

MRI can be used to reproduce the anatomical location and size of lung lesions to achieve complete removal of the lesion with adequate margins. It may be necessary to carry out CT and MRI to describe the lesion correctly to evaluate the feasibility of resection. Other helpful investigations are angiography (to ascertain the vascularity of the tumor), bone scintigraphy (to detect bony metastasis) and bronchoscopy (to find and biopsy endobronchial tumors). However, if a benign lesion cannot be differentiated from a malignant lesion by imaging, diagnostic biopsy is required. On the basis of the location of the tumor, the differential diagnosis and local expertise, the modalities of biopsy (excisional, incisional, needle) should be chosen.

36.6 Outcome and Follow-up

All lung nodules should be considered to be malignant until histopathological examinations indicate otherwise, so excision of the tumor is the mainstay of treatment. Management is similar for most paediatric patients with pulmonary tumors [2–3]. The aim of treatment is to remove the lesion and conserve most of the working lung parenchyma so as not to impair lung function.

Management of malignancies is based on the site and histological characteristics of the lesion. Sleeve resections can be the choice for bronchial adenomas, always remembering their potential for malignancy. In the case of malignant lesions, resections should involve complete removal of the lymphatics. Pneumonectomy may be done in severe cases.

In the case of benign lung tumors, conservative resection is preferred. Thoracoscopic resection should be considered on the basis of local expertise. Multimodal therapy (adjuvant chemotherapy with radiotherapy) should be considered in specific cases, in particular if metastases are found.

The prognosis is based mainly on the type and biological characteristics of the lesion. The most important factor for survival in metastatic and primary lung tumors is complete resection with a clear margin.

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Tumors of the Chest Wall

37

Riccardo Masetti, Daniele Zama, Luca Bertelli, Tamara Belotti and Andrea Pession

37.1 Introduction and Epidemiology

Chest wall tumors (CWTs) in children comprise a wide range of benign and malignant neoplasms. These tumors are rare in infants, children and young adults, accounting for 1.8% of solid tumors [1]. However, high proportions of CWTs are malignant, and represent a diagnostic and therapeutic challenge to pediatric thoracic surgeons. The chest wall can be affected by: primary malignant neoplasms arising from different structures; secondary tumors which can invade the chest wall from the adjacent structures (e.g., breast, pleura, mediastinum, lung); metastatic tumors [2].

37.2 Etiology and Pathogenesis

CWTs in children are rare tumors and little is known about their etiopathogenesis. CWTs are classified as "benign" or "malignant" based on behavior, tumor type, and tissue of origin. CWTs are primarily of mesenchymal origin and comprise a broad spectrum of lesions arising from the skeletal or soft tissues of the chest wall. Among malignant tumors, soft-tissue tumors of the chest wall are more common than skeletal bony tumors. More than half of malignant CWTs are soft-tissue sarcomas whose histological diagnosis, total resection and local control often represent a challenge [3]. The most commonly encountered primary CWTs in children are small, round-cell tumors, and include Ewing's sarcoma (which is also known as primitive neuroectodermal tumor, PNET, and Askin's tumor) [4]. The category of these tumors is so named due to the lack of distinction among these lesions with regard to their neuroectodermal differentiation. After the pioneering work of Shamberger et al, these tumors are also classified as a single entity: malignant small round cell tumors [5]. In this group are also included the less common chondrosarcoma, malignant fibrous histiocytoma, osteosarcoma, synovial sarcoma and fibrosarcoma.

Benign tumors are less common in most reported series, though they may be under-reported. Benign tumors such as eosinophilic granuloma, aneurysmal bone cyst, hamartoma, osteoma, osteochondroma, chondroma as well as metastatic tumors such as osteogenic sarcoma, neuroblastoma and Wilms' tumor, are rarer than primary malignant tumors. Complete resection is often the only method of oncological management in many of these tumors.

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Furthermore, reconstruction of the wide chest-wall defects in a child is a surgical challenge.

37.3 Clinical Features

Because of their low incidence, the time between symptom onset and the diagnosis of a CWT is often long [6]. The first symptom is often a palpable, enlarging mass (Fig. 37.1). Diagnosis of a CWT due to an incidental discovery on imaging as part of screening or for examination of an unrelated condition is less common. Pain is a common symptom of masses originating from the bone (benign and malign) due to their growth and periosteal damage, whereas soft-tissue neoplasms are often painless.

Neurological symptoms such as paresthesias and weakness, can be present if the growth of the mass involves neurological structures such as the spinal cord or brachial plexus. If eosinophilic granuloma and Ewing's sarcoma are also present, the systemic symptoms of fever, malaise, fatigue, and weight loss can also be observed.

There are no specific signs or symptoms that can be used to discriminate between benign and malignant neoplasms. Rapid growth, involvement of surrounding structures, fixation to underlying tissues and cortical destruction are indirect and non-specific signs of malignancy. Although clinicians often associate pain with malignant CWTs, pain is not a reliable predictor of malignancy, so the diagnosis must be arrived at very carefully [6].

37.4 Diagnosis

Accurate history-taking and a complete physical examination represent the first steps of the work-up. They provide important information on the location, size and features of the neoplasm. The rapidity of the growth of the mass, pain, local inflammation/infection signs, and neurological or systemic symptoms and/or signs must be evaluated carefully. Based on this information, imaging studies should be planned to define the: effect of the lesion on bone; response of bone to the tumor; characteristics and composition of the matrix and cortex of the tumor; evidence of a soft-tissue mass [7]. Frequently, the first imaging examinations are plain radiographs of the chest: they can reveal bony erosion of the lesion, lytic lesions, mediastinal lymphadenopathy or invasion, and the presence of large pulmonary metastases. Ultrasound echography can help in distinguish solid from cystic tissue hamar-

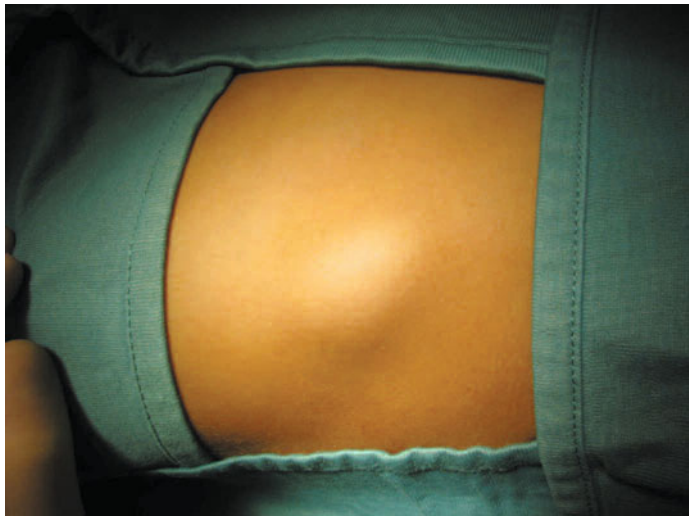

Fig. 37.1 Swelling of left side of the rib due to a benign lesion on the chest wall

tomas, hemangiomatous and lymphagiomatous lesions in superficial tumors. Computed tomography (CT) and magnetic resonance imaging (MRI) are considered essential for defining the mass and surgical planning. Chest CT can be used to assess the extent of bone, soft tissue, pleural and mediastinal involvement, as well as pulmonary metastases. It is also more sensitive than plain radiographs for defining calcification of the tumor matrix or bony cortical destruction [8].

MRI is more accurate than CT for defining soft tissues, vascular and nerve involvement, and spinal cord or epidural extension [9]. Typical malignant signs are destruction of bone and a "sunburst" pattern, whereas benign bony masses are generally smaller with distinct geographic margins. Malignant neoplasms are frequently deep to the fascia and look dark on T1-weighted MRI and bright on T2-weighted MRI. Benign soft tissue tumors are frequently small and superficial, and some benign tumors have classic features on MRI. Bone scintigraphy can be done to exclude bony metastases. Though imaging characteristics can be suggestive, a biopsy is often necessary for a definitive diagnosis of many soft-tissue tumors.

Many factors, such as the site, size, and type of lesion should be considered in the choice of the type of biopsy. Fine-needle aspiration (FNA) biopsy is a relatively inexpensive method with a low prevalence of complications and high diagnostic value for distinguishing between malignant and non-malignant neoplasms. In metastatic and primary bone tumors, FNA biopsy is quite easy to carry out and often accurate tissue diagnosis can be achieved. Unlike open biopsy, FNA does not require surgical incisions, so this procedure should be considered in the triage of bony lesions due to its low risk or morbidity [10]. False-positive results have major therapeutic implications; this is usually due to inadequate sampling or misclassification with regard to the exact subtype of malignant tumor. Nevertheless, the advantages must be balanced against the limitations of this procedure. Excision biopsy is advisable for all rib tumors and small lesions that can be removed without the need for the rebuild of bony structures. Incision or Tru-Cut® needle biopsy is recommended for soft-tissue and unresectable masses. An appropriate biopsy incision is important because the tumor may be resected later. Biopsy specimens should be taken from the peripheral and inner core of the mass to be analyzed for histological, cytogenetic and biological studies.

37.5 Therapeutic Management

37.5.1 Benign Soft-Tissue CWTs

Mesenchymal benign tumors include a heterogeneous group of soft-tissue lesions. In particular, the myofibroblast is the main cell in many fibromatoses tumors [11]. In this group of lesions, the most common neoplasm of early infancy is infantile myofibromatosis. In one study, 15% of patients with infantile myofibromatosis had multiple lesions. [12, 13]. The tumors are mainly present at birth or develop during the first week of life. They can be solitary or multicentric. Most of these tumors undergo spontaneous regression and are managed conservatively [14]. Notably, children with multicentric infantile myofibromatosis with visceral involvement are associated with a higher prevalence of morbidity and mortality.

The second most common lesion in this group is desmoid fibromatosis tumor. These tumors are slow-growing, bland fibrous neoplasms originating from the musculoaponeurotic structures throughout the body. The term desmoid, coined by Müller in 1838, is derived from the Greek word *desmos,* which means "tendon-like". Desmoid fibromatosis tumors often appear as infiltrative, usually well-differentiated, firm overgrowths of fibrous tissue. They arise from the muscle and fascia and extend along the tissue planes with aggressive behavior. The phrase "aggressive fibromatosis" describes their marked cellularity. This disease course and the tendency for recurrence makes the treatment of these relatively rare fibrous tumors challenging. These tumors typi-

cally present in the third decade, but 20–30% of cases have been reported in children, mostly in girls (probably due to the influence of oestrogen) [15]. Although considered benign, these neoplasms are often aggressive with multiple recurrences after incomplete resection. Hence, resection with negative margins is required to prevent local recurrence because they have local recurrence rates of ≤70% [6, 16]. Furthermore, they have been seen in association with Gardner's syndrome (mutation of the adenomatous polyposis coli gene) and in the scars of previous thoracotomies [9]. About 33% of patients with Gardner's syndrome develop desmoid fibromatosis tumors, whereas only 2% of children with desmoid fibromatosis tumor have a diagnosis of Gardner's syndrome [17]. Aggressive fibromatoses describes a more extensive infiltrative disease of fibrous scar tissue, and it has been treated with wide excision or, if unresectable, chemotherapy and radiation, without reducing the rate of recurrence [18].

Lipoblastomatosis is an uncommon benign tumor of brown fat that may be observed in childhood or infancy. It is diffuse lobulated, spreads along the tissue planes and typically recurs [19]. Lipoblastomatosis cannot be distinguished clinically from lymphangioma because they have a similar consistency. The differentiation between water-filled and solid soft-tissue tumors can be obtained by ultrasonography. Study of these masses should be completed with MRI to define the extension of the tumor and its relationship with surrounding tissues. After complete excision of the mass, the tissue should be sent fresh for histological and cytogenetic evaluation that allows differentiation between lipoblastomatosis and liposarcoma [20].

Giant-cell fibroblastoma is a rare type of soft tissue tumor characterized by painless nodules (usually 2–6 cm in diameter) in the dermis (the inner layer of the two main layers of tissue that comprise the skin) and subcutaneous (beneath the skin) tissue. It is a solitary, blue–gray, non-tender mass which is mostly located on the back, anterior chest wall, thigh, or groin. These tumors may come back after surgery but do not spread to other parts of the body. It is of important to distinguish giant-cell fibroblastomas from sarcomas to avoid inappropriately aggressive treatment [21].

In addition, a great number of hamartomatous lesions (e.g., lymphangioma, hemangioma, lipoblastoma, fibroblatic tumors) which involve the chest wall have been described in early infancy and childhood. These lesions are not described here because their presentation and management is not different from to those present elsewhere in the body.

37.5.2 Benign Bony CWTs

The chest wall can be affected by a wide group of benign bony and primary lesions that should be distinguished from non-neoplastic conditions such as cysts, infections, and fibromatoses because they require different management.

The most frequently observed benign neoplasm of the skeleton is osteochondroma. This tumor contains bone and cartilage and usually occurs near the end of a long bone. It accounts for almost half of all rib tumors [22]. This tumor takes the form of a cartilage-capped bony spur or outgrowth on the surface of the bone and frequently grows during the "pubertal spurt" until skeletal maturity. The most frequent clinical features are pain and asymmetry of the chest wall ("bony protuberance"). It is sometimes referred to as "osteocartilaginous exostosis". If an exophytic bone lesion contains a cartilaginous cap >1 cm in height, or if there is associated pain, there is thought to be a higher risk for the lesion being a chondrosarcoma. After puberty, complete resection should be done in patients with painful lesions or tumors that have increased in size [23–25].

Chondromas are benign tumors composed of mature hyaline cartilage. They generally have limited growth potential and are not locally aggressive [26, 27]. These tumors are called "enchondromas" if they occur in the

medullary canal of the bone [28] and "periosteal" or "juxtacortical" chondromas if they occur on the surface of the bone. Chondromas can also arise from the synovial sheaths of tendons or in the soft tissues adjacent to the tendons in the hand and feet of adults. In such cases, they are referred to as "soft-tissue" or "synovial" chondromas. The clinical and imaging features of chondroma and chondrosarcoma are similar and are seen as expansile lesions causing thinning of the bony cortex. Given appropriate treatment, patients with benign chondromas generally have a good prognosis, and most remain asymptomatic. Enchondromas are rare in the axial skeleton. If, however, they are found in the ribs, sternum, pelvis, or scapula, they should be treated with wide local resection and histopathological evaluation to rule out the possibility of chondrosarcoma, which is common at these sites [29].

Osteoid osteoma is a benign osteogenic tumor, typically noted in childhood [30], that rarely involves the chest-wall bones. Its hallmark is a local pain, which worsens during the night, and promptly improves after the consumption of aspirin or other non-steroidal anti-inflammatory drugs. Osteoid osteoma is more frequent in males and it is generally <1.5 cm in greatest dimension. Symptomatic lesions can be resected with excellent results. Osteoblastoma is a rare, benign, bone-forming tumor of the chest wall which is described as a "sternal tumor".

Fibrous dysplasia is a cystic expansive benign neoplasm characterized by a developmental anomaly of the medullary cavity of the rib. Fibrous replacement of the medullary canal is the hallmark of this disease. It is reported to be a solitary, slow-growing non-tender mass in the posterior–lateral aspect of the rib. It is associated with Albright's syndrome in which multiple bony cysts, skin pigmentations, and precocious sexual maturity are observed. The diagnosis is often incidental after radiography. The radiographic aspect is a cystic lesion with thinning of the cortex and a central "ground glass" appearance without calcification [31]. Local excision is curative and should be done for painful enlarging lesions that cause a diagnostic dilemma; conservative management is indicated for asymptomatic lesions [32].

Eosinophilic granuloma is an expansive lesion of the rib which involves the reticuloendothelial system. It is characterized by eosinophilic and histiocytic infiltrates. This tumor is commonly seen between 5 years and 15 years of age. Three types have been reported: eosionophilic granuloma, Letterer–Siwe disease, and Hand–Schuller–Christian disease. Eosinophilic granuloma is limited only to bone involvement, without the systemic symptoms that characterize Letterer–Siwe disease and Hand–Schuller–Christian disease [33]. The systemic diseases have a chronic course and require specific management, including corticosteroids and chemotherapy. The radiographic features of this lesion are: expansile bony lesion in the posterior–lateral aspect of the rib cage; irregular destruction of the cortex of the bone seen as "scalloping"; and new periosteal bone formation. The differential diagnosis should exclude Ewing's sarcoma or osteomyelitis, which requires different management. The excision biopsy of a lesion is indicated for the diagnosis and is curative in a solitary eosinophilic granuloma.

Mesenchymal harmartoma is a typical tumor found in infant which is present at birth in 40% of cases. It is a non-neoplastic proliferation of normal skeletal elements, predominantly cartilage [34]. Malignant degeneration has not been reported [34]. These lesions are mostly intrathoracic but extra-pleural, and can involve a single or multiple ribs (usually in their posterior or lateral portion). It has a typical appearance on chest radiography. However, the intrathoracic component is best evaluated with cross-sectional imaging [35], and the easiest imaging to carry out in infants is CT. The most common presentation is respiratory distress due to the mass effect [36]. Sometimes, it can be seen by prenatal ultrasound as a large thoracic mass or pleural effusion in the fetus [37, 38]. Conservative resection should be done only to relieve symptoms, whereas extensive resection

of multiple ribs should be avoided due to the risk of severe scoliosis. Spontaneous regression has also been reported [36–39].

37.5.3 Malignant CWTs

37.5.3.1 Ewing's sarcoma/PNET

Ewing's sarcoma/PNET is the most common CWT in all pediatric series. It was described for the first time by Askin in 1979 [40]. These lesions are known as malignant small-cell sarcomatous tumors or as PNET due the origin from embryonal neural crest cells. Histological differentiation is needed with other undifferentiated, small-round-cell tumors such as undifferentiated neuroblastoma, embryonal rhabdomyosarcoma, and lymphoma [41].

Ewing's sarcoma/PNET is an extremely aggressive tumor with frequent metastatic spread and local recurrence. It should be considered to be a systemic disease at presentation [42]. The peak incidence of Ewing's sarcoma is 13–16 years, with a male:female ratio of 2:1. Localization to the chest wall accounts for up to 6.5% of cases. The first presenting symptom is increasing pain that can be associated with cough, pain fever, malaise, anemia and increased erythrocyte sedimentation rate.

Plain radiographs highlight the non-pathognomonic signs of lytic destruction and regeneration. This tumor must be differentiated from other lesions such as osteomyelitis and osteogenic sarcoma by clinical and imaging findings. CT is the best method to evaluate the bony extent of the lesion (Fig. 37.2) and small pulmonary metastases. The imaging features are a round, ovoid, multinodular or lobulated neoplasm which can be circumscribed but is rarely encapsulated. Imaging also reveals areas of hemorrhage and necrosis in large tumors. Involvement of the soft tissue of the chest wall can be defined more precisely by MRI [43].

Three histopathological patterns have been defined: compact sheets of cells; a nesting arrangement of cells with an intervening fibrovascular stroma; and serpiginous bands of cells with necrosis. In all of these small cells, almost uniform nuclei with scant cytoplasm are found. The periodic acid–Schiff (PAS) negative cell profiles are arranged around an acidophilic focus of hyaline or fibrous nature rather than a neurofibrillary composition. Cy-

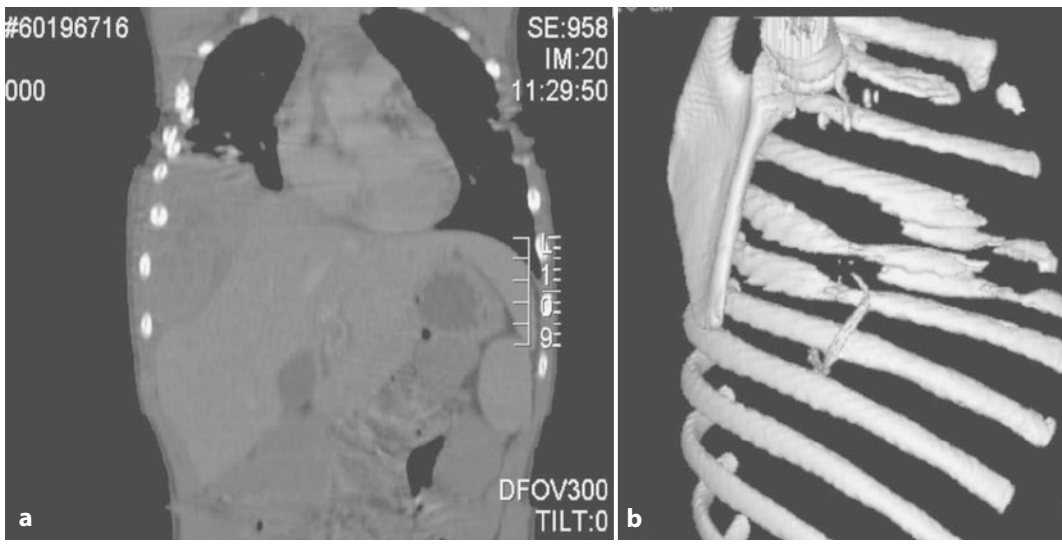

Fig 37.2 Coronal CT showing a large Ewing's sarcoma in the anterior–lateral region of the chest wall (**a**). 3D reconstruction permits the observation of the bone destruction in the ribs (**b**)

toplasmic glycogen is detected at PAS staining to distinguish Ewing sarcoma's from PNET. A characteristic balanced translocation between chromosome 11 and 12 [t(11:22)(q24;q12)] has been revealed in both tumors. The translocation points of these two tumors have now been evaluated: they are analogous [44].

These tumors should be treated using a multimodal approach (surgery, radiotherapy, chemotherapy) because they tumors have a high tendency to metastasize locally and also through hematogenous mechanisms mainly to the lungs and bones [45].

Ribs are expendable, so the whole rib from the vertebra to the costochondral junction can be removed. In lesions located laterally or interiorly on the chest wall, it is possible to leave the posterior portion of the rib. This might help in the reduction of long-term scoliosis. To achieve control of local and systemic micrometastasis, local resection of the entire involved rib with partial resections of the ribs on either side of the tumor, followed by radiotherapy on the site of the lesion, can be done. In general, the radiotherapy dose is 50–65 Gy [46]. Also, chemotherapy is employed to prevent recurrence and metastasis of the tumor [47]. Extra-osseous metastasis has also reported to be associated with an increased risk of distant metastasis and poor survival rates. Many authors have used radiotherapy after resection to improve outcome [48].

37.5.3.2 Rhabdomyosarcoma

Rhabdomyosarcoma is a typical tumor found in infancy. It accounts for 15% of all solid tumors in children, with two age peaks at 2 years to 5 years and around puberty. The prevalence in the chest accounts for 7.4% of all cases of rhabdomyosarcoma [49].

It appears as a rapidly growing mass which originates from the striated muscles of the trunk. At the beginning it is not painful, and sometimes it looks inflamed due to necrosis or hemorrhage. Hence, the diagnosis can be challenging and it should not be mistaken as an abscess.

Biopsy has the aim of confirming the diagnosis and characterizing the histological subtype of rhabdomyosarcoma. The most common type is the alveolar (which looks like pulmonary alveoli), followed by the embryonal subtype. There is also a mixed form where embryonal and alveolar components are present. The pleomorphic subtype contains large, elongated cells with many nuclei or giant nuclei, and it is rare in children.

Rhabdomyosarcoma of the chest wall is treated in a multimodal way that does not differ from the treatment in other localizations, and involves chemotherapy, surgery and radiotherapy.

Surgery has a pivotal role because complete remission cannot be achieved with chemotherapy alone in most cases, even if most tumors respond to vincristin, adriamycin and cyclophosphamide. Preoperative chemotherapy helps to reduce the size in a bulky tumor so as to achieve complete resection with a clear margin; this is fundamental because it has a significant impact on outcome. Debulking and mutilating surgery should be avoided. Radiotherapy has a role in residual, recurrent and metastatic disease.

The stage of the tumor at presentation is correlated with survival. In particular, chest-wall rhabdomyosarcoma has a poor prognosis [49-51]. Risk factors that affect the prognosis include an alveolar sarcoma subtype, advanced stage at presentation, difficulties in local resection and early relapse compared with other sites [52]. Overall five-year disease-free survival in children is 65% as reported by the results of the Third Intergroup Rhabdomyosarcoma Study. Local disease control on the chest wall is fraught with many difficulties, especially if relapse occurs. Radiotherapy is often undertaken to obtain local control of relapsing disease, but results in pulmonary fibrosis. A combination of radiotherapy and surgery may cause secondary restrictive defects that impair the development of the thoracic cavity and may cause scoliosis [53].

37.5.4 Other Tumors

Congenital infantile fibrosarcoma is present at birth, and most cases occur in the first 3 months of life. This tumor has a dense cellularity and mitotic activity but is less anaplastic than conventional fibrosarcoma and has good chemosensitivity. Hence, it must be differentiated from mesenchymal hamartoma and fibroblastomatosis. Preoperative chemotherapy makes resection possible with minimal morbidity. Resection is indicated in most instances of the residual tumor. Local recurrences have been reported with rare instances of metastasis [54].

Osteogenic sarcoma is a highly malignant bony tumour that is extremely rare in children. Osteosarcoma is a primary malignant tumor of the skeleton and is characterized by the direct formation of immature bone or osteoid tissue by tumor cells. Osteosarcoma arises predominantly in the long bones and rarely in soft tissues. Most patients present with a rapidly enlarging mass which is often reported as being painful. The age at presentation ranges from 10 years to 25 years. Plain radiographs, CT, MRI, angiography and dynamic bone scintigraphy are used for the: diagnosis; evaluation of the extent of tumour involvement; decision of the type of surgical procedure; type of reconstruction (if required). The management plan for these tumors is similar to commonly reported sites within the long bones of the limbs (i.e., incisional biopsy to confirm the diagnosis followed by chemotherapy). In the past, all patients with osteosarcoma were treated by amputation, but the cure rate was <10% and almost all patients died within 1 year from diagnosis. Today, for localized osteosarcoma at onset (80% of cases) treated in specialized Bone Tumor Centers with preoperative and postoperative chemotherapy in association with surgery, the percentage of patients cured is 60–70%. Surgery is conservative (limb salvage) in >90% of patients. The prognosis is more severe (cure rate, »30%) for tumors located in the axial skeleton and in patients with metastasis at onset.

Chondrosarcoma is a rare tumor in childhood, with a peak of incidence in men of 30–40 years [22]. It originates from the costochondral arch or the sternum on the anterior chest wall. It grows slowly, usually presenting with pain in a previously asymptomatic lesion with frequent local recurrence and a high risk of late metastasis. Well-differentiated chondrosarcoma is indistinguishable from chondroma. Given that misdiagnosis as chondroma is not uncommon in differentiated chondrosarcoma and results in inadequate excision, an accurate histological diagnosis is important. Plain radiographs show the tumor destroying the cortex (causing a mottled-type calcification within the tumor) whereas the tumor edges cannot be defined. CT gives better definition of the extent of the tumor, which is relevant for preoperative management to plan the resection biopsy (rather than incisional or needle biopsies). Chondrosarcoma does not respond to chemotherapy or radiotherapy, and an inadequate excision can be the cause of local recurrence. Therefore, the outcome of these patients is related to an initial wide excision, which results in cure as well as preventing local recurrences and distant metastasis [23]. Sometimes, complete excision with free margins cannot be done due to the size and location of the mass [52].

37.6 Outcome and Follow-up

The aim of chest-wall surgery is complete elimination of the local tumor with restoration of adequate protection of the thoracic organs without impairment of physiological functions. This will enable adequate growth in the lung and chest wall and an acceptable cosmetic result [55].

Given that most CWTs are treated primarily with resection, a correct surgical indication should be based on evaluation of the histology, location, degree of local invasion, and metastases of the tumor. A standard thoracotomy incision allows palpation of the lesion and enables a biopsy to be taken or resection to be

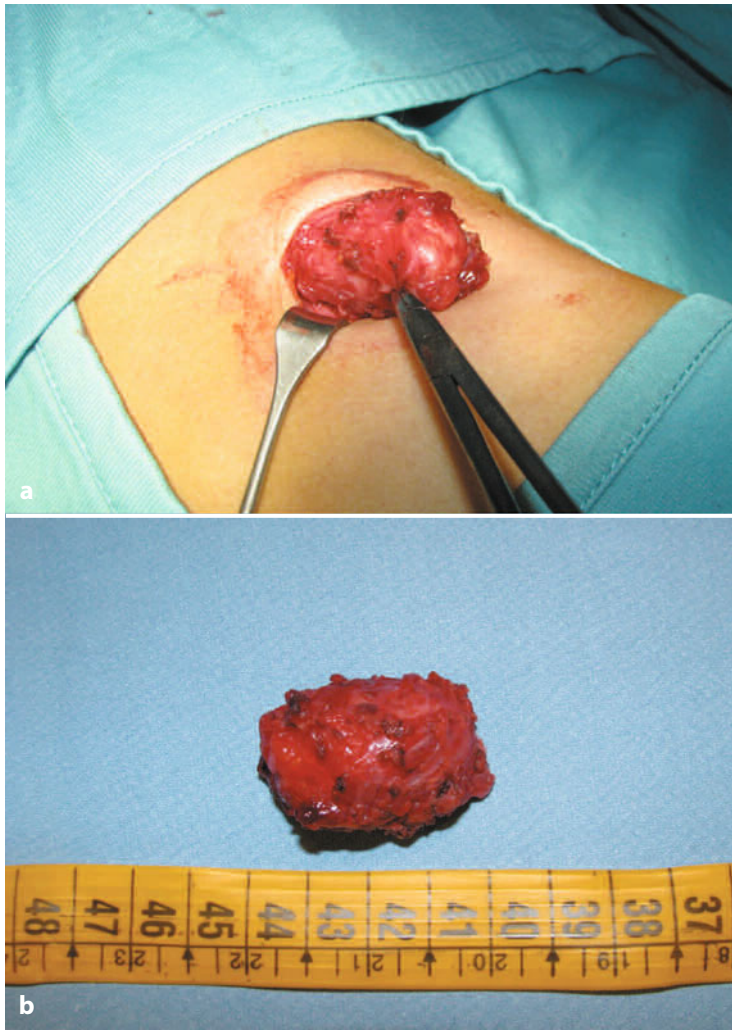

Fig. 37.3 Intraoperative image (**a**) of a standard thoracotomy in a child with rhabdomyosarcoma (**b**) of the chest wall

carried out (Fig. 37.3). Video-assisted thoracoscopic surgery may facilitate localization of the mass if it is detectable from the pleural surface. If the lesion is small and cannot be evaluated visually or by palpation intraoperative localization and resection can be done. This is achieved by placement of a coil wire by interventional radiology or injection of methylene blue into the surrounding tissues under imaging guidance.

Aiming to prevent local recurrence, resection of all tumors must ensure negative margins (even if the margin size depends on the specific tumor type). Benign tumors can be excised with negative margins, whereas a wide excision with a minimum 4-cm margin is required for malignant tumors. Thoracic and reconstructive surgeons are involved in the choice of reconstruction, which depends on the experience and preferences of the center.

Scoliosis is a well-known complication of chest-wall surgery. The severity of the curve is directly related to the number of ribs involved in the resection. In addition, the risk factors for severe scoliosis are resection of posterior segments or lower ribs and irradiation of the spinal column in patients affected by malignant tumors [56, 57]. The convexity of the

curve is towards the resected side. Scoliosis can be progressive until the child is fully grown, so it must be evaluated carefully in the long-term follow-up. This may require further surgical correction of scoliosis with insertion of a Harrington rod or the use of rib-expansion devices.

Severe scoliosis is also a risk factor for secondary impairment of pulmonary function [51] Thus, periodic evaluation of forced vital capacity, forced expiratory volume in one second, and functional residual capacities should be included in the follow-up of patients who undergo extensive chest-wall surgery.

A risk of 20% of secondary malignancy (including secondary sarcomas, acute myeloblastic and lymphoblastic leukemias) [58] has been reported. These tumors are most common within the first 5 years after the diagnosis in patients treated for Ewing's sarcoma/PNET [59–61]. Irradiation with a cumulative dose >60 Gy [62] and a chemotherapy regimen including alkylating agents are common risk factors [63, 64]. A typical complication is wound infection, in which the risk factors are tumor ulceration and use of omentum in soft-tissue reconstruction [65].

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