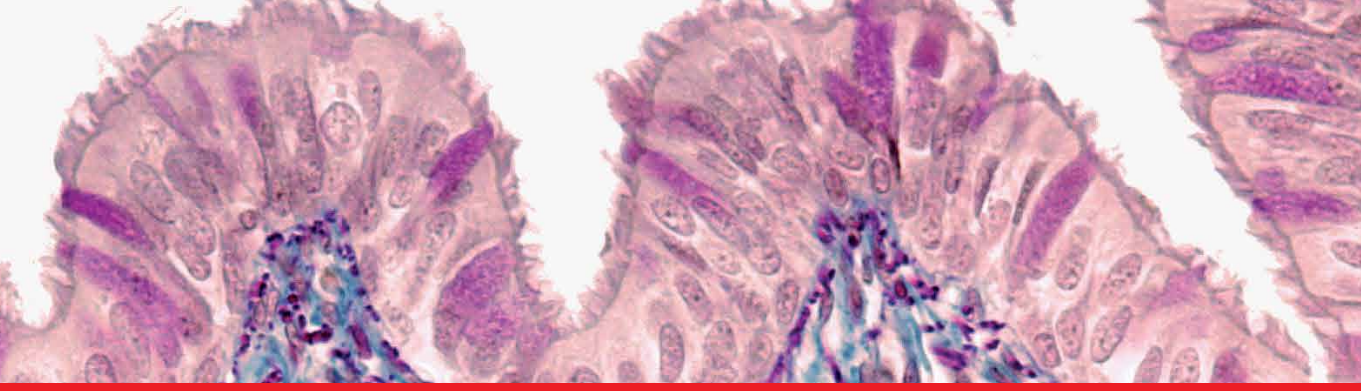

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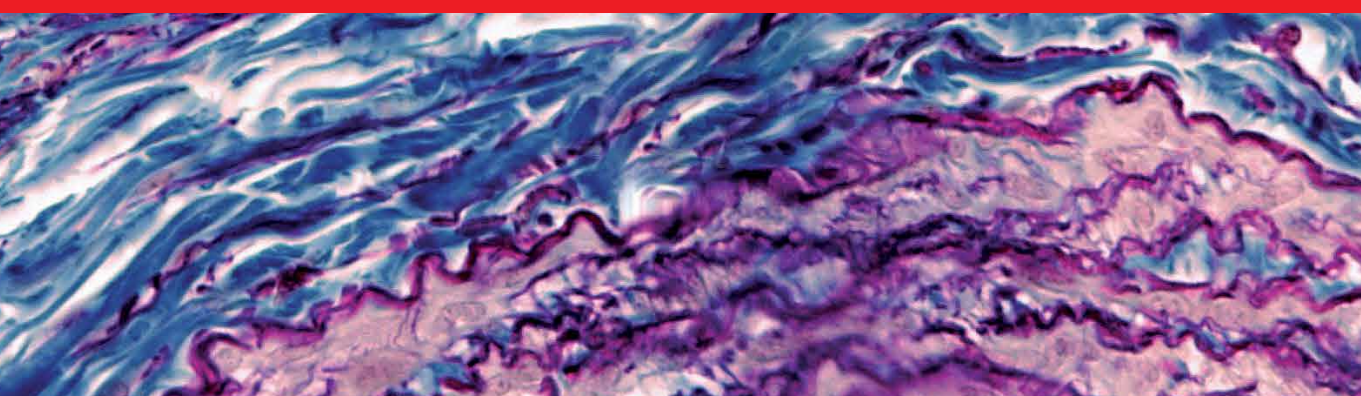
Pleura

A Surgical Perspective

Edited by Alberto Sandri



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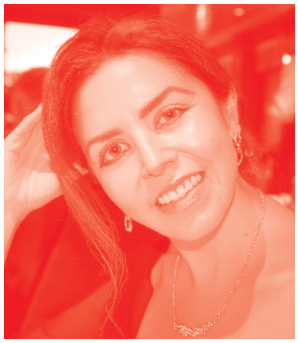

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Contents

Preface

Pleural pathology covers a wide range of benign and malignant thoracic diseases that may require invasive approaches for their diagnosis and treatment.

Advances made in the field of thoracic surgery go hand in hand with inexorable technological achievements, which have greatly improved the standards of diagnosis and treatment in patients undergoing thoracic surgery for benign and malignant diseases by increasing procedural safety, improving prognosis, and reducing potential peri-and postoperative complications.

This book examines pleural pathology from a surgical point of view, starting from the historical aspects, which are a reminder of where we were and where we presently stand in the management of pleural disease. It discusses in detail, and according to the most recent guidelines, the surgical aspects and management of pleural infection (empyema) and complications that may arise following lung surgery for cancer (i.e., bronchopleural fistula). One section covers all the aspects related to pneumothorax, with a special focus on secondary pneumothorax and pneumothoraces in children. Chapters deal with the indications, positioning techniques, and management of chest drains and indwelling catheters, which are commonly utilized in daily clinical practice for the management of pleural disease (pleural effusion, pneumothorax).

I am deeply grateful to the chapter authors for their contributions to this project, which I am sure will be much appreciated by the thoracic community worldwide.

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Section 1

Introduction

Chapter 1

Introductory Chapter: Pleura, A Surgical Perspective

Alberto Sandri and Francesco Leo

1. Introduction: a surgical perspective through the centuries

Pleural pathology covers a vast chapter of benign and malignant thoracic diseases which may require invasive approaches for their diagnosis and treatment.

However, the present role of the thoracic surgeon in the management of pleural/thoracic disease is the tip of the iceberg of a very long journey which dates back thousands of years. It is a journey that starts with no knowledge of the human anatomy, physiology and basic medical sciences and where mistakes, attempts, improvements and eventually successes were the fundamentals of the present medicine and surgery.

The very first pathologies related to the chest and pleura reported in history relate majorly to thoracic traumas and thoracic wounds (e.g., penetrating injuries), caused accidentally or during fights/wars, and infections (e.g., empyema). Their treatment was the cornerstone for the present modern thoracic surgery.

2. Early reports of thoracic wounds and infections

The first historical reports of chest wounds and infections treated by doctors are described in the Edwin Smith papyrus, during the Ancient Egyptian Era.

Other reports of chest injuries and attempts at their treatment have been reported and described in several historical books, in which it is clear how the limited knowledge of the human anatomy and physiology and the total absence of basic infection management because of the then ignored micro-bacterial world were causes of almost certain death.

The "*Iliad*" by Homer, copiously report wounds and infections during the Trojan War [1, 2], as well as the French knight saga *Chanson de Roland* (Song of Roland), provides a long list of usually deathly chest wounds, in which the clear description proves that contemporary witnesses, including barber-surgeons, were already aware of this kind of injuries and their poor prognosis despite the treatments available in those times.

3. Empyema and surgery

Thoracic empyema is defined as the collection of pus in the pleural cavity and it is one of the very first pathologies on the scene of history of surgically treated chest diseases [3, 4]. The first recorded descriptions of invasive approaches to the chest cavity are found in the medical texts of ancient Greece in regards to the treatment of empyema as suggested by Hippocrates of Kos, whose teaching *ubi pus (ivi) evacua* has remained relevant throughout the ages. Hippocrates' first treatment attempt

was a conservative one, based upon herbal medications and physiotherapy. If the patient did not improve, open evacuation of the empyema was then undertaken [5].

> *'First, cut the skin between the ribs with a bellied scalpel; then wrap a lancet with a piece of cloth, leaving the point of the blade exposed a length equal to the nail of your thumb, and insert it. When you have removed as much pus as you think appropriate, plug the wound with a tent of raw linen, and tie it with a cord; draw off pus once a day; on the tenth day, draw all of the pus, and plug the wound with linen. Then make an infusion of warm wine and oil with a tube, in order that the lung, accustomed to being soaked in pus, will not be suddenly dried out. When the pus is thin like water, sticky when touched with a finger, and small in amount, insert a hollow tin drainage tube. When the cavity is completely dried out, cut off the tube little by little, and let the ulcer unite before you remove the tube [6]'.*

Sequelae of chest injuries and post-pneumonic empyemas (unidentified until percussion and auscultations were introduced in the mid-nineteenth century) are reported in ancient medical sources. The great Roman doctor Galen of Pergamon (*Aelius Galenus* or *Claudius Galenus*) advised the usage of metallic tubes in order to drain an empyema cavity [7], a teaching that did not change significantly through the Christian and Muslim medical practices of the Middle Ages [8]. Barber surgeons like *Pietro d'Argellata* refined and improved the chest drain insertion and thoracic irrigation to wash out the purulent fluids from the chest cavity. In this context, further improvements were adopted in time, such as a thoracentesis syringe and cannula for the irrigation of empyema [9, 10]. Permanent windows of the chest wall was a competing way of treating empyemas, with modern surgeons such as Joseph Lister and Charles M.E. Chassaignc who refined the technique. Excision of a segment of the rib was endeavoured by German, French and English surgeons, such as Paget in his book Surgery of the Chest [11]. The challenge of empyema, usually tuberculous in origin, led to the emergence of chest surgery in the late decades of the nineteenth century. Basic treatment for empyema consisted of rib resection and loose tamponade of the chest cavity with a gauze soaked in antiseptic (mercury/iodine). Between 15 and 20% of post-traumatic patients need surgery (rib resection and debridement), with a mortality comprised between 20 and 50%, likely related to streptococcal superinfections [12]. As depicted later in this chapter, the belief of a transcostal approach (chest tube) for the treatment of empyema lasted until long after the first World War.

As a matter of fact, thoracostomy, i.e., the externalisation of the empyema cavity by unroofing, was another option that went through several modifications in the years, starting from the Eloesser flap introduced in 1935 [13] to the Clagett procedure which required daily packings [14, 15]. George R. Fowler and Edmond Delorme pioneered the exeresis of the thick visceral pleura (decortication) in 1894–95 [16]. It was Lilienthal who reintroduced lung decortication for early-stage empyema on the basis of his experiences in the American Expeditionary Force in Europe [17]. Debridement and decortication became an option as soon as general anaesthesia and intubation were established during and after the Second World War. Such surgical improvements along with the introduction in the 1930s of Sulphonamides and later on, in 1943, of Penicillin, drastically revolutionised the treatment of thoracic empyema and their outcomes [18].

4. Tuberculosis, artificial pneumothorax and surgery

Tuberculosis has been known since the Old Testament [19], properly defined clinical and pathologic features depicted in detail in the mid-nineteenth century [20].

In 1882, Robert Koch identified the organism responsible for tuberculosis, proving the *sine qua non* cause of the disease. Remedies for phthisis comprised supportive care provided mostly by sanatoriums and Carlo Fontanini's artificial pneumothorax.

4.1 Carlo Fontanini's artificial pneumothorax

During his entire professional career, Carlo Fontanini from Pavia, Italy, devoted a great deal of time and effort to the study of tuberculosis contributing extensively to the medical literature on this subject. Forlanini's epoch-making treatise on the rationale of artificial pneumothorax was printed in the *Gazzetta degli Ospedali & delle Cliniche di Milano, Volume 3, No. 68, Page 537, August 23*. His reasoning was based on the observations of other clinicians as well as of his own, noticing that spontaneous pneumothorax, with or without pleural effusion, had a favourable effect on the course of pulmonary tuberculosis [21]. His apparatus introduced nitrogen into the pleural cavity through a large hypodermic needle, and in doing so, produced a pneumothorax. However, an artificial pneumothorax was frequently unsuccessful as a therapy for tuberculosis because of the presence of pleuropulmonary adhesions. This complication was accounted for with the use of the thoracoscope, firstly utilised by HANS Christian Jacobaeus from Stockholm in 1910, who is considered the father of the thoracoscope. The thoracoscope favoured the identification and clearance of adhesions through their digital manipulation setting the basis, in due time, for minimally invasive thoracic surgery [22, 23].

However, Forlanini's artificial pneumothorax was challenged by another attempt of treating tuberculosis; in fact, in 1937, at the Brompton Hospital in London, James E.H. Roberts reported 33 operations of extrapleural pneumothorax, which is the collection of air in the space between parietal pleura and endothoracic fascia.

4.2 Thoracoplasties as a surgical treatment for tuberculosis

Extrapleural thoracoplasties, in those times, was preferred because of the lack of safe anaesthesia; this surgical procedure aims at definitely resecting the pleural space with ribs and periosteum, intercostal neurovascular bundles and intercostal muscles.

Several surgeons in the years modified the technique, even by performing them in several stages. In fact, by the 1920s, staged operations became favoured as a result of the publication of Ernst F. Sauerbruch, André Maurer (Paris) and Walther Graf (Dresden) [24]. Those procedures were performed either under local anaesthesia or ether/chloroform masks narcosis, in spontaneous breathing.

Sauerbruch added drainage to the cavity and performed it in two-three stages to avoid mediastinal shift.

Remodelling the chest wall following thoracoplasty was achieved by means of omentum or muscle apposition in the years to come. By the early 1950s, thoracoplasty plombage with or without pneumoperitoneum had replaced artificial pneumothorax as the primary procedure.

Caverna treatment was another pressing problem due to deadly haemoptysis. It was Vincenzo Monaldi who refined staged transmural drainage as a very safe procedure (1939). Following a partial rib resection as a first step, he obtained a debridement of parietal-visceral adhesions through the instillation of irritative agents and, after 7–10 days, he inserted a tube through the area of the adhesions into the cavity, creating a real cavernostomy [25, 26].

It was only in 1936 that the first successful pulmonary lobectomy and pneumonectomy for tuberculosis were performed. In those days, post-lobectomy and post-pneumonectomy mortality for the treatment of tuberculosis was 20–25% for the former and up to 40–50% for the latter [24].

5. Chest wounds, penetrating chest injuries, gunshot wounds

In 1395, *Guy de Chauliac*, a leading physician-surgeon of the French medieval times, completed the most important surgical book of that time, *Chirurgia Magna*. In the second Doctrine of *Chirurgia Magna,* there are several comments regarding the lack of ancient writings on thoracic wounds and their treatment, acknowledging then non-linear treatment strategies between his contemporaries.

Basically, there were two schools of thought regarding the treatment of chest wounds, one advocated the open treatment of penetrating thoracic wounds using tents and drains to allow food and pus to escape the pleural cavity, the other, instead, advocated the immediate closure of the wound to prevent the entry of cold air and loss of heat [27]. This debate persisted for centuries.

Chest injuries developed a decisively worse prognosis as the more fatal gunshot wounds dominated from the sixteenth century onwards [28]. Giovanni da Vigo, an Italian surgeon and physician of Pope Julius II, was one of the first surgeons to explore firearm wounds, including those to the chest, in Practica Copiosa of 1514 [27].

In accordance with Guy de Chauliac, Vigo too points out the dilemma of the "open" vs. "closed" treatment of penetrating thoracic injuries, among which he was more inclined to the latter. Vigos's work was accredited by a French military surgeon, Ambroise Paré, in the attempt of establishing guidelines to determine whether to choose an open or a closed treatment for penetrating thoracic wounds [29].

5.1 The introduction of aspiration to a chest drain

In 1707, Dominique Anel described a method for sucking wounds with a silver tube attached to a piston syringe which replaced a human mouth, a practice which was very common in those days, to such an extent that nobles and upper-class men would bring wound suckers with them when they had to fight duels [29, 30]. Following such invention, the surgical procedure now consisted of a cannula which allowed a catheter to be introduced into the pleural space, not only to the margins of the wound, and by applying an aspiration to it. In 1771, Adamus Birkholz added a reservoir container into Anel's suction line, creating an early Potain aspiration [29]. In the following years, despite the advances made, there was still a lack of consensus on the optimal treatment management of chest wounds, comprising different techniques, ranging from the hypothetical necessity of closing at first the wound to avoid blood loss from the lung but making a counter opening which would evacuate the retained blood, as Valentine did in 1772, to Gurthrie's method (early 1800s), which encompassed closing the wounds of the chest and watching for an increase in serous effusion for few days after the injury, indicating that the bleeding had likely stopped for, then, evacuating the blood with a trocar and cannula through a new opening or by reopening the original wound [31].

Larrey, a surgeon who treated Napoleon, believed that there was a danger of renewed bleeding if attempts were made to evacuate effused blood less than nine days from the initial injury [29].

It is therefore clear that, to this point of history, the only commonly accepted step forward in the management of penetrating injuries to the chest and consequent chest infections was to drain them. Regarding the how, that was still a dilemma.

During the American Civil War war, surgeons started to insert trocars in the chest to drain fluid retained in the pleural space while, in the same period, the Union forces were experimenting the use of airtight seals to impede airflow in open chest wounds. It is on Playfair, in 1873, the attribution to applying a water-sealed

chest drainage system for the first time, as a successful treatment of a child with thoracic empyema [32]. Until that time, scarce information was known in regards of the intrapleural negative pressure, the reason why the management of chest traumas was only just successful until then.

5.2 The first closed water-seal chest drain

In 1875, Gotthard Bülau applied a closed water-seal chest drainage to treat an empyema, as an alternative to the standard rib resection and open tube drainage in the acute phase or rib excision in the chronic phase [33]. In contrast to the popular opinion of the surgeons of that time, Bülau was the first to understand the importance of negative intrapleural pressure to obtain the re-expansion of a collapsed lung subsequent to thoracic empyema.

His method consisted in puncturing the pleural space and introducing a rubber catheter with a clamp inside the chest. The part of the drain outside the chest was then immersed in a bottle filled for one third with an antiseptic solution and unclamped, creating a siphon drainage which allowed pus to flow out from the chest [33–35]. The nineteenth century marked the advent of rubber tubes and the invention of standardised syringes and needles changed and improved the practice of chest tube thoracostomy.

During World War I, despite the above-mentioned improvements and treatment options (needle drainage of hemothorax, wound exploration and debridement, wound exploration for foreign body removal and closure of open pneumothorax with sutures), mortality was still high, estimated to be around 55% [36]. Furthermore, during World War I, recently invented tampons and Morelli's occlusive rubber cuffs, which allowed for closure and simultaneous suction drainage, were in use in the control of airflow in open chest wounds [29]. Also, by that time, post-thoracotomy evacuation of fluid in the pleural cavity was recognised as an important way to avoid infection, and the concept of a flutter valve for uni-directional air movement within a drainage tube was spreading, but tube thoracostomy was not widely used yet for treating hemothoraces or pneumothoraces [31].

During World War II, it was clear to the surgeons that lung function restoration was the primary goal of treatment, with emphasis on wound debridement and pleural cavity drainage [37]. The modern three-chamber thoracic drainage system was first described by Howe in 1952 and in the Korean War (1950–1953), mortality decreased to 0.6–1.9% of major thoracic trauma patients who survived to be evacuated and treated. Also, the frequency of empyema due to penetrating chest wounds was reported to be 25–30%, decreased to 9% as hemothorax was approached with a more aggressive attitude [38–41].

During the years, tube thoracostomy was finally accepted as the standard of care at the time of the Vietnam War. A significant improvement was developed by Heimlich in 1968, who designed a flutter valve to attach to catheters and replace the underwater drain bottles. Its advantages included sterility, disposability, simplicity, safety in the event of disconnection, and allowance for patient ambulation [42].

6. Conclusions

Thoracic surgery is a multi-fathered speciality, which gained recognition as a distinct surgical entity only in the 1950s. The development of such a specialistic surgery was possible because of the knowledge gained through, attempts, mistakes, improvements and eventually successes over hundreds of years. The post-war effect on the development of thoracic surgery was enormous. In the first decade after the

war, thoracoplasties and empyema treatments for tuberculosis dominated thoracic surgery, but it was in the 1930s that small but decisive steps were taken in the direction of lung parenchymal resection. It was right in those days that oncological cases became a priority over the tubercular ones because of the introduction of new medical treatments available, (i.e., streptomycin, 4-aminosalicylic acid, isoniazid, pyrazinamide, cycloserine, ethambutol and rifampicin 1963).

The contribution to the development of a dedicated thoracic anaesthesia was a cornerstone in consolidating the results of thoracic surgery, especially with the achievement and standardisation of the single lung ventilation through a double-lumen endotracheal tube.

Another crucial step was the establishment of thoracic societies in the world by the earliest pioneers in thoracic surgery, such as the American Association of Thoracic Surgeons (AATS) in 1917 and the Society of Cardiothoracic Surgeons of Great Britain and Ireland (SCTS) in 1934. The role of the Societies helped, in the beginning, through sharing surgical experiences and results to, then, cooperating in improving and standardising operating techniques, indications and treatments through an evidence-based methodology and teaching.

Such advances go hand in hand with the inexorable technological achievements in the thoracic surgery field, which greatly improved the standards of diagnosis and treatment in patients undergoing thoracic surgery for benign and malignant diseases, by increasing procedural safety, improving prognosis and reducing potential peri and post-operative complications.

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Section 2

Surgical Management of Pleural Infection

Chapter 2

Surgical Management of Pleural Space Infection

Alessandro Maraschi and Andrea Billè

Abstract

Pleural space infections are a common clinical entity affecting a large number of patients. These are associated with considerable morbidity and mortality rate and they require significant healthcare resources. In this chapter, we discuss the disease characteristics with regards to the etiology (primary and secondary), clinical presentation, radiological findings, different stages of the condition and treatment options according to stage at presentation. Conservative management (medical treatment, pleural drainage, with or without intrapleural fibrinolytic) may be effective in management of simple pleural space infections, but surgical management may be required in loculated complex empyema to prevent acute sepsis, deterioration and trapped lung. Surgical treatment of complicated pleural infections either by VATS or thoracotomy will be discussed in order to understand when to perform debridement/decortication of the pleural cavity or less frequently a thoracostomy.

Keywords: Pleura, Empyema thoracic, Pneumoniae, Thoracoscopic debridement, Decortication

1. Introduction

Pleural infections are a frequent clinical entity which affect a large number of patients. The annual incidence in the UK and USA combined is up to 80,000 cases. The overall incidence worldwide is increasing both in the adult and pediatric population [1].

Infection of the pleural space remains a serious condition which continues to be associated with high morbidity and mortality rate. The outcome is poor and it is reported to have one-year mortality of 20%, which rises up to 30% in the elderly population. Approximately 20% of patients with pleural space infection will require surgical treatment due to a failure in the conservative management [2, 3].

Pleural infections consist in a continuum spectrum of evolving disease through 3 different stages, starting from an uncomplicated pleural effusion to a complicated effusion and eventually established empyema.

The diagnosis can be obtained with a detailed anamnesis, biochemical analysis and radiological test, such as ultrasound or computed tomography.

The treatment choice is based on patient condition and disease stage at presentation. The treatment can be either conservative or surgical.

2. Pleural space infection - etiopathogenesis

Pneumoniae is an infectious process resulting from invasion and proliferation of microorganisms which elude the host defenses within the lung parenchyma and cause the production of intra-alveolar exudates. Pneumonia may cause the development of parapneumonic effusion followed by an empyema. A parapneumonic effusion occurs in 35–40% of hospitalized cases of pneumoniae, empyema only develops in 20% of these.

The pleural space infection and the subsequent empyema can be classified as primary or secondary:

- Primary pleural infection/empyema is defined as a complication of intrinsic infection of the lung. Most commonly, an empyema develops as a complication of bacterial pneumoniae.

- Secondary pleural infection/empyema occurs as a complication of invasive procedure to the chest: lung surgery, thoracocentesis, chest drain insertion, penetrating chest trauma. Other causes are esophageal rupture, mediastinal infection, sub diaphragmatic or paravertebral abscess. Bronchopleural fistula can also lead to an empyema.

Patients with risk factors have an increased risk of developing a pleural infection. The most common risk factors are:

- Diabetes mellitus
- Immunosuppression (including corticosteroid use)
- Gastro-esophageal reflux
- Alcohol misuse
- Intravenous drug abuse
- Poor oral hygiene (correlates with anaerobic infection)
- History of aspiration (correlates with anaerobic infection)
- Pediatric and elderly population
- Impaired conscious level (risk of aspiration)

Other risk factors for the development of lung infection and therefore, to the development of pleural infection, are: underlying lung disease (COPD, emphysema, interstitial lung disease, deficiency/aberrant alveolar surfactant), tracheal intubation and antibiotic treatment.

Pediatric and elderly population patients affected by chronic diseases are more susceptible to developing lung infection.

Smokers are also included in the high-risk category due to the impact of the smoke on the airway defense mechanism in clearing secretions (thick secretions and impaired ciliary motility) and increased susceptibility.

Patients in the community and patients hospitalized present different risk factors. Impaired conscious levels and higher risk of aspiration is far more common in hospitalized patients, which explains the higher rate of gram-negative gut bacteria.

These present relatively later in the infection with pneumonitis involving the superior segment of a lower lobe or posterior segment or an upper lobe.

The evolution from the simple pleural effusion to the complicated empyema usually occurs following three well defined stages.

1. **Exudative stage** (uncomplicated or simple parapneumonic effusion)

   This first stage of the disease is characterized by a simple pleural effusion with clear, free-floating fluid and usually too small to be sampled within the pleural cavity. The fluid is exudative, therefore, following the Light's Criteria:

   - Ratio of pleural fluid to serum protein is greater than 0.5.
   - Ratio of pleural fluid to serum LDH greater than 0.6.
   - Pleural fluid LDH value is greater than two-thirds of the upper limit of the normal serum value.

The fluid is a neutrophil-rich effusion and is the result of an increased pulmonary permeability in response to the inflammation associated with the infection.

The balance between production and reabsorption of the pleural fluid is impaired due to the inflammatory process, which causes increased vascular permeability and neutrophil chemotaxis.

The fluid is sterile and the glucose and pH level are maintained within the physiological range. No microorganisms are seen in Gram stain culture.

This stage occurs between 2 and 5 days from the onset of the pneumonia.

2. **Fibrinopurulent stage** (complicated parapneumonic effusion)

   This stage is characterized by the colonization of the microorganisms of the pleural fluid. The fibrin deposition causes loculation and pleural thickening, activation of the coagulation cascade and downregulation of fibrinolytic pathways. This process can create a uni-loculated or multi-loculated collection consistent in a separate pocket of infected viscous fluid within the pleural space. Bacterial invasion is often present, but Gram stain culture of the fluid may remain sterile due to the rapid bacterial clearance from the pleural space. The fluid is characterized by pH < 7.2, LDH > 1,000 U/L and a decreased glucose level (< 60 mg/dL). Bacterial infection increases the immune response, attracting more neutrophils which by killing the microorganisms increases the CO2 and lactate levels in the effusion, producing a self-maintaining process.

   This stage occurs approximately 5–10 days after the pneumonia onset.

3. **Organizing stage** (pleural empyema)

   In the final stage the pleural fluid begins to organize. Thick and viscous pus created by fibroblast chemotaxis, accumulates within the pleural space and creates a thick fibrinous rind (fibrous peel) covering the lung surface encasing the organ and preventing the re-expansion (trapped lung). The trapped lung causes decreased ventilation leading to a perfusion-ventilation mismatch, which causes a restrictive syndrome. Microorganisms are normally present in the pus and the disease at this stage is non-reversible.

Findings in analysis of pleural fluid include a pH < 7.2, glucose <50 mg/dL, LDH > 1,000 IU/L.

Even after eradication of the infection a functional impairment will persist. This stage occurs after 2–3 weeks from the onset of the disease.

3. Microbiology

Numerous microorganisms may be involved in pleural space infections. The incidence of these pathogens varies widely according to several factors including the source of infection (haematogenous diffusion, following invasive procedure in the chest cavity, such as, thoracic surgery procedures), community or hospital acquired infections, geographic location and age group.

Parapneumonic pleural infections secondary to community acquired pneumonia (CAP) tend to be caused by the same organisms responsible for the pneumonia. CAP is defined as a low respiratory tract infection (LRTI) in a patient who has not been hospitalized in the previous 14 days from the diagnosis. This can be classified as typical and atypical.

Although a causative organism is not always isolated, the most common pathogens responsible for typical CAP, accounting for 85% of cases are:

- Streptococcus pneumoniae (commonest)
- Haemophilus influenza
- Moraxella catarrhalis
- Pseudomonas aeruginosa
- Klebsiella pneumoniae

Atypical CAP is most commonly caused by:

- Legionella species
- Mycoplasma pneumoniae
- Chlamydia pneumoniae
- Coxiella burnetii
- Chlamydia psittaci
- Francisella tularensis

Hospital-acquired pneumoniae (HAP) is defined as a LRTI with the onset 48–72 hours after admission to hospital. In the context of hospital acquired infections (HAP) the most common species of bacteria isolated are:

- Pseudomonas aeruginosa
- Escherichia coli
- Klebsiella pneumoniae

- Staphylococcus aureus and methicillin-resistant S. aureus (MRSA)
- Streptococcus pneumoniae
- Haemophilus influenzae

Parapneumonic pleural infections that result from aspiration are often caused by several pathogens (polymicrobial) mainly including oral streptococci (S. anginosus, S. intermedius, S. constellatus) and anaerobes, which colonize the oropharynx.

Staphylococcus aureus methicillin-resistant is present in 25.8% of the CAP infections and 68.8% in HAP infections [4, 5].

The prevalence of the pathogens is also related to the selected patients. For instance, patients affected by diabetes mellitus have increased risk of empyema secondary to Klebsiella pneumoniae [6].

Mycobacterial infections are far less common than bacterial infections. Tuberculous pleural effusion must always be investigated in areas where tuberculosis is endemic and in patients who have risk factors for TB. Tuberculous pleural effusion is the second most common form of extrapulmonary tuberculosis (after lymphatic involvement). Tuberculous empyema needs to be differentiated from tuberculous pleurisy. In the former, the mycobacterium can be found by stain or culture in the effusion, while in the latter, a lymphocytic effusion is caused by the immunologic response to proteins released by the mycobacterium and TB organisms, which are scarce in the effusion.

This can occur as reactivation disease or primary tuberculosis whereas in children represents mostly a primary disease and in adults occur mainly due to a reactivation process [7, 8].

4. Presentation

As previously discussed most cases of parapneumonic effusion and empyema follow a previous case of pneumonia, with typical symptoms including productive cough, pleuritic chest pain, dyspnoea and fever.

The presentation may be insidious, with non-specific and delayed symptoms, especially when related to anaerobic infections. Some patients can present with loss of appetite and weight loss over a period of a few weeks to several months. Aerobic infections usually present with more acute onset.

The persistence of fever for more than 3 days following the initiation of adequate antibiotic treatment may indicate progression to pleural involvement and a necessity of more aggressive management.

Patients with empyema present with persistent fever and malaise for several days compared with those with pneumoniae alone or pneumoniae with simple parapneumonic effusion.

On physical examination decreased fremitus, dullness on percussion and decreased breath sounds related to the presence of pleural effusion are representative signs of pleural effusion. In case of overt empyema patients present with fever, tachypnoea and tachycardia, in combination with the above described findings of a pleural effusion.

Laboratory blood tests are nonspecific for parapneumonic pleural effusion and these usually are the common findings in an infection, such as, leukocytosis and elevated C-reactive protein.

The main markers for the diagnosis are pH, LDH and glucose in the pleural effusion, along with the symptoms and clinical presentation. The normal pleural fluid is

clear with pH ranges between 7.60 and 7.64. It contains a similar amount of glucose to that of plasma, LDH < 50% of plasmatic concentration, white blood cells <1,000/mm3 and scarce amount of protein (less than 2%, 1–2 g/dL).

However, since these are non-specific and require invasive test to be analyzed, numerous studies have investigated different biomarkers, inflammatory cytokines and enzymes to enhance and expedite the diagnostic process of empyema. These have not proven any diagnostic advancement compared to the traditional analysis [9–13].

A recent study by Wu et al. assesses the performance of four proteins (BPI, NGAL, AZU1 and calprotectin) in the diagnosis of complicated parapneumonic effusions. This study highlighted the superiority of BPI (bactericidal permeability-increasing protein) compared to LDH, glucose and pH in the diagnosis of complicated parapneumonic effusion [14].

5. Radiological findings of parapneumonic effusion and empyema

Chest radiography, ultrasonography (US) and computed tomography are paramount in the diagnosis and management of parapneumonic effusion and empyema, as well as, in their post-treatment and post-operative monitoring.

All patients diagnosed with pneumoniae should undergo new imaging considering the chest radiography as the first step in the diagnosis process to show presence of pleural effusion.

CT is generally performed when loculations are demonstrated or suspected at the US and also, when a surgical procedure is planned.

Magnetic Resonance Imaging (MRI) and positron emission tomographic scanning are not useful and they do not usually have a role in the diagnostic and management process of pleural effusions.

Occasionally, if esophageal perforation or intra-abdominal processes, such as, liver abscesses are suspected, contrast imaging may be required. Specifically, to identify an esophageal perforation: fluoroscopy with a low-osmolar water-soluble agent like barium for esophageal perforation; CT scan with water-soluble oral contrast administered 20 minutes before scanning to demonstrate extraluminal contrast leak and intravenous contrast to delineate the esophageal wall.

5.1 Chest radiography

Uncomplicated parapneumonic effusions are characterized by:

- Pulmonary consolidations or infiltrates
- Free pleural fluid which is characterized by:
- Blunt costophrenic angle. This indicates an amount of pleural fluid greater than 200 ml
- Dense linear shadow layering between the lung and the chest wall

Free-flowing fluid collects in the dependent areas of the chest cavity. To measure with good approximation the amount of fluid in the chest cavity with a radiography, the following details can be noted:

- In an upright standing patient in posteroanterior projection blunting of the costophrenic angle indicates an amount of fluid greater than 175 ml
- In a lateral chest radiograph blunting of the posterior costophrenic angle indicates amount of fluid greater than 75 ml
- Large effusions may obscure the diaphragm (> 500 ml) and demonstrate a meniscus sign

A pleural fluid depth ≥ 10 mm from the chest wall on the chest X-ray suggests sufficient fluid is present to perform diagnostic pleural aspiration.

Complicated parapneumonic effusions (**Figures 1-3**) are characterized by:

- Lung consolidations or infiltrates as in the previous stage
- Uni-loculated or multi-loculated pleural effusion. These can be identified by:
  - Pleural opacity in a non-dependent area
  - Linear densities in the pleura
  - No changes or minor changes in the imaging comparing erect and decubitus radiographs

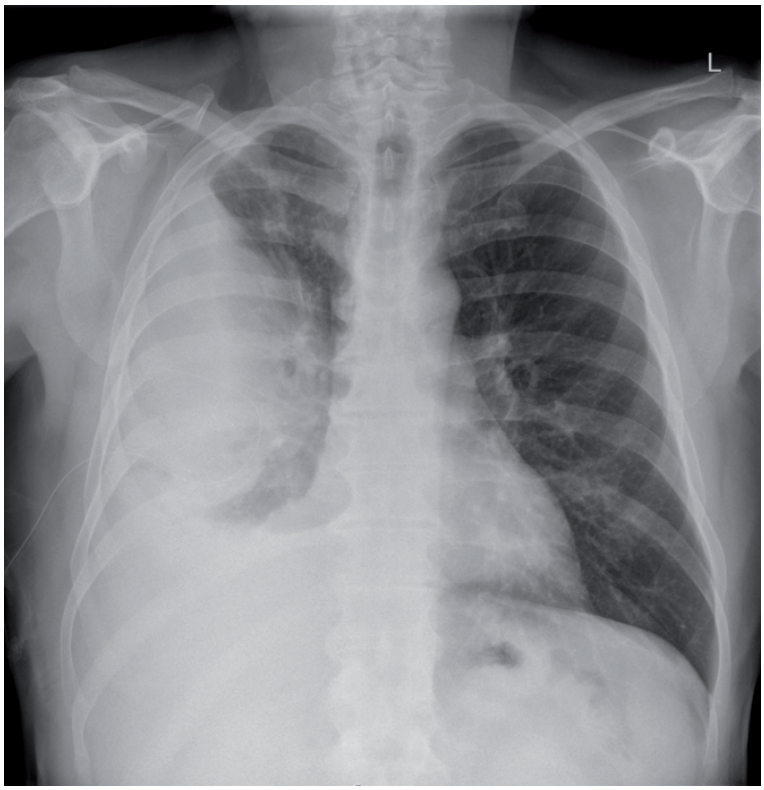

Figure 1.
Chest radiograph of a patient with complicated parapneumonic effusion, demonstrated by restricted expansion of the underlying lung in the right hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

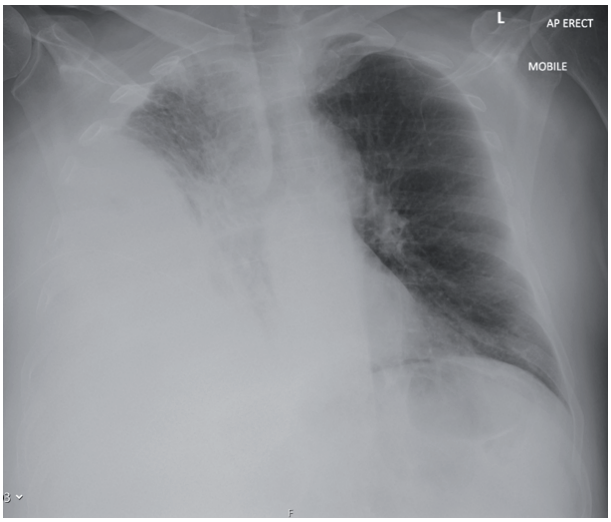

Figure 2.
Chest radiograph of a patient with empyema, demonstrated by lenticular opacity in the pleural cavity of the right hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

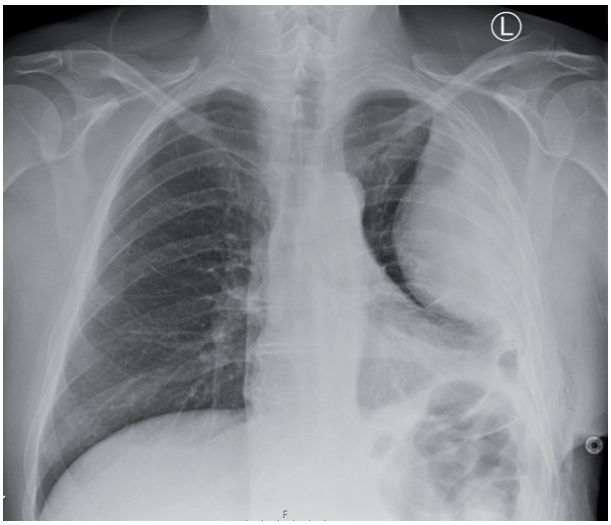

Figure 3.
Chest radiograph of a patient with empyema, demonstrated by lenticular opacity in the pleural cavity of the left hemithorax. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

Empyema is characterized by:

- Lenticular opacity in the pleural cavity, convex towards the lung
- Incomplete expansion of the lung

5.2 Ultrasound scan features of a parapneumonic effusion and empyema

US is reported to be superior to radiography and computed tomography to identify the presence of septations. It is also more sensitive than decubitus radiography in detection of the amount of fluid being capable of detecting a minimum of 5 ml of

fluid. Sonography has been reported having a sensitivity of 93% and a specificity of 96% in the diagnosis of pleural effusion [15].

Moreover, the US is particularly useful in critically ill patients allowing supine examinations when the patient cannot be mobilized [16].

It is also valuable in confirming the presence and size of pleural effusion and allows to determine the precise location of the fluid for needle-guided aspiration and drainage.

Tu and colleagues demonstrated the utility of the portable sonography in Emergency Departments and Intensive Care Units in critically ill patients. This allowed, based on the ultrasound features of the effusion, to indicate whether or not thoracentesis was necessary or could safely be deferred [17].

Four different patterns of imaging can be described in sonography evaluation, accordingly to the stage disease: [18].

- Homogeneous anechoic consistent with transudative effusion
- Complex non-septated effusion with internal echogenic foci consistent with fibrinopurulent phase
- Complex septated effusion with echogenic foci consistent with fibrinopurulent phase
- Homogeneously echogenic consistent with presence of blood or frank pus

5.3 Computed tomography features of a parapneumonic effusion and empyema

Chest CT is considered the gold standard to assess a complex pleural effusion. It is better performed with medium contrast in order to better identify the pleural membranes. This is the most sensitive method for detecting a small amount of fluid (limit of resolution 2 ml).

Computed tomography allows:

- Differential diagnosis between pleural empyema and parenchymal lung abscess
- Diagnosis of underlying etiology, such as, pneumoniae, endobronchial lesions or esophageal rupture
- Determine the extension of the infective process and allows to determine any spread into other structures including chest wall (empyema necessitans), mediastinum (determining a mediastinitis) or pericardium (pyopericardium)
- CT guided chest drain insertion, identify the pockets of fluid
- Pre-operative planning for surgery

Specific findings of an empyema include:

- A thick and contrast-enhanced pleural rind
- Pleural effusion which is loculated, septated, lenticular and with high density. Occasionally gas bubbles are seen within the effusion of pockets
- "Split pleura" sign due to pleural enhancement and fluid separating the parietal and visceral pleura surfaces

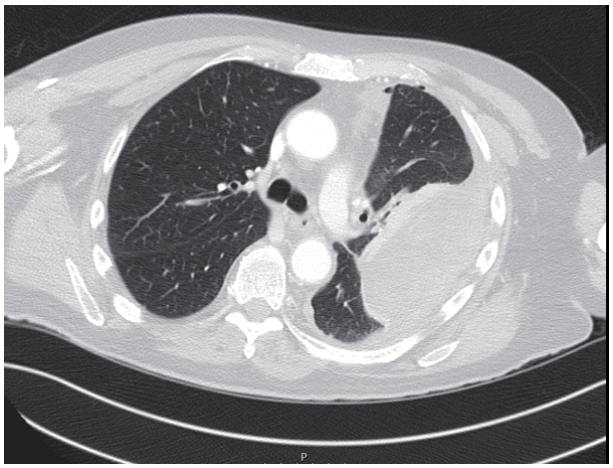

Figure 4.
Lung window computed tomography representative of a loculated left empyema. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust.

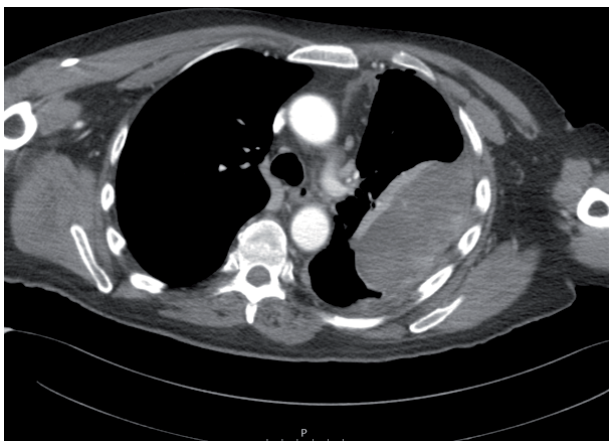

Figure 5.
Mediastinal window computed tomography representative of a loculated left empyema. Guy's and St. Thomas' Thoracic Surgery NHS Foundation Trust

Although pleural thickening is found in both parapneumonic effusion and empyema, the pleural thickness is greater in purulent effusions, with the absence of pleural thickening suggesting an uncomplicated parapneumonic effusion (**Figures 4** and **5**).

6. Principles of management for parapneumonic effusion/empyema

Our Unit follows the guidelines of the British Thoracic Society, which are in accordance with the American College of Chest Physician guidelines.

The parapneumonic effusion and empyema are categorized according to radiological, biochemical and microbiological criteria. The staging of the disease based upon these criteria guides the management (**Figure 6**).

Patients can be divided in four categories which require different management:

Category 1: includes uncomplicated parapneumonic effusion with minimal free-flowing fluid (< 10 mm at the chest X-ray) and undetermined microbiology

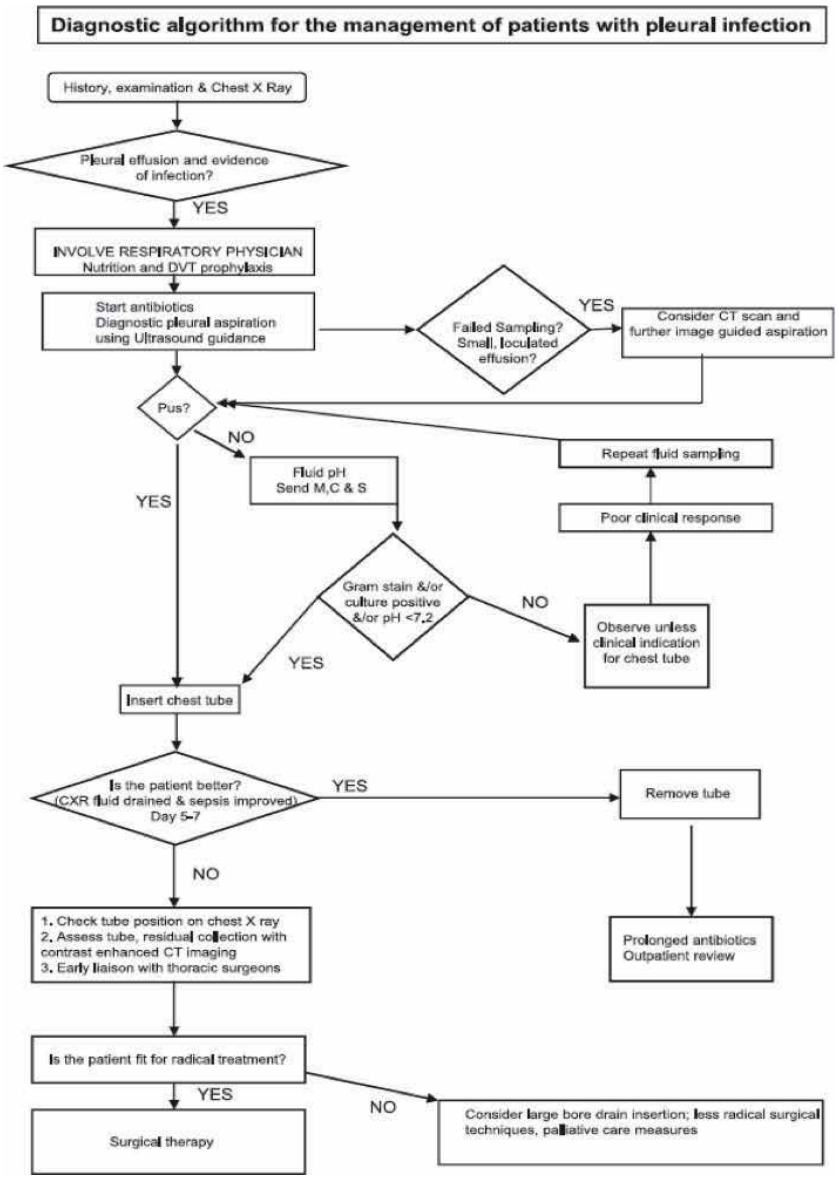

Figure 6.
Management of pleural infection in adults: British Thoracic Society pleural disease guidelines 2010, © British Thoracic Society, 2010.

and biochemistry. Patients in this category can be treated with antibiotics only for the underlying pneumoniae.

Category 2: includes uncomplicated parapneumonic effusion with small to moderate free-flowing fluid (more than 10 mm of collection on the radiography). These patients have a negative culture and Gram stain. pH ≥ 7.2 and glucose ≥3.4 mmol/L.

Patients in this category are treated with antibiotics regimens as the previous category with an addition of a thoracocentesis (to determine the fluid quality) and a chest drain insertion if the effusion is large and the patient is symptomatic.

Category 3: includes complicated parapneumonic effusion with large or loculated collection and thickened parietal pleura. The cultures or Gram stains are positive. Acidotic effusion (pH < 7.2) and glucose level < 3.4 mmol/L.

These patients require, as the previous categories, antibiotic treatment, thoracocentesis followed by chest drain insertion in symptomatic cases.

In presence of a pH < 7.2 a chest drain insertion is mandatory.

Multi-loculated effusions may require multiple chest drains and/or intrapleural thrombolysis.

Early surgical intervention with video-assisted thoracoscopic surgery (VATS) is recommended for evacuation of pleural fluid, debridement with the disruption of the loculations and decortication in presence of an immature pleural cortex. Early surgical intervention can minimize the impact of the lung restriction in long term effects, allowing a better and faster resolution of the infection and can also reduce the mortality.

Category 4: presence of frank pus which determines empyema. Also, radiological evidence of empyema on the CT scan.

These patients require antibiotic treatment of the underlying pneumoniae, chest tube insertion followed by surgical washout, debridement and decortication aiming for the re-expansion of the underlying lung.

7. Conservative management

When the patient presents in stage I, in most cases, uncomplicated parapneumonic effusions resolve with appropriate antibiotic therapy and drainage is not generally necessary.

It is important to strictly monitor the clinical and radiological evolution to decide if the patient does not respond to conservative treatment. Further pleural fluid sample should be taken to test possible resistance to antibiotics and further imaging considered.

For most community acquired complicated parapneumonic effusions and empyema an empiric intravenous antibiotic regimen that cover S. pneumoniae and the oropharynx pathogens including microaerophilic streptococci and anaerobic bacteria is instituted.

This consists in a third-generation cephalosporin associated with metronidazole or a combination beta-lactam/beta-lactamase inhibitor (amoxicillin-clavulanate, ampicillin-sulbactam).

In case of penicillin hypersensitivity who cannot have cephalosporin, options include carbapenem in single therapy, combination therapy with fluoroquinolone and metronidazole or a monobactam with metronidazole.

Clindamycin has been used for treatment of anaerobic lung infections, however, the increasing rates of resistance among anaerobes makes this antibiotic no longer routinely used for empiric treatment of anaerobic infections.

In case of hospital acquired parapneumonic effusions and empyema the empiric IV antibiotic regimen targets MRSA, gram-negative bacteria (including Pseudomonas spp) and anaerobic bacteria. Vancomycin with metronidazole associated with an antipseudomonal cephalosporin is appropriate. A combination of vancomycin and beta-lactam/beta-lactamase inhibitor is an alternative. However, since the combination of vancomycin and piperacillin-tazobactam is highly nephrotoxic, sometimes linezolid is used in place of vancomycin when piperacillin-tazobactam is used.

In case of penicillin allergy, an appropriate protocol can be vancomycin with metronidazole and an antipseudomonal fluoroquinolone or an antipseudomonal carbapenem.

While most uncomplicated effusions respond well to antibiotic treatment alone, there may be an indication for drainage in selected circumstances: in symptomatic and frail patients early drainage can be considered.

After the establishment of an appropriate antibiotic regimen, a good clinical response with improvement of signs and symptoms is expected. The antibiotic course is usually maintained for at least 7 days and in most of the times the coverage for the anaerobic species is not needed.

Radiographic improvement usually requires 2 to 4 days, especially with no chest drain inserted.

As a general principle, for self-resolving uncomplicated bacterial parapneumonic effusions, the antibiotic therapy can be protracted with good results and resolution, up to 1–2 weeks. Complicated parapneumonic effusions and empyema usually request longer treatment ranging from 3 weeks for a complicated effusion and 4–6 weeks for empyema.

The initial IV antibiotic regimen can be switched to an oral regimen with similar spectrum when the clinical response is clear, and more invasive procedures such as drainage are no longer needed. There is no demonstrated optimal duration of therapy. The duration of treatment is individualized and it is based upon the type of effusion, the adequacy of drainage, clinical and radiographic response to treatment. On top of that, the immune status and efficacy of immune response of the patient plays a primary role in the duration and efficacy of treatment.

7.1 Intrapleural fibrinolytics

In case of complicated parapneumonic effusions (stage 2) which demonstrate difficult resolution with the sole drainage and antibiotics, including circumstances when septations are proven at the imaging, intrapleural t-PA/DNase can be considered.

These are also a valid option in patients not fit for surgery.

These agents are not exempt from side effects, these include chest pain, fever, allergic reactions (more frequently with streptokinase) and pleural hemorrhage (the risk is increased in presence of renal failure, thrombocytopenia, anticoagulation).

Fibrinolytics are neutralized (usually within an hour) by plasminogen activator inhibitors that are increased during pleural infection.

The first Multicenter Intrapleural Sepsis Trial (MIST1), a double-blind prospective and randomized controlled trial of patients with pleural infection randomized in 2 groups

- Group 1 received streptokinase (250,000 IU b.d. for 3 days)
- Group 2 received a placebo

demonstrated no significant difference between the two groups for mortality percentage requiring surgery, radiological outcomes and lengthy hospital stay; therefore, reporting no benefit of the use of intrapleural streptokinase [19].

7% of patients in the treatment group reported serious adverse effects (chest pain, fever, allergy), compared to 3% in the placebo group.

The median length of stay in the streptokinase group was 13 days while in the control group was 12 days, reporting no significant difference.

Death and the need for surgical intervention data were analyzed separately and no difference was found between the groups at 3 or 12 months.

MIST2 analyzed 210 patients with pleural infection assigned randomly to four groups to receive: double placebo, intrapleural tissue plasminogen activator (t-PA) and DNase, t-PA and placebo, or DNase and placebo.

However, the MIST2 trial found that the intrapleural use of tissue plasminogen activator (t-PA) and DNase improved the drainage of infected fluid in patients affected by pleural infections [20].

This study reported that combination of TPA and DNase improves the drainage of empyema reducing the length of hospital stay (6.7 days less than the placebo groups) and the need for surgery (4% of surgical referrals at 3 months in the double treatment group, compared to 16% of surgical referrals at 3 months in the placebo arm).

8. Surgical treatment

Surgical treatment is often indicated in patients with stage III empyema with cortex encasing the lung or empyema that fails to resolve with antibiotics, chest drain insertion and if indicated t-PA/DNase (stage II) or in symptomatic patients despite control of infection and sepsis.

Failure of resolution of the pleural effusion and the sepsis within 5–7 days despite drainage (+/– t-PA/DNase) and antibiotics is indication for surgical treatment.

This involves minimally invasive approach or thoracotomy according to the stage of the disease. VATS is preferred as first approach. Thoracotomy and thoracostomy remain valid alternatives in patients with advanced staged empyema.

8.1 VATS/thoracotomy debridement and decortication

Thoracoscopy has been proven an effective procedure for the treatment of pleural infection and reporting high successful rate around 91% with few complications compared to thoracotomy.

In their study, Brutsche et al. [21] analyzed a retrospective series of 127 patients over a period of 4 years affected by empyema and treated with medical thoracoscopy.

Empyema was defined by frank pus on thoracocentesis or by pH < 7.2 with signs of infection. Chest radiography and CT scan were used to confirm the diagnosis.

Thoracoscopy was performed with a zero-degree scope through a 7 mm trocar.

Post-operative active suction of minus 20 cm H2O was applied together with IV antibiotics for at least one week. They reported 9% of complications (surgical emphysema and prolonged air leak). No mortality was observed. 6% of cases required a thoracotomy and pleurectomy post thoracoscopy.

In a single centre, prospective study, Wait et al. [22] considered stage 2 empyema only. 20 patients were randomized to undergo either video-assisted thoracoscopic surgical decortication (11 patients) or chest tube drainage with streptokinase (9 patients). The VATS group reported higher treatment success (10/11, 91% vs. 4/9, 44%), lower chest tube duration (5.8 ± 1.1 vs. 9.8 ± 1.3 days), and decreased total hospital days (8.7 ± 0.9 vs. 12.8 ± 1.1 days). One death was reported in each group.

The authors concluded that VATS was the preferred primary approach for complex fibrinopurulent parapneumonic empyema.

In a recent Cochrane review, the authors [23] compared surgical with non-surgical treatment for pleural empyema.

The study included eight randomized controlled trials for a total of 391 participants comparing open thoracotomy versus drainage.

Six trials were focused on children and two on adults comparing tube thoracostomy drainage with or without intrapleural fibrinolytics, to either VATS or thoracotomy.

Of note, one trial, in children, showed a statistically significant reduction in mean hospital stay of 5.90 days (mean hospital stay of the control group was 15.4 days) and in complications for those treated with primary thoracotomy.

Seven studies were focused on the comparison between VATS versus thoracostomy drainage. No significant difference in mortality or complications between groups for both adults and children, with or without fibrinolysis, were reported. There was a significant reduction in mean length of hospital stay for patients who underwent VATS, 2.5 days less than the thoracostomy group.

A meta-analysis [24] based on 14 papers comparing VATS to traditional thoracotomy to perform decortication for the treatment of persistent pleural collections, in adults, demonstrated the superiority of VATS in terms of postoperative morbidity, complications and length of hospital stay, and gave equivalent resolution when compared with thoracotomy and decortication.

In 2005, Luh et al. [25] in a retrospective single centre study compared VATS decortication in the treatment of complicated parapneumonic effusion (stage 2) in 145 patients and loculated empyema (stage 3) in 89 patients, over a period of 8 years. Those with empyema had a conversion rate to thoracotomy and decortication of 21.3% compared with 3.5% with complicated effusion. The study reported also a significant reduction in postoperative length of stay on patients with complicated effusion (9.1 days) compared to patients with empyema (18.5 days). Reported perioperative morbidity; effusion group 6.2% vs. empyema group 11.2%. Perioperative mortality: effusion 2.1% and empyema 5.6%.

6.8% needed further surgery for empyema and 9 patients required open drainage or thoracoplasty, 7 patients needed re-decortication or repair of bronchopleural fistula.

Shahin et al. [26] in their single centre study over a period of 3 years reported a 3.5% conversion rate from VATS to thoracotomy to perform a decortication of 3.5% in patients with fibrinopurulent empyema (stage 2) and 19% in those with advanced organized empyema. Postoperative stay was shorter with VATS than thoracotomy (5 vs. 8 days) and no mortality was reported in both groups.

The authors conclude that we should consider VATS debridement and decortication as a first-choice treatment for primary empyema.

Another single centre study [27] analyzed a 10 years-experience comparing VATS decortication in 326 patients and 94 patients after thoracotomy and decortication. 11.4% of VATS cases were converted to thoracotomy. The VATS group reported reduced median post-operative hospital stays (7 vs. 10 days) and significantly reduced postoperative complications (atelectasis, prolonged air-leak, reintubation, ventilator dependence, need for tracheostomy, blood transfusion, sepsis,) and 30-day mortality. The mean operative time was VATS-thoracotomy 97 min – 155 min.

The study concluded that VATS approach is an effective and reasonable first-line option for most patients with complex pleural effusions and empyema.

Cardillo et al. [28] reported for VATS (185 patients) better results than thoracotomy decortication (123 patients) in terms of operative time, pain, postoperative air-leak, hospital stay and time to return to work. Conversion rate to open surgery was 11/185 (5.9%). Empyema recurred only in VATS group 3/185 (1.6%). The analysis of postoperative pain at six months follow-up showed no significant differences.

In conclusion, VATS and thoracotomy (open surgery) show similar postoperative outcomes, however, in terms of morbidity and hospital length of stay VATS is superior to open surgery. Therefore, when possible, VATS is preferred over the thoracotomy approach.

In advanced stage empyema open decortication should be considered: patients with stage III empyema or previous VATS procedures with still trapped lung or symptoms.

8.1.1 Our data

In our Institution regarding a single surgeon experience 103 patients were treated for empyema from August 2015 to May 2021: 33 were female and 70 males, with a median age of 58 years.

34 thoracotomies (33%) and 69 VATS were performed (28 decortications and 75 washout and debridement), Between VATS cases. The average operating time was 82 minutes. The average blood loss was 250 ml, ranging from 0 ml to 2500 ml. We reported 3 (4.3%) conversions for bleeding (one from parenchymal abscess and 2 from the lung surface).

The Median length of chest drain was 4 days and median length of hospital stay of 9 days (range 2 to 38 days): 8 and 9 days in the VATS and thoracotomy group respectively. Postoperative in-hospital mortality was 4.8% (n = 5): One COVID-related and one for progression of malignancy. One intraoperative mortality was due to bilateral PE.

9.7% of patients presented with postoperative complications: pneumoniae, bleeding (one required re-intervention), prolonged air leak, chylothorax and respiratory arrest due to mucus plug. Five patients were re-admitted within the first 30 days post discharge: 3 recurrent chest infections, one PE and one wound infection.

8.1.2 VATS washout and debridement technique

The main goal of the surgery is to achieve an adequate drainage of empyema and full re-expansion of the lung. This is easier if early intervention and adequate antibiotic treatment is undertaken.

Thoracoscopic debridement allows direct vision of the chest cavity facilitating the drainage. Usually the thoracoscope introduction is best performed after opening the pleura under direct vision.

Often, the best place to insert the first port is the intercostal space from which a needle exploration is positive for pleural fluid/pus. Alternatively, the creation of a pleural window by open dissection is requested, in presence of thickened pleural rinds. Subsequently, the port is inserted through the incision.

The risk of blind insertion of a thoracoscopic port in absence of confirmatory exploratory aspiration is to enter into the adherent lung parenchyma with a subsequent damage to the lung surface which will result in a postoperative air leak. Hence, blind port insertion should be avoided.

Following the first port insertion the pleural space is debrided, a second port can be inserted in order to achieve the complete debridement of the chest cavity. With the use of Yohan forceps, endoscopic ring-grasper or the swiping action of the scope itself, all the adhesions and loculations are separated and dissected in order to create space and have a clear vision of the chest cavity.

Repeated warm saline irrigations help loosen adhesions as well as improve vision by sucking and draining blood and purulent material.

A helpful maneuver to release adhesions is the use of endoscopic instruments to hold the membrane and twisting it from outside the port, which allows to peel the fibrinopurulent membrane effectively.

Most of the time, two ports are sufficient in case of early intervention, to clear the cavity. In presence of thick membranes, a third port may be required in order to achieve complete release of the trapped lung.

When satisfied with the debridement and subsequent lung re-expansion, port sites are closed and chest drain is inserted in the pleural cavity.

These procedures are often related to considerable bleeding related to the inflammatory state of the tissues. This generally stops following lung re-expansion. However, bleeding from intercostal vessels need to be controlled with coagulation

diathermy, endoclip or bipolar diathermy device. Arterial bleeding needs careful identification and control before intercostal drain insertion and ports closure.

It is generally preferred to start with a keyhole approach and then convert to an open thoracotomy if required by emergency or impossibility to complete the debridement/decortication.

Conversion to open thoracotomy is also appropriate in patients who do not tolerate single lung ventilation, uncontrollable bleeding or damaged structures not accessible by VATS.

Timing is crucial when surgery is discussed in the management on stage II or III empyema. Decortication is associated with prolonged hospital stay, bleeding, bacteremia and hypotension. The need of decortication may be less than expected if early treatment is started with antibiotics and VATS debridement of the pleural space. Na open decortication should be probably deferred when infective process is resolved and natural remodeling of the pleural space is completed. An open decortication in presence of chest infection and not defined cortex can cause worse sepsis, prolonged air leak and poor lung re expansion.

Aquamantys © bipolar sealer uses radiofrequency energy and saline simultaneously to provide hemostasis and it is useful to control bleeding from the chest wall surface, as well as, from the lung parenchyma. It is provided with endoscopic handpiece and can be used in keyhole surgery, such as, VATS.

8.2 Thoracostomy

Rarely, when all the other interventions fail (antibiotics, tube thoracostomy, fibrinolytic therapy) and in patients not fit for major surgery with advanced stage empyema with thick cortex, an open thoracostomy should be considered, this can be obtained with a small rib resection and creation of thoracostomy. The empyema resolving process takes approximately 60–90 days.

The stoma needs multiple daily dressing changes, sometimes, a wound vacuum-assisted closure (VAC) device facilitate drainage of the empyema. However, this device can facilitate or worsen the creation of a bronchopleural fistula.

When compared with conventional management of open window thoracostomy, VAC therapy accelerates wound healing and improves re-expansion of residual lung.

Palmen et al. [29] retrospectively analyzed all 242 patients with empyema in a 19.5 years' experience. 19 patients had a recurrence of empyema, which required a thoracostomy. 11 patients were treated with VAC therapy in addition.

The non-VAC group consisted in 8 patients.

Thoracostomy-only group received saline-soaked gauzes application in the cavity, with daily dressing changes.

The total duration of open window thoracostomy and the duration of VAC therapy were 39 ± 17 and 31 ± 19 days, respectively.

All 11 patients were amenable for subsequent closure using pedicled muscular flaps.

In 2 patients, VAC therapy alone resulted in complete closure of the thoracostomy.

Four patients died from complications (1 bleeding, 3 recurrent infections) during follow-up. The average duration of OWT was 933 ± 1,422 days.

9. Conclusion

Parapneumonic effusion stage I can be managed conservatively with antibiotics treatment and chest drain insertion, in stage II VATS debridement and fibrinolytics

are recommended, in stage III VATS decortication should be considered the first treatment option considering better outcomes compared to thoracotomy. In case of septic patients or severely trapped lung open decortication should be considered. The preference is to delay the open decortication at a later phase if VATS failed to reduce the risk related to open decortication: bleeding, prolonged air leak and worsening sepsis.

Conflict of interest

The authors declare no conflict of interest.

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Section 3

Chest Tubes and Indwelling Catheters

Chapter 3

Chest Tubes

Mohit Kumar Joshi

Abstract

Insertion of intercostal drainage (ICD) tube is one of the commonest surgical procedure that is life saving in certain circumstances. Although the procedure is being used for long, yet there is no consensus in its management. The procedure is simple to perform but the incidence of the complications, which primarily occur due to improper positioning of the tube and poor post-procedural care, is as high as 40%. It is therefore essential that all clinicians should be familiar with this simple, common and lifesaving procedure. This chapter provides a comprehensive overview of various aspects of intercostal drainage including the prerequisites, technique of insertion, post-procedural care, complications and common pitfalls in the management of chest tubes in the light of the recent advances and updates.

Keywords: Chest tube, Tube thoracostomy, intercostal drainage tube, ICD tube, Thoracentesis, Thoracostomy drainage

1. Introduction

Insertion of intercostal drainage (ICD) tube is a common procedure that is required to drain the abnormal intrapleural collection. As the name implies, it is insertion of a tube through the intercostal space to facilitate the drainage of abnormal collection in the pleural cavity. The procedure is also known as tube thoracostomy and thoracostomy drainage. The earliest reports of thoracic drainage dates back to 5th century BC [1, 2].

The aim of thoracostomy drainage is to:

i. Remove fluid and air from pleural cavity as promptly as possible.

ii. Prevent drained air and fluid from returning to pleural cavity.

iii. Restore negative pressure in pleural cavity to help re-expand the lung.

Although, the procedure has been in practice since long, there is still no consensus in the management of chest tubes and there remains great variability in practice. The procedure of inserting a chest tube is simple, definitive in treating a majority of thoracic pathologies and may be life-saving in certain situations. However, improperly placed chest tubes and poor post-procedural care may increase the morbidity and is associated with complications in up to 40% of patients [3, 4]. It is therefore imperative that all clinicians should be well versed with this simple yet life-saving procedure.

In this chapter, we will discuss various aspects of intercostal drainage including the prerequisites, technique of insertion, post-procedural care, complications and common pitfalls in the management of chest tubes in the light of the recent advances and updates.

2. Characteristics of an ideal thoracostomy tube

An ideal thoracostomy tube should:

i. Allow collected air and fluid to drain out from the chest.

ii. Contain a one-way valve to prevent air and fluid from returning back into the chest.

iii. Allow maintenance of negative intra-pleural pressure (the normal intrapleural pressure is −3 mmHg that decreases further on inspiration).

iv. Have provision for applying higher negative pressure to help in expanding the lung.

v. Allow accurate measurement of drained fluid and air.

3. Indications for inserting chest tube

Tube thoracostomy is required to drain any abnormal collection in the pleural cavity, that includes:

i. Air: Pneumothorax

ii. Fluid: Pleural effusion

iii. Blood: Hemothorax

iv. Pus: Empyema

v. Chyle: Chylothorax

vi. Prophylactically following cardio-thoracic surgery to drain post-operative collection of air, fluid or blood

4. Commercially available chest tubes

The modern, commercially available chest tubes are soft and pliable that are either made up of Polyvinyl chloride (PVC) or silicone (**Figure 1**).

The red rubber or malecot tube drains (**Figure 2**) are sometimes used as thoracostomy tubes mostly in resource constraint settings because of their low-cost, however their use is not advisable as they are difficult to retain, get kinked easily, wither rapidly and at times may break.

Chest tubes come in various sizes from 6 French gauge (F) to 40 F. Larger the size of the tube, greater is its diameter. One F is equal to 0.033 cm. To know the diameter of the tube from the F size, one need to multiply F size by a factor of 0.033, so a chest tube of size 24 F will have an internal diameter of approximately 0.8 cm.

Some chest tubes are available with metallic trocar that has a pointed end (**Figure 3**).

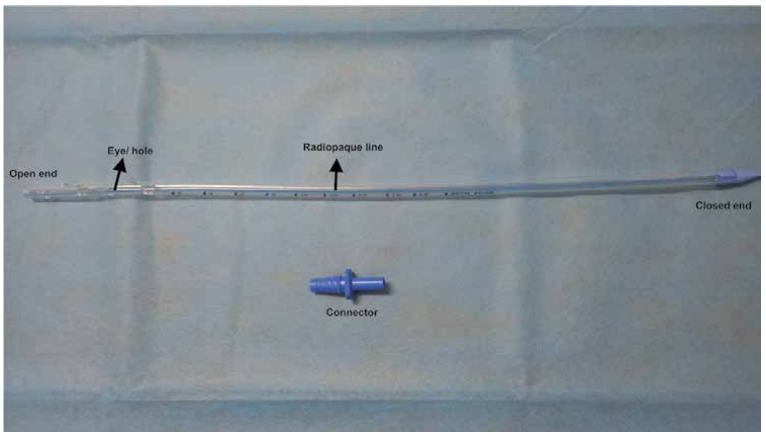

Figure 1.
Intercostal drainage tube (chest tube).

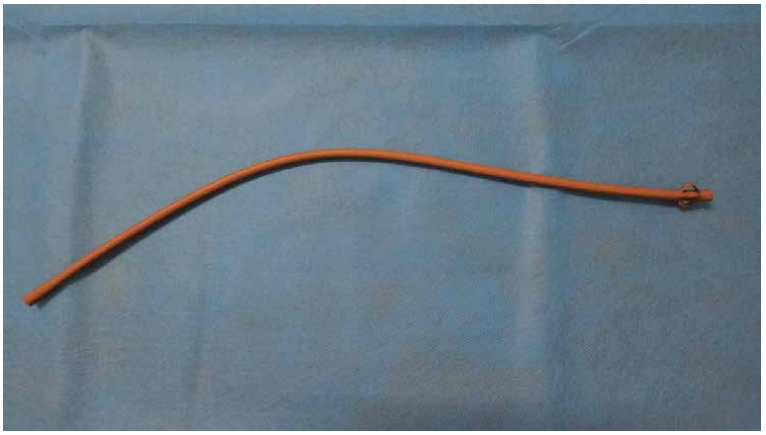

Figure 2.
Malecot (red rubber) tube drain.

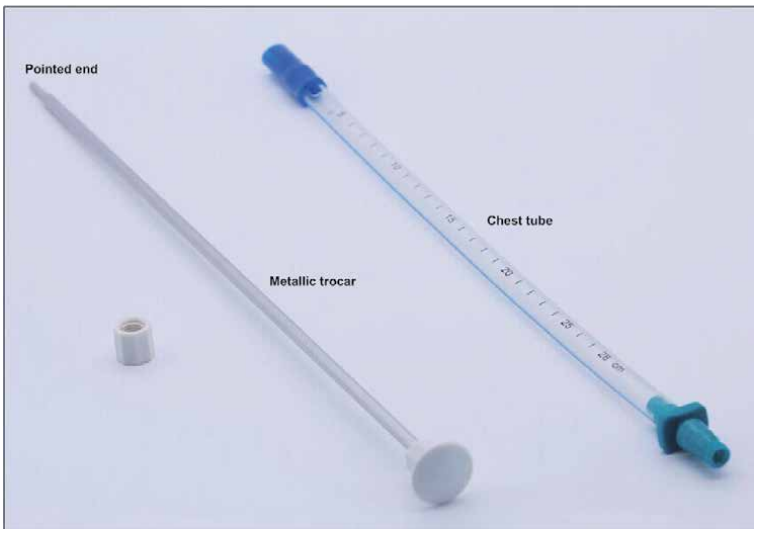

Figure 3.
Chest tube with metallic trocar.

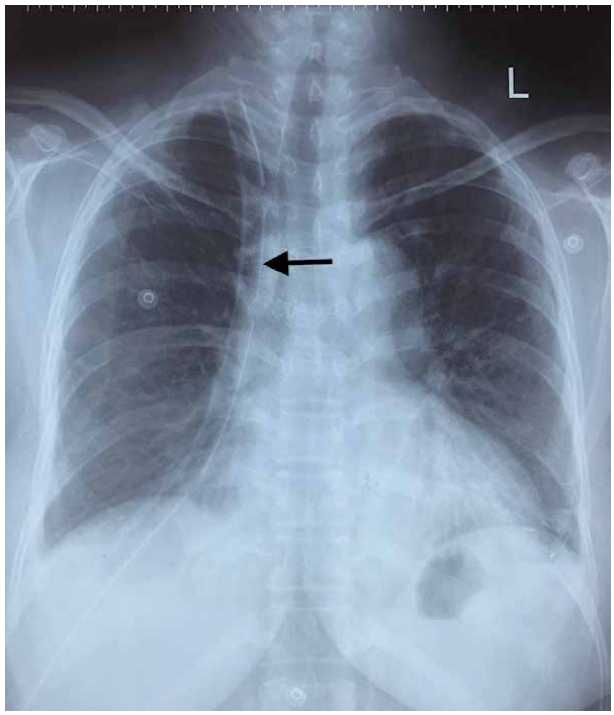

Figure 4.
Radiopaque line in the chest tube visible on x-ray (arrow).

These are meant to insert in intercostal space after making a small skin incision, without dissecting the intercostal muscles. Although, this makes the procedure fast, there is a higher risk of injury to the intrathoracic organs and as such use of chest tubes with trocars should be discouraged [3, 5, 6]. Most of the chest tubes are open from one end while the other end is sealed. There are side holes or eyes on the tube and the markings are printed on it. There also is a radiopaque line all along the length of the tube that helps in identifying the position of the chest tube on X-ray (**Figures 1** and **4**).

5. Before inserting the chest tube- the preparation

5.1 Consent

Insertion of ICD tube is a surgical procedure and like any other surgery, a written informed consent is required prior to the procedure. Consent may not be possible in cases where the patient requires urgent tube thoracostomy as a lifesaving measure and when he/ she is unconscious, unattended or is in extremis.

5.2 Preparing the trolley: Equipment required

Following instruments and equipment are required for inserting the chest tube. One must ensure the availability of all necessary equipment beforehand to avoid any difficulty during the procedure.

1. 5 ml syringe with a suitable local anesthetic. Preferably 2% lidocaine with adrenaline.

2. Sponge holding forceps
3. Bowl with solution for painting
4. Number 11 surgical blade with handle
5. Sheets for draping
6. A pair of medium sized curved artery forceps
7. An appropriately sized chest tube: See the section on 'selecting the size of chest tube.
8. Silk No.1 suture on cutting needle
9. Needle holder
10. A pair of tooth forceps
11. Prepared underwater seal bottle or bag.
12. Gauze pieces
13. Adhesive tape for dressing

5.3 Selecting the size of chest tube

The chest tubes are available in various sizes ranging from 6 F to 40 F. There is a general understanding that large-bore tubes are required to drain fluid and small-bore tubes are sufficient to drain air. There have been numerous studies on this issue, however there is no conclusive scientific data to support this idea. Large-bore tubes have been related to higher incidence of pain and patient discomfort without any significant advantage in draining the intra-pleural fluid. In various studies, small-bore tubes have been found to be equally effective to drain pleural effusion and hemothorax [7–11]. This has generated wider interest in use of small-bore tubes for thoracostomy. Conventionally, for most of the clinical conditions requiring tube thoracostomy a 24–32 F chest tube is inserted, depending on the expected underlying pathology, however tubes smaller than 24 F may be sufficient to drain pneumothorax.

5.4 Preparing the under-water seal

The reservoirs for collecting the pleural drainage are available either in the form of bags or single or multiple chambered plastic bottles (**Figure 5A** and **B**).

In both of these reservoirs, there are markings for calculation of effluent. In addition, there is also a marking for 'initial fluid level'. Before connecting the reservoir to the chest tube, a sterile fluid like normal saline should be filled till this mark. As the chest tube is connected with the tube in the reservoir that remains below the 'initial fluid level', the air from the environment cannot gain access to the pleural cavity, however the intrapleural collection may egress easily into the reservoir, thus it functions as a one-way valve or 'under water seal'.

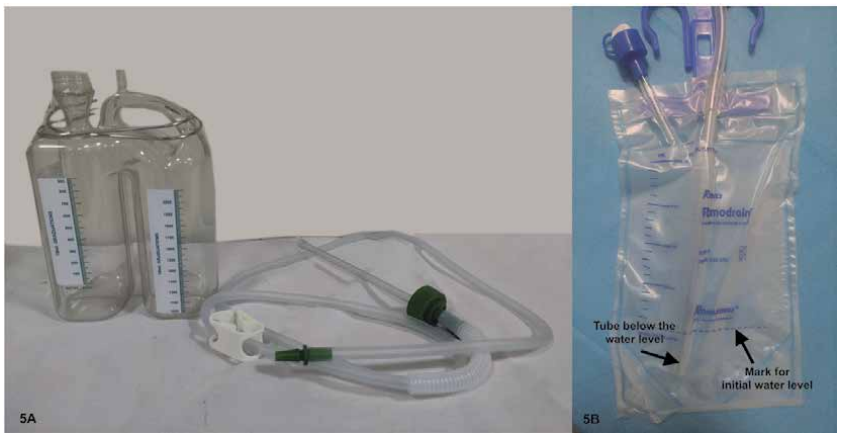

Figure 5.
A: Two chambered plastic bottle and B: ICD bag.

5.5 Local anesthesia: type, amount and technique

Any suitable local anesthetic is appropriate for the procedure. Plain Lidocaine 2% solution and Lidocaine 2% with adrenaline are commonly used drugs for ICD insertion. A volume of nearly 5 ml is sufficient to anesthetize the local site. Local anesthesia may not be required where the patient is obtunded or unconscious and ICD insertion is required urgently.

6. Inserting the chest tube

The step by step procedure is demonstrated in the video supplemented with this article.

Inserting Intercostal drainage tube: step by step.

6.1 Position of the patient

Although the ICD can be inserted while the patient is sitting, leaning forward with the forearms resting over a stool, the supine position is less cumbersome and more comfortable for both patient and the doctor. In addition, the patient may not be able to sit for the procedure due to the underlying clinical condition. We prefer to insert ICD tube in supine position. The patient lies on the table close to the edge with arm abducted over the head if possible.

6.2 Identifying landmarks

The ideal site of inserting ICD is 4th or 5th intercostal space just anterior to the mid axillary line. One may calculate the desired intercostal space by considering sternal angle as landmark. The rib attached to the level of sternal angle is the second rib, subsequent ribs can be counted while palpating the chest wall distally and laterally. There is an alternative way of counting the ribs and the intercostal

spaces which is quick and is particularly helpful in obese patients and in presence of subcutaneous emphysema. The level of the nipple in males and inframammary crease in females can be taken as a reference point- a line drawn from this point laterally to a point where it intersects the mid-axillary line is marked and the site for insertion of the chest tube is just anterior to this.

In case, the chest tube is being inserted prophylactically during thoracic surgery, the site of insertion is selected under vision in appropriate intercostal space.

6.3 Steps of the procedure

A wide area around the predetermined site of ICD insertion is painted with a suitable antimicrobial solution (Chlorhexidine or Povidone-iodine) and is draped. If the patient is awake and conscious, 5 ml of local anesthetic solution (preferably 2% lidocaine with adrenaline) is infiltrated in the overlying skin, intercostal muscles and pleura at the site of ICD insertion. Before injecting the local anesthetic, one should ensure that the needle is not in a blood vessel by pulling the plunger of the syringe back. For the adequate effect of local anesthesia, it is prudent to wait for at least 2 minutes before making the incision.

An incision measuring nearly 1.5–2 cms is made by a number 11 surgical blade at the predetermined site of ICD insertion along the long axis of the rib in the inter-costal space just over the upper border of the lower rib. This is done to prevent injury to the neurovascular bundle that runs along the lower border of the ribs.

Using a medium sized curved hemostatic clamp, the subcutaneous tissues and inter-costal muscles are dissected bluntly till the parietal pleura is reached. By the tip of the closed hemostatic clamp, gentle pressure is then applied till there is a feeling of 'give way' which marks the entry into the pleural cavity. The entry into the pleural cavity is also confirmed by the escape of intra-pleural collection like air, fluid or blood (as the case may be). One should be careful enough not to apply undue force while puncturing the pleura as this may cause injury to lungs or mediastinal structures. The jaws of the hemostatic clamp are then opened while withdrawing the instrument to increase the size of the thoracostomy wide enough to allow the entry of index finger. This should be followed by 'finger thoracostomy'. The index finger is inserted through the thoracostomy site to explore the pleural cavity for presence of any pleuro-pulmonary adhesions. In case they are present, adhesiolysis is performed to create space inside the pleural cavity for the chest tube. This step is important as attempts to insert a chest tube without ensuring space between the lung and the chest wall may injure the lung, cause air leak from the damaged lung parenchyma and such improperly placed tube may fail to drain the intra-pleural collection.

Following finger thoracostomy and ensuring safe space inside the pleural cavity to accommodate the chest tube, an adequately sized chest tube is then taken. The tip of the tube from the open end (the end that should lie inside the thoracic cavity) is held with the tip of the hemostatic clamp and the rest of the tube is held parallel to the instrument. The tube is introduced inside the pleural cavity, the instrument is then released and the tube is inserted gradually by guiding it to lie posteriorly and superiorly by using the same instrument aided by the index finger of the opposite hand to the point till the last eye (hole) on the chest tube is at least 5 cms inside the pleural cavity (this can be confirmed by looking at the markings over the chest tube). The limit to which the ICD tube needs to be put in depends on the build of the patient. In a patient with an average built a length till 8–12 cms inside the chest is sufficient.

The tube is then clamped by using an artery forceps (hemostatic clamp) close to its distal (closed) end. The end of the chest tube is now cut and is connected with

the tubing of the underwater seal using the connector provided with the chest tube. The length of the tube of under-water seal apparatus should not be unduly long as the fluid column in the tube will provide resistance to the egress of intrapleural collection compromising the drainage. A good rule is not to allow any loop in the draining tube between the connector and the tubing of the reservoir.

The chest tube is then fixed by silk suture no.1. For better fixity, it should be anchored on either side. While fixing, one must ensure to take deep bites through the soft tissues close to the tube. Fixing the tube by taking superficial bites (including skin only) may leave potential space around the tube at the site of entry in the intercostal space which may lead to subcutaneous emphysema in cases of pneumothorax and may increase morbidity. Some clinicians prefer purse string suture for fixation of the tube but that leaves an ugly scar following removal of the chest tube and as such is not necessary. A dressing is now applied at the ICD site and the tube may then firmly be reinforced at the site by using adhesive tapes. This completes the procedure.

The free drainage of the collected material from the pleural cavity and the movement of the column of the fluid in the tube confirms the adequate position of the chest tube. The chest should now be auscultated, improvement in the breath sounds suggests success of the procedure. A chest X-ray is then performed for confirmation of proper positioning of the tube radiologically.

Some authors advocate creation of an oblique passage or 'tunnel' in the chest wall to insert the tube, primarily to decrease the incidence of recurrent pneumothorax following removal of the chest tube [12]. In this technique incision is made one intercostal space below the pre-determined site of thoracostomy, the skin and soft tissues of the chest wall are then bluntly dissected to reach the site of thoracostomy thereby creating a curved passage through the chest wall for introduction of the chest tube. This requires additional time at the expense of no added advantage and therefore is not required.

7. Post-procedural care

7.1 Nursing the patient with chest tube

Utmost care should be exercised while nursing a patient with chest tube. The reservoir should remain below the level of the chest at all times. Raising the reservoir above the chest level may result in passage of the fluid from the reservoir back into the pleural cavity. While turning or shifting the patient, one must ensure that the tube is not held or entangled in the patient's bed. This may result in accidental displacement or dismantling of the tube. The outlet of the reservoir should remain open at all times especially in patients with pneumothorax or air leak. The closed outlet of the reservoir may lead to failure of decompression of pneumothorax leading to development of life-threatening tension pneumothorax. For the same reason, the tube should not be clamped at any time except while changing the fluid in the reservoir, collecting a sample of effluent or while planning to remove the chest tube. The patient should be closely monitored during this period.

The patient should be motivated for active physiotherapy and incentive spirometry (**Figure 6**).

This aids in faster resolution of pleural collection and thereby early removal of the ICD tube. In case, the patient is unable to do active physiotherapy, passive physiotherapy should be performed. All efforts must be made to ambulate the patient early. The chest tube must be secured carefully while patient mobilizes and the drainage bag (reservoir) should be kept well below the thoracostomy site.

Figure 6.
Patient performing incentive spirometry.

The ICD site should be carefully examined every day for signs of local infection like peri-tubal inflammation or tenderness. The dressing needs to be changed in case it is soaked. Extreme care must be taken while dressing the ICD site lest the tube is displaced or dismantled. The patient should be clinically monitored every day and the volume of drained fluid should be charted carefully in the patient's record. The reservoir should be emptied once it is full up to 3/4 of its capacity. A new reservoir with prepared under water seal or disposable reservoir (in case of digital chest tube drainage systems) is kept ready while changing the reservoir. In resource constraint settings the same reservoir may be reused. It is important to follow universal precautions while changing the reservoir. The chest tube is clamped and the filled reservoir is disconnected from the tube, the new reservoir is then connected or fluid is filled up to the 'initial water level' mark (or till the outlet tube is at least 2 cms below the water level) in case one contemplates to use the same reservoir. Once the reservoir is reattached, the tube is unclamped. It is important to prepare the equipment beforehand while changing the reservoir to keep the time of occlusion of the chest tube to minimum possible.

The practice of performing daily x-ray has been questioned by many authors and it is suggested that this may not be required if there is pleura to pleura apposition in the post-procedure x-ray and the patient is improving clinically [13].

7.2 Use of analgesics and antibiotics

Appropriate oral or parenteral analgesics are administered depending on the underlying condition for which tube thoracostomy was necessitated. There has been much debate on the use of antibiotics following tube thoracostomy. There is no evidence to support the routine use of prophylactic antibiotic therapy following the procedure [14, 15]. However, the antibiotics may be needed for other associated causes for which tube thoracostomy was performed like in empyema thoracis or in a patient of trauma with soft tissue injuries.

7.3 Use of suction

The use of controlled suction (−10 to −15 cm saline) to the outlet of the reservoir may help in faster resolution of intrapleural collection and promote early pleura to pleura approximation. This is most useful following pulmonary resections

and may decrease the incidence of persistent post-operative space problems. In our practice, we apply overnight suction in patients undergoing pulmonary resection surgery (except following pneumonectomy). At times, the application of suction may result in pleural pain, the amount of suction should be decreased in such situations. In case of increased air leak on application of suction, the suction may be decreased or avoided altogether.

7.4 What to do in case the tube is blocked?

Blockage of thoracostomy tube is not uncommon and occur frequently in hemothorax. Careful observation of the ICD tube and the ensuring drainage of the fluid are paramount to detect this complication early. If appropriate measures are taken in time, the possibility of maintaining the tube patency are high.

Various manipulations can be performed to restore the patency of blocked ICD tube. These include tapping, milking and stripping of the tube. These measures are successful only with partial blockage of the tube and should not be performed routinely to prevent blockage. There is theoretical possibility of generation of high intrapleural pressures with stripping and milking. Some authors have raised concern that this may cause pulmonary injury, however we have not observed any clinically significant adverse effects of these procedures. The practice of flushing the blocked tube by instilling sterile solutions should be discouraged as this may increase the chances of introducing infection from outside with resultant increase in the incidence of empyema. Some clinicians have used novel methods like using a fogarty balloon catheter to unblock the chest tube [16] or use of advanced systems to either prevent clot formation inside the tube [17] or wipe the inside of tube to unblock it [18].

7.5 How to collect a sample from the chest tube

A loop is formed in the ICD tube and the intrapleural fluid is allowed to accumulate in this loop. The tube is then clamped proximal to this collected fluid. With all aseptic measures the external surface of the ICD tube near its connection with the tubing of the reservoir is cleaned with alcohol based antiseptic solution. The tube is then disconnected from this end and the sample is collected in a sterile container. The ICD tube is then reconnected with the reservoir tube and is unclamped.

8. Removing the chest tube: when and how?

There are no fixed or universally agreed criteria that applies to all patients for guiding removal of the thoracostomy tube. There is great heterogeneity in practice, however the rule of thumb is that the chest tube should be removed once it has served its purpose. If the patient is clinically well, there is no more air leak than on forced expiration, no expanding subcutaneous emphysema, no blood, pus or chyle in the effluent and the volume of the fluid being drained is less than 250 ml, the tube can be safely removed. In case of residual space following pulmonary resection with persistent low volume air leak (no more than on forced expiration) beyond day 5, the chest tube may be clamped for up to 24 hours and a repeat x-ray is performed. The patient should be closely monitored during this period for tachypnoea or dyspnea. In case the patient remains asymptomatic and the pneumothorax does not worsen, the chest tube may be removed. The same may be done in case of persistent non-expanding effusion. This practice however, carries the risk of serious side effects if the patient monitoring following clamping of the tube is not diligent. The use of digital chest tube drainage devices might obviate this risk. The chest tube

may be safely removed if the air leak is <40 ml/ min over 24 hours [19]. Alternatively, in patients with prolonged air leak (beyond day 5), a Heimlich valve may be applied to the chest tube and the patient may be followed on outpatient basis with a plan to remove the tube later allowing more opportunity for the residual lung to expand. We have recently proposed a protocol for removal of chest tubes following thoracic surgery that have enabled us to decrease the chest tube indwelling time [20].

In some specialties like Colorectal and Gynecological Surgery, the Enhanced Recovery After Surgery (ERAS) protocol has been well established. This has recently been proposed for patients undergoing oncological major lung resection surgery too. The guidelines suggest that chest tubes may safely be removed with a non-chylous fluid output of up to 450 ml/ day in absence of air leak or minimal air leak detected by the digital chest tube drainage systems [21].

The view is equally divided regarding removal of the chest tube during end-inspiration or end-expiration [22, 23]. In a Randomized Controlled Trial by Bell RL et al., there was no significant difference between the complications following removal of the chest tube at either the height of inspiration or expiration and both methods were considered safe [23]. The incidence of recurrent pneumothorax is likely to be multifactorial and correlates poorly to the method of chest tube removal alone [23, 24]. We prefer to remove the chest tube by a swift motion followed immediately by sealing of the thoracostomy wound by appropriate dressing material irrespective of the phase of respiration.

9. Complications

The complications of tube thoracostomy may be divided into 3 phases:

1. During insertion of the tube:
    i. Hemorrhage from the ICD site
    ii. Injury to the lung and the mediastinal structures
    iii. Misplacement of the tube
2. During the indwelling time of the chest tube:
    i. Displacement or dislodgement of the tube
    ii. Subcutaneous emphysema
    iii. Kinking
    iv. Blockage
    v. Fracture of the tube
    vi. Empyema thoracis
    vii. Wound infection
    viii. Re-expansion pulmonary edema

3. Following removal of the tube

    i. Recurrent pneumothorax or pleural effusion

    ii. Thoracostomy site pain

Hemorrhage from the ICD site may be avoided by carefully siting the thoracostomy incision on the upper border of the lower rib in the desired intercostal space. This avoids the damage to the neurovascular bundle that runs along the lower border of the rib. All aseptic measures should be taken while inserting the chest tube and later while handling the tube during the post procedural care to prevent wound infection and empyema. Care should be exercised while nursing and mobilizing the patient with chest tube to prevent accidental displacement or dislodgement of the tube.

To prevent re-expansion pulmonary edema, the pleural cavity should be gradually decompressed. Sudden evacuation of more than one liter of fluid from the thoracic cavity should be avoided. It is desirable to monitor the intrapleural pressure while draining large amount of fluid from the pleural cavity. The intrapleural pressure should not be allowed to fall below −20 cm saline at any point of time.

10. Common pitfalls in chest tube management

A pitfall is different from complication and is defined as a hidden or unsuspected danger or difficulty that may lead to adverse events. The awareness of a pitfall and preparation to act swiftly in such eventuality may help in averting the complication arising from it. Following are the common pitfalls in ICD tube management:

i. Missed diagnosis: ICD tube placed in a patient with large diaphragmatic hernia suspecting it to be a loculated pneumothorax. A careful history and diligent look at the x-ray will avoid this pitfall (**Figure 7A** and **B**).

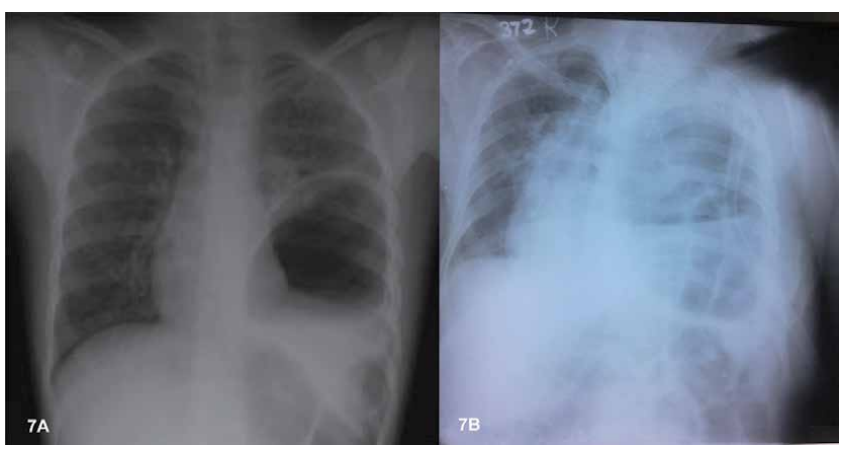

Figure 7.
A: Left sided diaphragmatic hernia with large gastric shadow. B: Chest tube inserted in a patient of diaphragmatic hernia misdiagnosed as hydropneumothorax.

ii. Placement of ICD on wrong side: One should confirm the side with pathology before putting the chest tube. The history of the patient, clinical notes and the radiological findings should be correlated to correctly identify the side of pathology.

iii. A large thoracostomy incision may result in potential space around the chest tube. This coupled with fixation of the tube by superficial skin suturing results in development of a closed plane in the subcutaneous tissues. Peri-tubal air leak in this situation may lead to massive surgical emphysema with attended morbidity and mortality.

iv. Avoiding digital exploration of the pleural cavity may result in injury to pulmonary parenchyma in addition to improper positioning and kinking of the tube (**Figure 8**).

v. One must perform 'finger thoracostomy' before inserting the chest tube to avoid this from happening.

vi. Use of tubes with trocar and applying undue force while gaining entry to the pleural cavity may result in injury to various thoracic, mediastinal or intra-abdominal organs.

vii. Poor placement result in a tube that may be:

a. Too in: may impinge on to the mediastinal structures (**Figure 9A** and **B**).

b. Too out: the eye (hole) of the tube may lie in the subcutaneous tissues with resultant subcutaneous emphysema (**Figure 10**).

c. Mispositioned or kinked resulting in poor drainage (**Figures 11–14**).

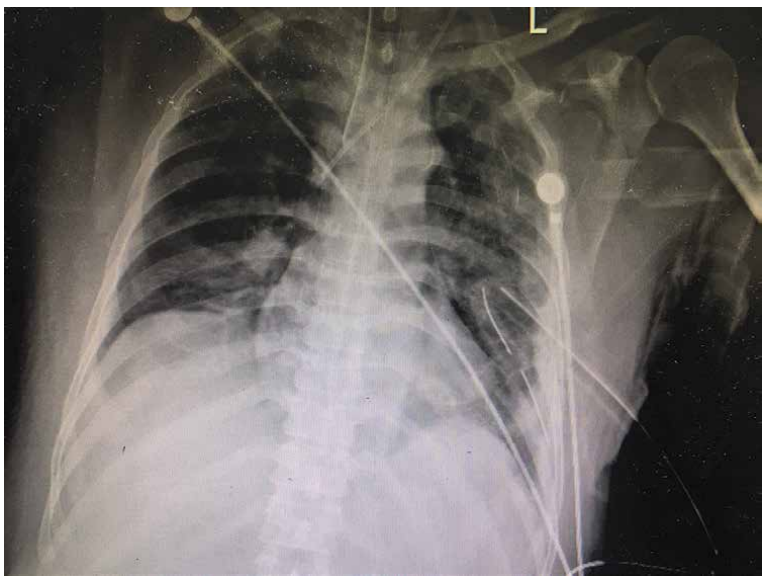

Figure 8.
A kinked chest tube.

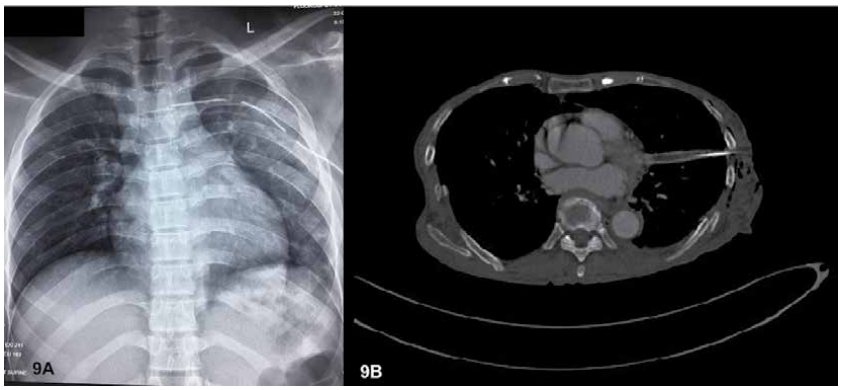

Figure 9.
A & B: Chest tube impinging on mediastinal structures.

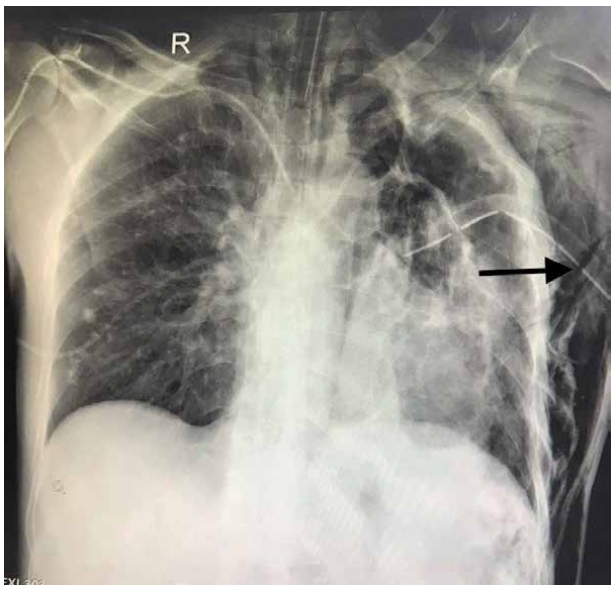

Figure 10.
Eye of chest tube in subcutaneous tissues with subcutaneous emphysema.

d. Poor fixation of the chest tube may result in accidental displacement or dislodgement (**Figure 11**). The chest tube should be anchored properly with number 1 silk suture. An additional suture from the opposite side improves the fixation and decreases the chances of this mishap.

e. Improper filling of the reservoir (under water seal) with sterile solution so that the outlet tube is not beneath the water column may result in pneumothorax.

f. Raising the reservoir above the level of the chest may result in drainage of the collected material back into the thoracic cavity. The reservoir should remain below the chest level of the patient at all times.

g. Clamping the tube while shifting or mobilizing the patient may result in tension pneumothorax. The outlet of the reservoir should be kept open at all times to prevent this.

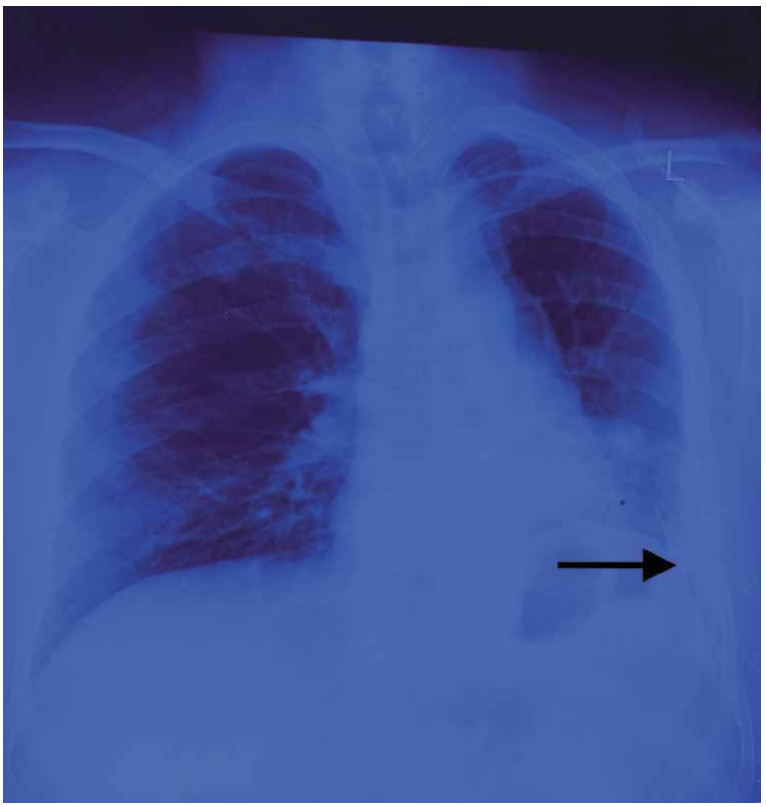

Figure 11.
Chest tube (arrow) about to come out.

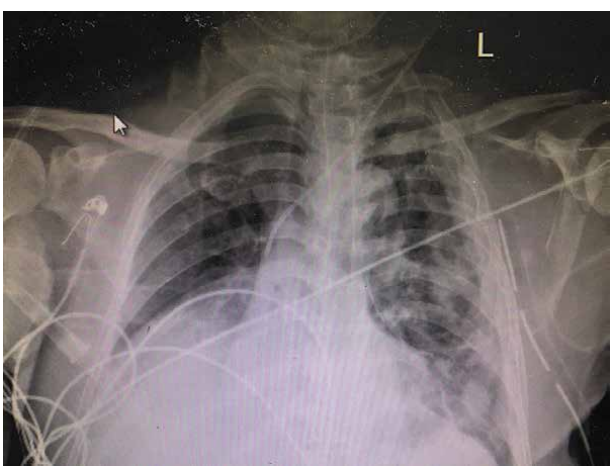

Figure 12.
Chest tube lying outside the chest wall.

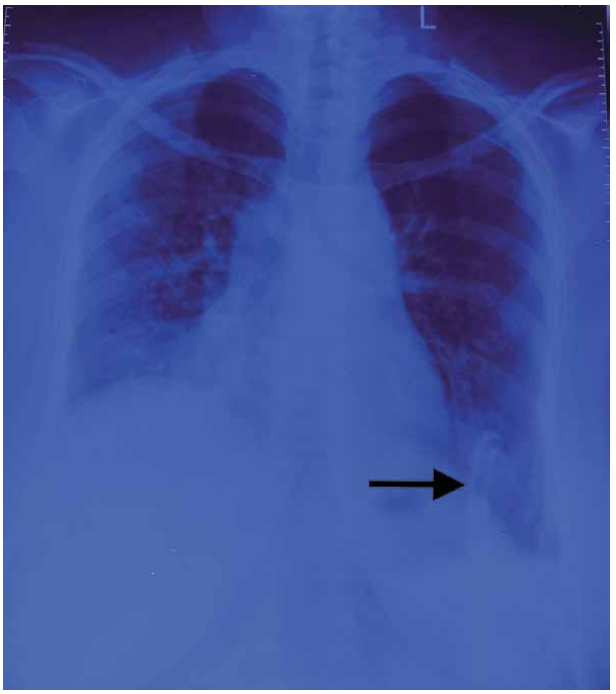

Figure 13.
Mispositioned tube over the diaphragm (arrow).

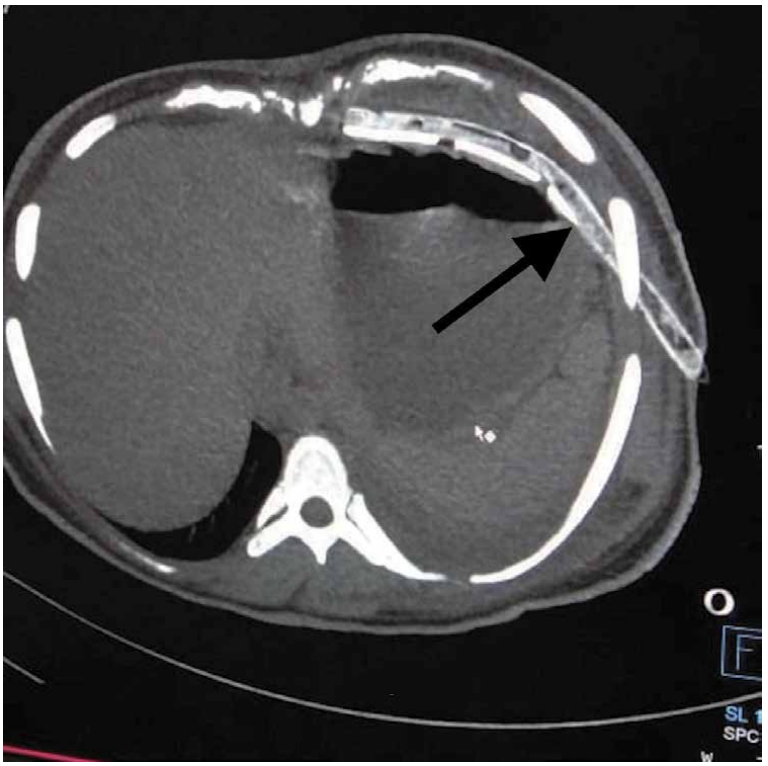

Figure 14.
Mispositioned tube lying in abdomen (arrow).

11. Advances in chest tube drainage systems

With the advancement in technology, newer equipment has become available that may help in decreasing some of the complications associated with the tube thoracostomy, make the assessment of drainage more objective and accurate thus helping in better management of ICD tubes. Some of the advancement in the recent times are:

i. Devices for better fixation of the chest tubes: Some devices are available that claim better fixation of the chest tubes [25], others have been tested on animal models and may soon become available [26].

ii. Digital chest tube drainage systems: This has been perhaps the most significant advancement that is now the part of most modern thoracic surgery units (**Figure 15**).

The use of these drainage systems has been associated with improved decision-making regarding chest tube management, decrease complications, improved quality of life and reduce the hospital stay [27–29] These are light weight, portable system with a disposable reservoir that may be replaced once full. The main advantages of this system are:

- It does not require an 'underwater seal' thus eliminating the risk of accidental pneumothorax and passage of drained material from the reservoir back to the chest.

Figure 15.
A patient being managed on digital chest tube drainage system following thoracotomy.

- It allows accurate measurement of drained fluid and air over time and thus helps in assessment of the trend of drainage (**Figure 16A** & **B**).

This may help the clinician in making decision for removal of chest tube more objective and accurately.

- Continuous controlled suction may be applied to the chest tube that remains constant irrespective of the position of the drainage system.

- The patient may easily carry the device while ambulation without the risk of changes in pressure effecting drainage or accidental drainage of the collected material back in chest.

    i. Chest tube systems with inbuilt mechanism to keep the inside of the tube clean to prevent clogging [16, 18].

    ii. Motion activated systems for prevention of clot formation inside the chest tube: This system uses motion-activated energy (vibration) primarily to prevent early adhesion of clots within the internal chest tube surface and thus maintains the patency of the chest tube [17].

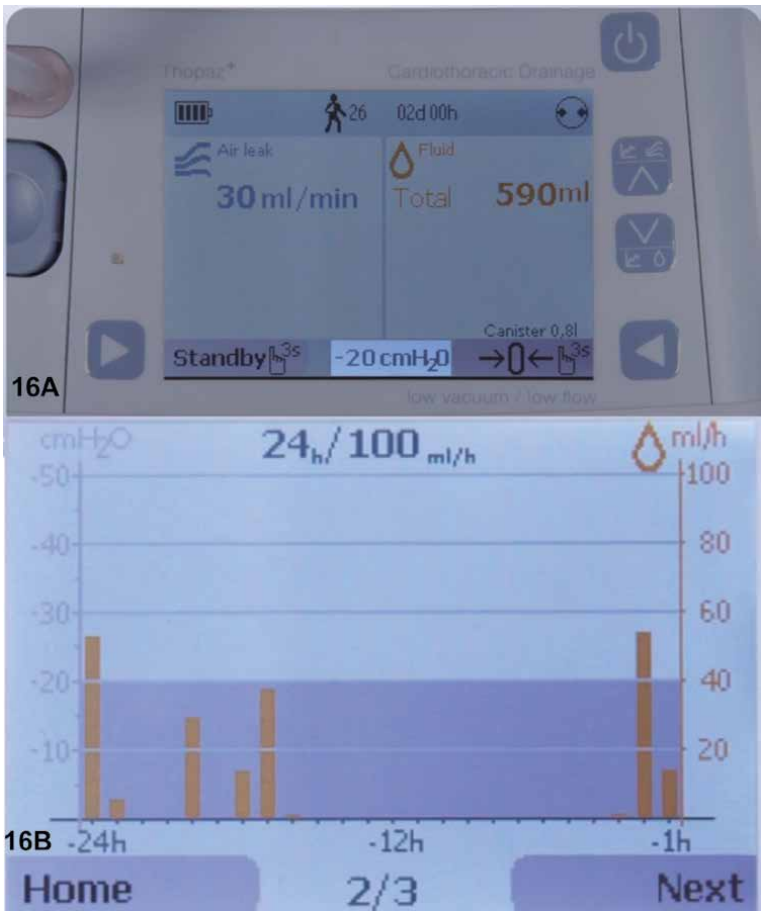

Figure 16.
A & B: Objective depiction of air and fluid drainage and trend of drainage in digital chest tube drainage system.

12. Conclusion

Insertion of ICD is a common, simple yet lifesaving procedure. All clinicians should be well versed with the appropriate technique of inserting the thoracostomy tube and various aspects of its management. Although simple, it is associated with high rate of complications that primarily occur due to improper technique of insertion or poor post-procedural care. Awareness of these factors will make the procedure safer with improved outcome.

Conflict of interest

There are no conflicts of interest.

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Chapter 4

Indwelling Pleural Catheters

Yuvarajan Sivagnaname, Durga Krishnamurthy, Praveen Radhakrishnan and Antonious Maria Selvam

Abstract

Indwelling pleural catheters (IPC) are now being considered worldwide for patients with recurrent pleural effusions. It is commonly used for patients with malignant pleural effusions (MPE) and can be performed as outpatient based day care procedure. In malignant pleural effusions, indwelling catheters are particularly useful in patients with trapped lung or failed pleurodesis. Patients and care givers are advised to drain at least 3 times a week or in presence of symptoms i.e. dyspnoea. Normal drainage timing may lasts for 15–20 min which subsequently improves their symptoms and quality of life. Complications which are directly related to IPC insertion are extremely rare. IPC's are being recently used even for benign effusions in case hepatic hydrothorax and in patients with CKD related pleural effusions. Removal of IPC is often not required in most of the patients. It can be performed safely as a day care procedure with consistently lower rates of complications, reduced inpatient stay. They are relatively easy to insert, manage and remove, and provide the ability to empower patients in both the decisions regarding their treatment and the management of their disease itself.

Keywords: indwelling pleural catheters, recurrent pleural effusion, malignant effusion, pleurodesis

1. Introduction

Indwelling pleural catheters (IPC) are now being considered worldwide for patients with recurrent pleural effusions [1]. It is commonly used for patients with malignant pleural effusions (MPE) and can be performed as outpatient based day care procedure. Talc pleurodesis and indwelling pleural catheters are the standard of care therapeutic options for the patients presenting with symptomatic malignant pleural effusions. In malignant pleural effusions, indwelling catheters are particularly useful in patients with trapped lung or failed pleurodesis. IPCs are effective, both in terms of symptom control and costs, and can dramatically improve the quality of life for patients who have traditionally needed lengthy hospital admissions.

2. Background

Indwelling pleural catheter (IPC) is a multi-fenestrated flexible silicone elastomeric chest drain with a polyester cuff which envelops the medial portion of the

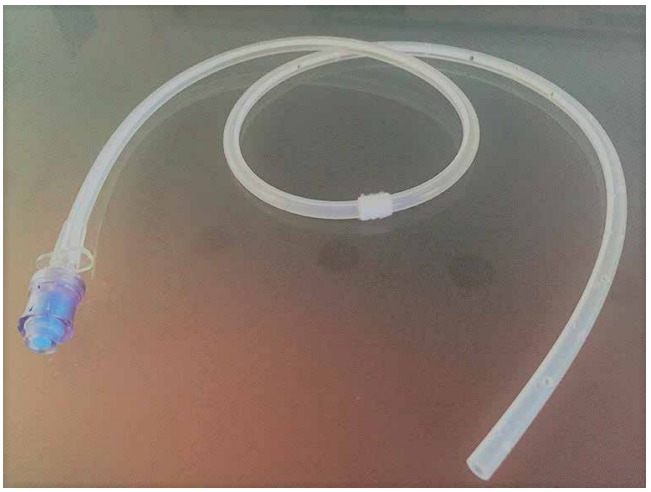

Figure 1.
Indwelling pleural catheter (IPC).

tube. The proximal end of tube has a one-way access valve designed to be attached to vacuum drainage bottles. Its distal part is tunneled through the subcutaneous tissue before placing it in the pleural space (**Figure 1**). Most widely used IPCs are pleurx catheter and IPC by Rockett medical. Pleurx catheter was approved by FDA in 1997 for patients with symptomatic malignant pleural effusions to relieve Dyspnea [2].

Before the advent of IPCs, conventional method for managing recurrent pleural effusions is to place a large bore chest drain with pleurodesis/multiple pleural aspirations. Some centers were able to offer more invasive procedures, such as parietal pleurectomy or pleuro-peritoneal shunting, but these inevitably carried a risk of morbidity and were limited to patients who were fit enough to undergo general anesthesia [3, 4].

3. History of indwelling pleural drains

A widely recognized precursor to indwelling pleural catheter was first described in 1994. Robinson et al. [5] treated 9 patients with recurrent MPE, who had previously failed pleurodesis, with a Tenckhoff catheter, which was tunneled into the pleural space under local anesthesia. Implantable Porta cath was also used in olden days for some patients for intrapleural immunotherapy used in mesothelioma [6].

4. Indications

- Recurrent pleural effusion predominantly due to malignant etiology.
- Trapped lung with symptomatic pleural effusions.
- Recurrent pleural effusion due to benign etiologies such as hepatic hydrothorax [7], chylothorax [8], CKD related effusions, loculated effusions [9], and empyema [10].

5. Contraindications

- Inability for the patient and care givers to handle or tolerate the drain.
- Significant coagulopathy.
- Parapneumonic effusion/empyema.
- Local cellulitis in the insertion site.
- Track metastasis over the proposed insertion site.
- Individuals in immunocompromised state due to systemic diseases.

6. IPC insertion

Most of this procedure can be performed as a day care procedure in outpatient settings. There is no need to admit the patient for IPC insertion unless clinically warranted. It is advisable to stop antiplatelet/antithrombotic medications before the procedure to minimize the risk of bleeding (Aspirin-withheld for 5 days, Clopidogrel—withheld for 7 days. IPC can be inserted in any position which is suitable for drainage. It is preferable to moniter his oxygen saturation and vitals during the procedure. Supplemental oxygen can be given to those patients who are dyspneic with hypoxemia. We often prefer to give supplemental oxygen to all our patients during the procedure.

It can be performed under conscious sedation with local anesthesia. The patient is typically placed in the lateral decubitus position, with the patient lying on the side contralateral to the effusion, although they can be inserted in other patient positions. Bedside ultrasound thorax is to be done which facilitates the site of entry and also helps to quantify the pleural effusion.

Under aseptic precaution, after local anesthetic (Lignocaine 1–2%) infiltration, two small incision are made, one at the pleural insertion point and another one 7–10 cm anterior to this, which will form the proximal end to the tunneled track. The IPC catheter is tunneled along this track with the pro-fibrotic cuff which promotes tissue growth and keeps the drain in-situ, situated approximately a third along the track.

The distal end of the catheter is then inserted into the pleural cavity, using the Seldinger technique. The incisions are then sutured closed, although the catheter itself is not sutured in place. A one-way valve on the external end is then attached to a drainage bag or vacuum bottle system.

7. Drainage

Patients and care givers are advised to drain at least 3 times a week or in presence of symptoms i.e. dyspnoea. Normal drainage timing may lasts for 15–20 min which subsequently improves their symptoms and quality of life. Drainage bottles are commercially available which are connected to proprietary one-way access valve on the external portion of the drain. Training to the patients and their family members has to be done for proper dressing and drainage by connecting the bottles with aseptic precautions. This drainage bottle is primed with a vacuum (**Figure 2**) in order to draw out the pleural fluid usually to a maximum of 1000 ml.

Figure 2.
Vacuum drainage bottles.

8. Complications

Complications which are directly related to IPC insertion are extremely rare [11].

9. Immediate complications

It is common to see a small pneumothorax in the post procedure chest X ray as a result of air being drawn into the chest during insertion. Such appearances may also be produced by trapped lung if significant volumes of fluid have been removed or trapped lung itself is seen in 20–30% of patients with malignant pleural effusion.

Large significant pneumothorax should prompt consideration of Iatrogenic injury to underlying lung and may warrant an extended period of observation before discharge.

Subcutaneous emphysema is also been documented post procedure. This demonstrates another reason why careful consideration should be given to track length, as if it is made too long there is the possibility of a fenestration remaining in the extrapleural space.

Post procedure pain can be seen in significant number of patients which can be usually managed with analgesics. Severe pain and discomfort should prompt concerns over irritation or damage to intercostal nerves. Patient may experience pain and discomfort at the end of drainage which indicates complete drainage of the pleural space which is often seen in those with underlying trapped lung. Wound Dehiscence in IPC is rarely reported.

10. Late complications

Initially there was a concern surrounding the risk of associated infections with indwelling pleural catheters. However, data from the observational and randomized studies have demonstrated a reassuring low incidence of associated infection

with one large multicenteric multinational retrospective study of over a 1000 patients, demonstrating a 4.8% IPC-related pleural infection rate [12]. Common organisms implicated are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and Enterobacteriaceae which differ from the pattern what we usually expect in parapneumonic effusions [12].

Usually the infectious complications are reported after 6 weeks after the insertion of IPC which indicates they are not secondary to the insertion but due to later spread of pathogens from the patient's skin or lung parenchyma [13]. Proper care, IPC dressing and drainage techniques would help to minimize the risk. Reassuringly, the mortality rate from IPC-related infection is low (0.29%) and most of these patients can be managed with oral antibiotics [12]. There is no need to remove IPC as most patients responds very well to the therapy. If this approach is unsuccessful, then patient may require hospital admission for intravenous antibiotics and placing the catheter on continuous free-drainage to facilitate resolution of the infection. In case of loculated pleural effusions, Intrapleural thrombolytics like tissue plasminogen activator and DNAase can also be given via IPC [13].

In malignant pleural effusion insertion of IPC may lead to track metastasis usually occurs in malignant mesothelioma [14]. Reported cases in the literature are sparse, but the incidence of metastasis occurring appears to be just below 1% [15]. Diagnosis can be made clinically or using ultrasound-guided biopsy [16], followed by prophylactic radiotherapy to prevent track metastasis. There is nothing to suggest that radiotherapy damages the IPC [14] and treatment, based upon small case series, tends to be successful, obviating the need for drain removal [17].

IPC blockage is another concern one need to consider since patency of the tube is important for effective drainage. This can be managed by daily saline flushing and on rare occasions in presence of thick loculated collection, one may use intrapleural fibrinolytics. The loss of electrolytes, immune factors or proteins has occasionally been raised as a concern of the long-term use of IPCs [18].

Catheter fracture is rare and may occur when an IPC is removed. The polyester cuff promotes inflammation and fibrosis which leads to tight anchoring of the catheter makes it difficult to remove. The risk of catheter fracture is reported to be about 10% [19]. This is usually managed by surgical exploration or just leaving the catheter fragments inside the body. No complications have been reported from retained fragments of IPC.

11. Use of IPC in malignant pleural effusions (MPE)

Conventional approach to the patients with symptomatic MPE is therapeutic pleurocentesis and subsequent pleurodesis. Various pleurodesis agents can be used but the most commonly used agent is talc which can be guided by thoracoscopic talc poudrage or instillation via standard chest tube. Option of IPC insertion is given to the patients who had developed trapped lung. IPCs are the ideal way for palliative care as they can be sited easily and quickly, and can be drained as often as is required to alleviate symptoms, allowing for consistent improvement in the breathlessness which will afflict the vast majority of patients with a malignant effusion [20] and improvements seen even in those with trapped lung [21].

Davies et al. [22] compared the use of IPCs to standard talc slurry via chest drain in patients who had not previously undergone pleurodesis. The trial used self-reported dyspnoea scores as its main outcome measure, showing that 6 weeks after randomization there was no significant difference between the two treatment arms. Some of the secondary endpoints appeared more favorable in the IPC group, including the proportion of patients who achieved a clinically significant relief

in their symptoms (86 vs. 74%); the median length of initial hospital stay (0 vs. 4 days), and the median number of days spent in hospital for drainage over the following 12 months (1 vs. 4.5 days). Eventhough the study is underpowered, similar findings were reported elsewhere. Intrapleural Fibrinolytics can also be guided with IPC in case of multiloculated/septated effusion.

It also holds the potential to allow direct anti-cancer therapy. Sterman et al. [23] showing that patients with MPE or mesothelioma can be safely given both single- and repeated-dose interferon-β gene therapy and another group reporting the administration of monthly rituximab via an IPC for a patient with non-Hodgkin's lymphoma [24]. Jones et al. [25] and Rahman et al. [26] studied the use of Docataxel and Lipotechoic acid -T via IPC (Pleurx) respectively with favorable clinical response.

IPC can be combined with pleurodesis agents to achieve higher success rates and early pleurodesis in patients with high output effusion. Tremblay et al. [27] have demonstrated that low-level, repeated doses of intrapleural silver nitrate in a rabbit model can maintain the pleurodesis efficacy of a drug without raising the side effect profile. Dierdre B Fitzgerald et al. studied the use of talc via IPC with malignant pleural effusion and concluded that IPC combined with inpatient talc slurry pleurodesis, followed by daily home drainage provided good success rates [28].

12. Spontaneous pleurodesis

Spontaneous pleurodesis is also possible in patients with IPC which is an added advantage. In a study by Yuvarajan et al. [29] Spontaneous pleurodesis was achieved in 55% of the patients with hepatic hydrothorax who were placed on IPC. Mean time for spontaneous pleurodesis is around 120.8 days. Collated data from various studies suggest an overall spontaneous pleurodesis rate of around 45% for patients with MPE [15], however, some studies have reported significantly higher [30, 31] or lower values [32]. Higher pleurodesis rates, often exceeding 70%, have been noted when more aggressive drainage regimens (daily or more frequent) have been used, or when patients undergo a talc pleurodesis at the same time as IPC insertion [31].

13. Impact of chemotherapy in patients with IPC

Usage of IPC significantly improves the dyspneoa, quality of life and their performance status which is crucial for initiating chemotherapy, as chemotherapy is usually deferred in patients with poor performance status. In spite of this, there is huge concern in the risk of infectious complications post chemotherapy in those patients with IPC. There was no difference in the pleural infection rates in a retrospective analysis of 170 patients who were receiving chemotherapy with IPC when compared to those patients who did not receive chemotherapy [33]. But the decision to place an IPC in those who is already on chemotherapy needs multidisciplinary discussion with oncologist, oncosurgeon, pulmonologist and infectious disease specialist.

14. IPC in benign effusions

The most common causes for nonmalignant pleural effusions are Parapneumonic effusions, effusions due to congestive heart failure (CHF), hepatic hydrothorax (HH) secondary to cirrhosis of the liver and effusions due to renal failure. IPC's are

being recently used even for benign effusions in case hepatic hydrothorax and in patients with CKD related pleural effusions. Yuvarajan et al. [29] did a retrospective analytical study on the use of IPC in hepatic hydrothorax. 30 patients with hepatic hydrothorax were placed with indwelling pleural catheters. Spontaneous pleurodesis was achieved in 18 patients (60%) and IPCs were removed in these patients. Most of the patients (70%) who achieved spontaneous pleurodesis with IPC received at atleast one TIPS (Transjugular Intrahepatic porto systemic shunt) procedure. Mean time in which pleurodesis achieved was 120.8 days (range, 15–290 days). Thus TIPS procedure increases the success rate of pleurodesis with indwelling pleural catheters in hepatic hydrothorax.

IPC placement may be a reasonable clinical option for patients with refractory HH, but it is associated with significant adverse events in this morbid population. Potechin et al. [34] did a cohort study on IPC usage in patients who presented with recurrent effusion in end stage renal disease and concluded that IPC insertion for pleural effusions associated with end-stage renal disease appears safe and effective.

15. IPC removal

Removal of IPC is often not required in most of the patients. However, spontaneous pleurodesis is one of the potential causes for considering its removal. Other indications include pleural sepsis, nonfunctional/defective IPC and Severe pain with local cellulitis which cannot be managed with conservative approach. Removing indwelling pleural catheter is not an easy task. Since the polyester cuff attached to the drain is designed to promote local fibrosis and the removal of a drain can become more difficult with long standing IPC. In addition, advanced malignancy promotes ingrowth of fibrotic strands into the fenestrations of IPC further making the extraction of catheter difficult. For removal, one need to do careful and meticulous dissection of the fibrous material around the cuff following appropriate incisions. In those circumstances of difficulty in removal of IPC, an alternative is to simply leave the drain and to remove only the proximal portion. Fysh et al. [35] described 2 cases of this being undertaken in a small series of complicated removals. In none of the cases in which tubing was left intrapleurally did the patient experience any infective or pain-related complications during follow-up.

16. Conclusion

So IPCs plays a major role in patients with recurrent pleural effusions especially malignant pleural effusions. It is particularly useful in palliative care of the patients with trapped lung and failed chemical pleurodesis. It can be performed safely as a day care procedure with consistently low rates of complications, reduced inpatient stay and the recognition that significant improvements in patients' symptoms. They are relatively easy to insert, manage and remove, and provide the ability to empower patient's in both the decisions regarding their treatment and the management of their disease itself.

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Section 4

Bronchopleural Fistula

Chapter 5

Bronchopleural Fistula after Pulmonary Resection: Risk Factors, Diagnoses and Management

Kristina Jacobsen

Abstract

Bronchopleural fistula (BPF) after a pulmonary resection is rare with some of the most life-threatening consequences and a high mortality rate. Contamination of the pleural space resulting in empyema and spillage of the infected fluid into the remaining lung leading to respiratory distress remain the biggest concerns with BPF postoperatively. There are many patient characteristics and risk factors that can be evaluated to decrease the chance of a postoperative BPF. Presentation of BPF can be early or late with the late BPF more difficult to diagnosis and manage. Many options to treat BPF include surgical repair, conservative management, and endoscopic treatment.

Keywords: bronchopleural fistula, pneumonectomy, empyema, lung cancer, thoracic surgery

1. Introduction

Bronchopleural fistula (BPF) is defined as a central fistulous connection of inspired air between trachea, major, lobar, or segmental bronchus into the pleural space [1, 2]. Or a BPF can occur peripherally when there are connections between the distal segmental bronchus or lung parenchyma and the pleural space [1, 2]. Although rare, managing a BPF is challenging and represents a high morbidity and mortality.

2. Etiology

After an anatomical lung resection, a BPF is rare but severe complications can occur and may be fatal. The BPF incidence after a pneumonectomy for lung cancer is between 4.5% and 20% and 0.5–1% after a lobectomy [1, 3, 4]. The mortality rate after a pneumonectomy is estimated to be 18–71% with a much lower rate for lobectomy [2, 4]. The pleural space is exposed to the endobronchial bacterial flora with the pleural effusion leaking into the major airway and into the peripheral alveolar space. The main cause of death is aspiration pneumonia, empyema, and subsequent respiratory distress [4, 5]. Treatment for BPF after surgery requires emergency

treatment due to patient's lung volume loss and short-term poor respiratory function with surgical damage to the respiratory muscles [5].

The less common causes of BPF include suppurative lung processes such as septic pulmonary emboli, infected pulmonary infarctions, or tuberculosis [6]. Neoplasms with tumor invasion into the pleural space may also lead to BPF. Iatrogenic etiologies due to complications with chest tube insertion, thoracentesis or lung biopsies may result in BPF [6].

When considering different surgical approaches and incidence of BPF, one study evaluated the Society of Thoracic Surgeons and General Thoracic Surgery Database (STS-GTD) to compare outcomes of video-assisted thoracoscopic surgery (VATS) and robotic-assisted lobectomy (RATS) for primary clinical stage I or II non-small cell lung cancer (NSCLC) at high volume centers from 2009 to 2013. This study identified 1,220 RATS and 12,378 VATS patients. The incidence of BPF between these two groups was not statistically significant (0.6% vs. 0.3%, $p = 0.08$) [7]. Another study that included 737 cases of VATS lobectomies and 748 cases of open lobectomies for the surgical treatment of resectable non-small cell lung cancer showed no statistical difference in incidence of BPF postoperatively [8].

3. Risk factors

Certain anatomic, technical, and patient factors lead to increased risk for BPF (**Table 1**). Generally, right-sided pneumonectomy is associated with high risk of BPF. Devascularization of the bronchial stump, diabetes, malnutrition, steroids, neoadjuvant chemoradiotherapy, stump closure, residual carcinomatous tissue, presence of empyema and postoperative mechanical ventilation all lead to increased risk of bronchial stump dehiscence [9, 10].

3.1 Right sided surgery and right pneumonectomy

Generally, right-side pneumonectomy and right lower lobectomy are associated with high risk of BPF and are multifactorial. The right upper pulmonary artery is made up of the apical, anterior, and posterior ascending branches [11]. The apical and anterior branches are located in the front of the hilum and the posterior is located at the posterior segment of the horizontal fissure [11]. The right lower pulmonary artery is divided into the dorsal and basilar segment and is located at the corresponding position of the posterior ascending branch in

Anatomic Factors
Right pneumonectomy
Technical Factors
Devascularization of bronchial stump
Long bronchial stump
Stump closure
Residual carcinoma at bronchial margin
Patient Factors
Preoperative radiotherapy
Presence of empyema
Postoperative mechanical ventilation
Diabetes
Chronic Steroid Use
Nutritional status

Table 1.
Risk factors for bronchopleural fistula after pulmonary resection.

the horizontal fissure [11]. This single bronchial artery supplies the entire right mainstem bronchus whereas the left mainstem bronchus has a vascular supply by two bronchial arteries [9]. During lymphadenectomy if the single artery of the right bronchus is damaged, the bronchial stump becomes ischemic [4].

After a right pneumonectomy, the risk for BPF increases due to the diversion of the entire cardiac output going through the smaller left lung and increased load on the right ventricle [12]. This compensation results in decreasing circulating blood volume, pulmonary hypertension, increased pulmonary pressures, increased pulmonary vascular resistance and right ventricular failure [12, 13]. Loss of the larger right lung may compromise pulmonary function resulting in respiratory failure predisposing the patient to the postpneumonectomy edema syndrome [12, 14, 15]. Larger perioperative fluid resuscitation causes overload of the pulmonary circulation and right ventricle and has been reported to be a poor outcome predictor [14, 15].

Anatomical differences in the right bronchus versus the left are significant factors in increased risk of BPF. The right main bronchus is more vertical and wider than the left increasing the accumulation of secretions in the bronchial stump [4]. The right mainstem bronchus is not naturally buttressed by mediastinal tissue coverage and therefore likely to be exposed to the thoracic pleural free space [9, 15]. The left main bronchial stump tends to be protected and covered by the aortic arch with its surrounding vascularized mediastinal tissue [9, 15]. The left bronchial stump retracts within that tissue under the aortic arch after dissection giving protection from the pleural free space.

3.2 Lymph node dissection

The surgical approach to mediastinal lymph node dissection at the time of pulmonary resection for NSCLC has been a subject of interest for several decades. Accurate pathologic lymph node examination offers the most accurate staging and survival benefit and provides the most significant prognostic factor [16]. Accurate nodal staging increases survival by improved risk categorization, increased detection of candidates for adjuvant therapy and possibly resection of oligometastatic disease [17]. Staging NSCLC may have lymph node metastases even after appearing localized by imaging which makes the extent of mediastinal lymph node removal controversial [18]. Patients with negative nodes by systematic lymph node dissection with early stage NSCLC did not have improved survival with complete mediastinal lymph node dissection [17–19]. Intraoperative lymph node sampling is removal of one or more lymph nodes decided by preoperative or intraoperative findings and is determined by the surgeon [19]. Systematic nodal dissection contains all mediastinal tissue containing lymph nodes and is removed systematically within anatomical landmarks. To meet minimal recommendations, for right-sided cancers, mediastinal lymphadenectomy should contain stations 2R, 4R, 7, 8, and 9. Left side stations 4 L, 5, 6, 7, 8 and 9 should be included [17–19]. Patients should have N1 and N2 node resection with a minimum of N2 stations sampled [17–19]. Some argue that systematic mediastinal lymph node sampling versus mediastinal lymph node dissection is adequate for staging and that complete dissection does not provide survival advantage as most patients with N2 disease die from systemic disease [18, 19].

Lymph node dissection removes tissue from adjacent organs and skeletonization of intrathoracic structures. It includes enblock removal of tissues with cancer cells that includes lymph nodes and fatty tissue within bronchus, trachea, superior vena cava, aorta, pulmonary vessels, and pericardium [17, 20].

Healing of the bronchial stump is delayed due to decreased post-operative blood supply after lymph node dissection. Superior and inferior mediastinal lymph node

dissection for NSCLC is widely performed adjunct to pulmonary resection [21]. Vascular supply to the suture line is watershed from the descending thoracic aorta across the mediastinum and is decreased after mediastinal lymph node dissection [11]. Ischemic bronchitis after lymph node dissection due to decreased bronchial microvascularization negatively influences bronchial stump healing [11, 21]. Lymph node sampling rather than complete lymphadenectomy leading to devascularization of the bronchial stump can permit adequate blood flow to the bronchial stump [21]. Meticulous technique while dissecting around the bronchus is necessary. Preventing devascularization of the bronchus during lymph node dissection can decrease the incidence of fistulization [9, 21].

3.3 Stump closure

The Sweet principles on bronchial closure, emphasized in 1945 are still followed today. Trauma to the end of the bronchus should be minimized and the blood supply must be preserved all the way to the end cut of the bronchus [22]. The cut edges of the bronchus should be carefully approximated [22]. Tissue reinforcement of the bronchial closure should be provided. Clamps should not be used on the proximal bronchus [22]. The major change to Sweet's original description has been leaving the posterior membranous wall longer when cutting the bronchus so it can be used as a flap to decrease tension on the closure [22].

Typically, when the bronchus is pulled to place a stapler, an abrupt onset of vagal-induced atrial fibrillation or bradycardia may occur, along with hypotension that leads to releasing the bronchus [23]. There is a natural tendency with the next attempt to reduce bronchial traction allowing for a longer stump. Using a Roticulator linear stapler is useful to suture and clip the main bronchus close to the carina [23]. To avoid pooling of secretions within the bronchial stump, the stump should be resected back to its origin and for a pneumonectomy divided as close to the level of the carina as possible [9, 24]. This is critical to avoid secretions pooling resulting in infection and stump breakdown.

When closing a very proximal right bronchial stump or thickened bronchial wall, attention must be directed to ensure there is no closure under tension [25]. Closure under tension can be implicated in right sided BPFs at the point of transection of the right mainstem bronchus as it is generally larger than the left [25]. By the Law of LaPlace, the tension on the curved cartilaginous membranes and the fluid within the crenelated surface is higher in the larger orifice of the right bronchial stump [18, 26, 27]. Elimination of the stump diverticulum may reduce surgical line tension [18, 26, 27]. The cartilaginous ring at the origin of the right mainstem bronchus tends to keep the bronchus open and closure should be parallel to the bifurcation spur of the resected bronchus [21, 28]. This decreases the intraluminal deformity of the remaining bronchi with the straightened angle of the longitudinal axes [21,28].

3.3.1 Suture vs. staple closure

The surgical technique of bronchial closure remains controversial and has been studied extensively. The preferred technique of pulmonary hilum vessel ligation and bronchial stump closure has troubled thoracic surgeons for years. In 1909, regarding bronchial stump closure, Meyer advised his inversion technique [29]. In 1945, Sweet described the longitudinal, single interrupted silk suture closure [29, 30]. Dr. Mark Ravitch started using staplers in the United States in 1964 after having observed their early development in Russia [29]. In 1970, Kirksey reported 147 patients who underwent pulmonary resection with disposable and plastic

American staplers called Thoraco-Abdominal (TA) [29]. Reluctance to use vascular staplers due to fear of fatal hemorrhage because of malfunction continued the debate concerning pulmonary hilum vessel manual ligation versus stapled division for many decades [29]. The cessation of the alarm resulted after Asamura et al., in 2002 published results of 842 vascular divisions using endoscopic staples with 0.1% incidence of stapling failure and Yano et al., in 2013 reported 3393 pulmonary vein and artery stapling uses with a failure rate of only 0.27% [29].

It is decided by the surgeon perioperatively to use either manual suturing or stapling methods [31]. None of these have proven superiority in reducing the incidence of BPF and around a 4% rate of BPF has been reported for mechanical stapling and suture technique [31, 32]. Ucvet et al., 2011 reported the weakest part of the line are the end points of the stapler and it may incompletely close the tissue [31]. The staple line that exceeded the length of the bronchus caused a detachment in this end site creating a microfistula. These microfistulas can lead to large BPF along with infections [31]. To provide stump safety, lateral suturing to the weak and risky stump end points was required [31].

Endoscopic staplers have 2 differences compared to conventional TA type staplers: proximal and distal ends can be closed, both division and stapling can be performed simultaneously in one firing motion [31, 33]. The advantages of using endostaplers during a pulmonary resection are: (1) Time required for closure can be reduced, compared to the TA stapler when closure of the distal end of the bronchus and division are required; (2) Both proximal and distal ends of the bronchi are simultaneously and tightly closed without purulent or contaminated discharge which minimizes contamination of the operative field; (3) By selecting the appropriate cartridges, endostaplers can be used safely in vascular division [31, 33].

Suture closure is considered when the bronchial wall is hardened due to calcification [10, 21, 33]. Suture closure is also used with position difficulty due to hilar adenopathy or when the tumor is close to the pulmonary hilum due to a more extensive proximal dissection or a technically difficult bronchial stump [10, 21, 33]. Manual suturing may have the advantage of allowing inspection and assessment of the bronchial mucosa quality. Tumor fragments may also be recovered after the main bronchus is clamped [34].

3.4 Tissue coverage of the bronchial stump

Generally, wound healing has three phases: (1) inflammatory phase (2) proliferation phase (3) remodeling phase [35]. The inflammatory phase is marked by the aggregation of platelets, infiltration with leukocytes and coagulation. This phase begins soon after injury and is followed by the proliferation phase. The proliferation phase is characterized by reepithelialization, fibroplasia, angiogenesis, and wound contraction. Persistent inflammation can last about 2 weeks and likely causes robust adhesion. The remodeling phase takes place over months when the epithelium produces collagen and matrix proteins responding to the injury [35]. The phase of wound healing needs to be considered when deciding which type of bronchial closure is used.

Several options are available for coverage of bronchial closure. To reduce the incidence of postpneumonectomy BPF with soft tissue buttressing after bronchial closure has been debated. Many suggest stump reinforcement in patients with increased risk factors for BPF [36]. Cerfolio et al., 2005 suggests the best way to treat postoperative complications is to prevent it [37]. Local soft tissue coverage may provide vascular ingrowth to promote stump healing and effectively contain a small bronchial stump dehiscence [38]. Algar et al. 2001, found that the absence of bronchial stump tissue coverage was an independent predictor of BPF in the final multivariable model ($p = 0.039$) [32].

3.4.1 Intercostal muscle flap

The intercostal muscle flap causes no functional disability, is easy to harvest, has adequate length to reach most sites, has adequate vascularity and is harvested through the same thoracotomy incision [39]. Sfyridis et al., discovered the group that received an intercostal muscle flap had a lower incidence of development of BPF (0% versus 8.8%; $p < 0.02$) [40]. This flap is harvested prior to chest retraction to not crush the flap and cause damage to the blood supply. The use of cautery to harvest this flap is necessary because it is lacking periosteum and over time will not calcify [9, 37, 40]. The intercostal muscle flap is harvesting by cutting approximately two-thirds of the posterior aspect of the latissimus dorsi and the entire serratus anterior muscle is spared [37]. The rib is not shingled or cut. For harvesting, rib instruments are not used. The intercostal muscle flap, usually overlying the sixth rib is harvested using cautery prior to chest retraction from the under surface of the fifth rib. Starting at the distal end of the muscle under the serratus anterior muscle, cautery is lowered from 40 to 70 and carefully the muscle is dissected with both hot and cold cautery. So the intercostal vein is not injured, the cautery tip is positioned so it is almost parallel with the surface of the fifth rib. The intercostal is posteriorly freed from the sixth rib, past the lumbar-dorsal fascia but not freed from the undersurface of the fifth rib past this structure due to risk of injury to the vein posterior of the fifth rib with any further dissection. The bronchial stump is then tested [37].

3.4.2 Pericardial fat pad

In a retrospective study, Taghavi et al., found 93 patients who underwent pneumonectomy for primary lung cancer, identified no BPF during follow up after using a pedicled pericardial flap for bronchial stump coverage [41]. A pericardial fat pad is harvested from the anterolateral pericardium, pedicled at its cranial part, avoiding inclusion or injury to the phrenic nerve [9, 42]. A wide based pedicle should be used to assure vascularity of the flap. Careful attention should be used to avoid twisting the pedicle. The flap is attached caplike over the bronchial stump with numerous single mattress stitches to avoid devascularization when tied down over the four corners of the bronchial stump. The defect in the pericardium is then reconstructed with mesh [9, 42].

3.4.3 Serratus anterior flap

Bronchopleural fistula is exceedingly rare when a pedicled muscle flap is used to buttress the lobar bronchus, even after preoperative radiation doses of 60Gy or higher are administered [43]. To provide sufficient protection after preoperative radiation, using omental or serratus as a prophylactic buttress for the highly irradiated right main stem bronchus after a right pneumonectomy is recommended [43].

If the patient is believed to be at extraordinary risk of stump complications, larger muscle or omental flaps are used. The serratus anterior flap and omental flap are also used to treat a postoperative bronchopleural fistula to close the fistula [43, 44].

The serratus anterior muscle, one of the workhorse flaps is easily harvested, reliable, often preserved during the initial pneumonectomy due to its utility in dealing with potential complications [44]. The vascular pedicle that runs on the lateral undersurface of the scapula is where the serratus anterior muscle is based [25]. This muscle is mobilized and placed between the ribs in the second or third interspace where it will reach the hilum without tension. The thoracodorsal vascular pedicle is protected throughout the dissection [44]. With tight interspaces, compromising the

vascular supply of the flap, a segment of the third rib can be removed to allow the flap to enter the pleural space easily [25]. The serratus anterior flap is secured with interrupted absorbable sutures to the mediastinal areolar or peribronchial tissue [25] (**Figure 1**). This tissue helps with infection control and healing due to its blood supply emanating from regions beyond the inflamed field [25]. The flap is placed over the bronchial stump with uninterrupted suture to secure the closure [9, 25, 44].

3.4.4 Omental flap

The omentum has superior blood supply and plasticity which allows for a very safe and easy bronchus closure even in the presence of fibrotic tissue or infection [45]. The omentum with a rich blood supply assures adequate antibiotic and oxygen delivery [46]. Delivering potent angiogenic factors, the omentum improves neovascularization of the bronchial suture lines in experimental models. Omental transposition does not impair muscle function or produce chest wall deformities seen with major muscle flaps [46].

The disadvantage of tradition omental flap transposition extends the surgical procedure into the abdomen, requiring laparotomic access. Usually the omentum is mobilized through the upper midline abdominal incision, transposed into the chest via a substernal or anterior transdiaphragmatic route [46]. This description applies a transdiaphragmatic harvesting technique of the greater omentum performed through the standard thoracotomy [46].

The five centimeter incision in the diaphragm is performed radially between its anterior insertion and central tendon through the standard thoracotomy [46, 47]. Oval forceps are used to slide through the diaphragm into the abdominal cavity. Once confirmation the omentum is free of adhesions, the greater omentum gently can be retracted through the diaphragm into the chest. The omental insertion of the transverse colon is identified and divided as extensively as possible. The most distal omental extremity is identified in the chest cavity by gentle traction and subsequently isolated carefully inspecting its vascular supply. After confirming the omental flap has no traction on the stomach or colon, the omentum is sutured to the bronchial stump in the usual fashion. The diaphragmatic incision is closed leaving a large enough opening to avoid strangulation of the omentum. The omental flap is sutured with interrupted sutures to the diaphragmatic opening to further relieve

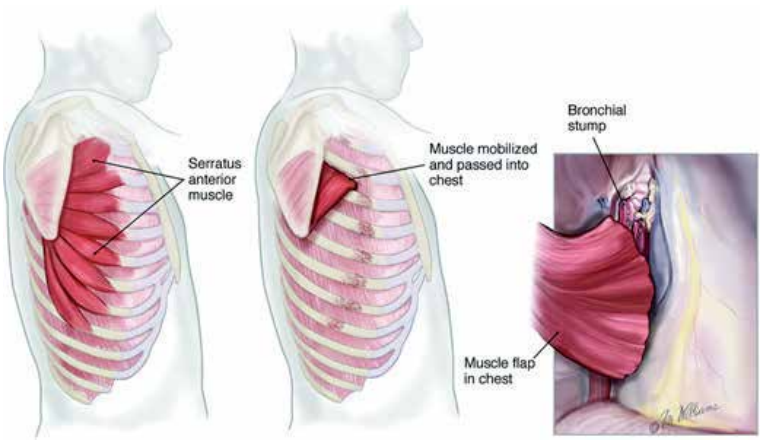

Figure 1.
The serratus anterior muscle is harvested and mobilized into the chest between the ribs in the second or third interspace with rib segmentation. (Sugarbaker D, Bueno R, Burt B, et al, editors. Adult chest surgery. 3rd edition. New York: McGraw-Hill Education; 2020; with permission).

any tension. This technique is appropriate to reinforce the bronchial stump and can be large enough to fill the pleural space [46, 47].

3.5 Residual carcinoma at bronchial margin

Residual disease is characterized by residual carcinomatous tissue within the margin of resection either under visible inspection or under microscopy [48]. Residual disease at the bronchial stump may cause poor prognosis with the increased risk of lung cancer recurrence both distantly and locally [48]. It may also decrease the bronchial stump anastomosis which can lead to a fatal bronchopleural fistula or empyema [48, 49]. In all pulmonary resections, the estimated incidence of residual disease left at the bronchial stump is 4–5% [49]. Asamura et al. reported in 2359 patients that the most important risk factor for a BPF was resection type, followed by presence of residual microscopic tumor at the resection margin ($p < 0.01$) [28]. Survival is worse in patients with bronchial margin residual disease; 1 and 5 year survivals range between 20 and 50% and 0–20% respectively [48]. Mediastinal lymph node involvement is associated with the poor survival in 75–85% of patients with residual bronchial margin disease [48]. Radiotherapy or reoperation may be considered in these patients [48, 49].

3.6 Neoadjuvant chemoradiotherapy

Neoadjuvant chemoradiotherapy is a crucial strategy in multidisciplinary treatments to improve the survival rate and resectability for patients with lung cancer [50]. Especially for patients with advanced lung cancer, chemoradiotherapy can eliminate or reduce the micro-metastasis. Previously published randomized control trials have been integrated with recent systematic reviews and have concluded that neoadjuvant chemoradiotherapy can significantly benefit the survival outcomes in operable patients [50]. Relative to other pulmonary resections, pneumonectomy has been associated with increased morbidity and mortality. The mortality for a pneumonectomy after neoadjuvant therapy has reports with very low mortality (<5%) countered by other reports with alarmingly high mortality (>20%) [51]. For the patient with N2 disease who requires a pneumonectomy, the correct approach can be unclear with the postoperative and intraoperative complications remaining a debate [50, 51]. Bronchial mucosa ischemia is induced by radiotherapy but the mucosal blood flow can recover in eight to ten days after completion of therapy. Early effects of radiation can cause mucosal edema and inhibit capillary angiogenesis [52]. Late effects of radiation cause fibrotic small vessel disease through radiation vasculopathy [52]. Radiation pneumonitis, poor wound healing, and fibrosis can occur in previously irradiated bronchial tissue with a higher perioperative and postoperative complication leading to a bronchopleural fistula [53, 54]. Induction therapy may cause injury to the bronchial microvascularization predisposing to airway complications but published literature does not support the notion that all pneumonectomies after therapy are associated with postoperative mortalities [51, 55].

3.7 Empyema

Empyema is the presence of purulent fluid in the postpneumonectomy pleural space. Postpneumonectomy empyema occurs in 2–16% of patients and can be life threatening [55]. This postoperative complication is associated with BPF which can further increase morbidity and mortality [56]. Most BPFs associated with empyema is monomicribial with most pathogens being Streptococcus or

Staphylococcus species and occur within 10 to 14 days of surgery [52, 57]. A late empyema can occur more than three months to 40 years after a pneumonectomy and is most often acquired via a hematogenous route [52, 57]. After a pneumonectomy, to avoid spillage of infected fluid into contralateral lung the patient should be kept upright at least 45 degrees [52]. An early empyema withing 10 to 14 days after surgery presents with expectoration of purulent sputum and fever [57]. Radiographic findings show a shift of the mediastinum away from the post-pneumonectomy space, development of a new or sudden change in the existing air-fluid level, and failure of the mediastinum to shift normally in the immediate postoperative period [57]. Empyema diagnosis is confirmed by fluid sample in the postpneumonectomy space [57].

3.8 Mechanical ventilation

Mechanical ventilation in patients after a pneumonectomy, subjects the bronchial stump line to increased wall tension and continuous barotrauma [1]. Positive pressure ventilation can be challenging in these patients and the aim is to prevent further lung injury by keeping the airway pressure below the critical opening pressure of the fistula, optimizing pleural suction pressures and provide adequate alveolar ventilation of sufficient gas exchange [58, 59]. To decrease the flow across a BPF, reducing the proportion of minute ventilation provided by the ventilator, minimal levels of positive end expiratory pressure (PEEP), low tidal volumes and respiratory rate are helpful [1, 59]. Adverse effects in mechanically ventilated patients with BPF include loss of effective tidal volume, incomplete lung expansion, inability to remove carbon dioxide and prolonged ventilatory support [59]. The majority of reported studies report a significant relationship between the occurrence of BFP and mechanical ventilation after pneumonectomy [60].

3.9 Diabetes, chronic steroid use, nutritional status

Typically, surgeons consider diabetes mellitus in patients requiring surgical intervention an important contributor to some fatal adverse events [61]. Diabetic microangiopathy alters the vascular bed causing small vessel ischemia impairing proper wound healing [40]. This decreases the oxygen diffusion capacity and the bronchial stump circulation is particularly prone to poor wound healing [52, 61]. The largest retrospective analysis reported by Asamura et al. in 1992, showed statistical results from both univariate and multivariate analysis indicating significantly increased risk of postoperative BPF in patients with diabetes [28].

Preoperative use of corticosteroids is believed to contribute to several postoperative complications which include impaired bronchial healing [62]. In a study by Algar et al. 2001, patients with preoperative steroid therapy were associated with higher risk of BPF ($p < 0.001$) [32]. This same study found hypoalbuminemia to also be related to higher risk of BPF ($p < 0.017$) [32]. Hypoalbuminemia has a negative effect on the healing process, and in order to decrease the BPF risk, an albumin level above 3.5 mg/dl is the goal [63]. Patients requiring a pneumonectomy are usually very catabolic and nutritional assessment is essential in their management [1]. Metabolic alterations induced by the lung cancer tumor affects the nutrition in these patients [64]. These alterations lead to cachexia syndrome with higher levels of the proinflammatory cytokines interleukin-6 and tumor necrosis factor and lower levels of albumin [64]. Malnutrition increases the risk of 90-day mortality rate, postoperative infection and length of hospital stay after a pneumonectomy and a thorough preoperative evaluation is crucial [64].

4. Pathophysiology: clinical features and diagnosis

4.1 Early/acute bronchopleural fistula

An early BPF has a peak incidence within 8 to 12 days after surgery but can occur at any time in the postoperative period [59]. Surgical closure of the BPF is the cornerstone of management. If a BPF is seen within the first 4 days after surgery, it requires exploration as it is likely due to a mechanical failure of the bronchial stump [59]. Early BPFs are normally approached urgently through the previous thoracotomy incision. An acute BPF can be life-threatening due to asphyxiation from pulmonary flooding or tension pneumothorax due to a massive air leak [59, 65, 66] (**Figure 2**). Acute BPF should be suspected in patients who present with fever, dyspnea, subcutaneous emphysema, excessively productive cough of purulent fluid, hypotension, trachea or mediastinal shift, disappearance, or reduction of pleural effusion on the chest radiograph or persistent air leak [25, 59, 65]. Chest radiography monitors the efficacy of BPF therapy and plays an essential role in evaluating the possibility of a BPF after a lung resection [2]. These symptoms appearing should raise the index of suspicion and quick and accurate diagnosis must be made before there is an overwhelming amount of aspiration into the remaining lung [25].

4.2 Late/chronic bronchopleural fistula

Late bronchopleural fistula present in the postoperative period more than 14 days [59]. The subacute and chronic forms present with more insidious symptoms and is characterized by fever, malaise, wasting, minimally productive cough, dullness to percussion on the affected side and reduced air entry with progressive clinical deterioration and varying levels of respiratory compromise [2, 59, 65]. A late BPF is often seen in debilitated or immunocompromised patients with many comorbidities [59]. In the chronic form that is associated with empyema, there is fibrosis of the mediastinum and pleural space preventing the mediastinal shift [59, 65].

Causes of late BPF include foreign body aspiration, refractory infection, chemotherapy and radiotherapy, and blunt chest trauma [67]. The time of interval is 2 months to 20 years between the surgery, therapy or injury and the onset of the late BPF [67].

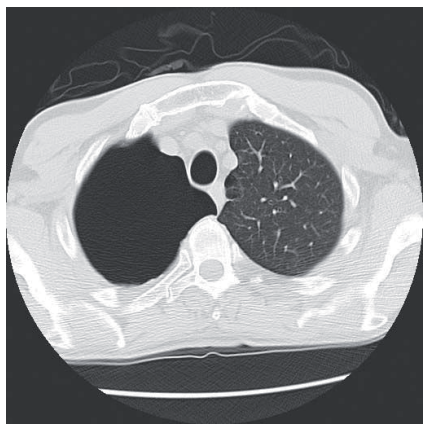

Figure 2.
Axial lung window after right pneumonectomy with large pneumothorax with evidence suggesting communication of the bronchial stump and pleural space. Case courtesy of Radswiki, Radiopaedia.org, rID: 11262.

In late BPF, due to the relatively stable mediastinal structures, conservative treatment is accepted by many investigators as the first step. Closure of the bronchial fistula with endoscopic treatment should be considered [67]. Proper antimicrobial coverage is mandatory along with proper nutrition with patients frequently requiring parenteral or enteral feeding [65]. Aggressive nutritional support and physical rehabilitation should be started early to optimize patients and enhance their recovery [65]. If surgery is indicated for a late BPF, the previous transthoracic approach may be unsafe due to fibrosis with associated inflammation with risk of bleeding and injury to vital structures [68, 69]. With a median sternotomy, approaching well vascularized, healthy, virgin tissues to reach the carina and bronchi may be preferrable and necessary. The advantages to the transsternal approach for BPF closure are avoidance of an inflamed operative field, scarring and adhesions in previous surgical fields and deformities of the thorax with thoracoplasty [68, 69]. The disadvantage of this approach is the infected empyema space is not managed at the time of closure. Previous cardiac surgery is not recommended for this type of approach [68, 69].

Once a BPF is suspected, a Computerized Tomography (CT) Scan with intravenous contrast to map the vasculature and better define the air-fluid levels and the peripheral rind enhancement is necessary [70]. This scan will identify the fistulous tract and will allow evaluation of the potential causes of BPF (i.e. recurrent tumor, staple line dehiscence, pneumonia, abscess, devascularized stump). It will also be simultaneously used to define the anatomic relationship of the adjacent mediastinal structures, vasculature, and diaphragm. A large fistulous tract can be clearly identified and a vigilant search must take place to look for subtle signs of a small BPF such as a change in the appearance of pre-existing pleural air-fluid levels and extraluminal air bubbles adjacent to the bronchial stump. Care must be taken to ensure while the patient is lying flat during the scan that they do not aspirate the pleural fluid through the BPF to the healthy lung [70].

All patients should undergo diagnostic bronchoscopy whether the BPF diagnosis is apparent radiographically or clinically [25]. A large fistula can be visualized but smaller 1 to 2 mm fistulas may be difficult to recognize [25]. Bronchoscopy provides information about the tissue at the level of the stump and condition of the remaining bronchial stump and can assist in deciding definitive repair [25].

5. Management of BPF

Management varies according to the individual patient, but the importance of addressing the risk of contralateral aspiration pneumonia and tension pneumothorax by drainage of the pleural space at time of diagnosis has to be emphasized [69]. The most important action when an acute BPF is suspected is protecting the contralateral lung from spillage of pleural fluid [2]. The primary principle is drainage of the pleural space by chest tube thoracostomy and care should be taken to place the chest tube above the previous thoracotomy incision as the diaphragm will be elevated with the normal thoracic remodeling that occurs after pneumonectomy [25, 59, 71, 72]. Pleural fluid should be sent for total protein, complete blood cell count, glucose, cytology, lactate dehydrogenase, triglycerides, gram stain and culture to evaluate for pleural infection [59]. Although integral for drainage, the chest tube can predispose the pleural space to infection and function as a foreign body [59]. Connecting the chest tube to a digital chest drainage system allows for more accurate and objective assessment of air flow and larger flow values and trend evaluation would provide more detailed information about the size and severity of the BPF [73]. For patients who are mechanically ventilated, the chest tube can

be used for occlusion during the inspiratory phase or to add positive intrapleural pressure during the expiratory phase [59]. These interventions decrease BPF during inspiration and decrease air leak during expiration to maintain positive end-expiratory pressure (PEEP) [59].

5.1 Acute failure of the bronchial stump

Acute failure of the bronchial stump is usually due to bronchial stump dehiscence and expeditious surgical repair with this single-staged intervention is recommended once clinical stabilization is achieved [71, 74, 75]. Given the relative integrity of the tissue, early stage of the infectious process, minimal pleural contamination and no problematic residual space, early reoperation is warranted to reestablish an airtight stump [25, 71, 74, 75]. Exploration with surgical revision by posterolateral thoracotomy with selective intubation and lung isolation of the contralateral mainstem bronchus to prevent further spillage of the remaining lung is recommended [25, 71, 75]. The fistula, if not readily visible can be identified with the assistance of positive pressure ventilation while covering the bronchial stump with irrigation [25]. The pleural space should be completely debrided and irrigated to remove all necrotic tissue [25]. The bronchial stump is refashioned and carefully dissected to decrease trauma to the blood supply [25, 71]. Measured from the carina, all efforts are made to made for the final stump to be less than 1 cm in length [25] (**Figure 3**). The stump may be reclosed with a stapler if their remains sufficient length on initial exploration. In cases where there is too much inflammation to allow stapling, the bronchial stump is mobilized and reclosed with interrupted monofilament sutures [25, 71]. A balance between avoiding too much exposure that may damage blood supply and exposing enough bronchus to avoid tension on the closure much be achieved [25].

5.2 Transposition of muscle flaps to treat BPF

Using a vascularized tissue to reinforce the suture line is the most important aspect of closure [25, 76]. Stump coverage was previously discussed as a preventive measure for BPF. The objective in treating a BPF with vascularized tissue is to obliterate the postpneumonectomy pleural space [25, 71, 75, 77]. Deciding which muscle flap to use depends on which muscle was preserved or damaged from the previous thoracotomy and the amount of space to be filled [71, 75, 77]. The most common muscles used in the pleural space to treat a BPF are serratus anterior, pectoralis major, pectoralis minor, latissimus dorsi, and intercostal muscles [25, 71, 75, 77, 78]. The latissimus dorsi is the most reliable and largest muscle but

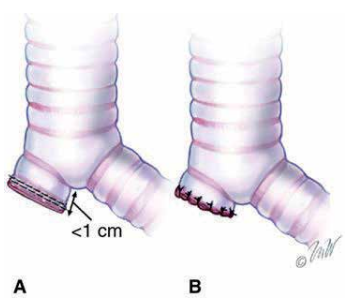

Figure 3.
A. The bronchial stump should be less than 1 cm. After inspection, if there is enough length on the stump, it can be closed with a stapling device. B. With too much inflammation, the stump may need to be sutured closed. (Sugarbaker D, Bueno R, Burt B, et al, editors. Adult chest surgery. 3rd edition. New York: McGraw-Hill Education; 2020; with permission).

may not be sufficient to obliterate the postpneumonectomy cavity if it was already divided in the original thoracotomy [77, 78]. The greater omentum consists of a large fold of peritoneum with excellent blood supply and antibacterial effect, lymphoid tissue, and fat [76, 78]. Using large muscles as the latissimus dorsi, greater omentum and serratus anterior has the advantage to contribute bulk to fill some of the dead postpneumonectomy space sugar [76–78]. In a study by Mazzella et al. 2017, fourteen patients with early BPF were treated with surgical repair of the bronchial stump via thoracoscopy (2) or thoracotomy (12) with omentum and fibrin glue (2) parietal pleural (3), intercostal muscle (1) or pericardial patch (2) with no recurrence of BPF after surgery [79].

5.3 Clagett window and eloesser flap

Treating a BPF with empyema and sepsis may require an Eloesser flap for patients too debilitated or too ill for a decortication or prolonged procedure involving muscle flaps [25, 80, 81]. The difference between the Clagett open-window thoracostomy (OWT) procedure and Eloesser flap is that the Clagett procedure is larger than the Eloesser flap and the Clagett window is temporary to allow complete drainage of purulent drainage in the pleural space [80] (**Figure 4**). The Eloesser flap creates a permanent drainage window in the pleural space [80].

5.3.1 Clagett procedure

In 1963, Clagett and Geraci described a technique as a two-step procedure for the management of postpneumonectomy empyema [81, 82]. This procedure combined an open-window thoracostomy pleural drainage with repetitive irrigation of the infected cavity with obliteration of the space with antibiotic fluid without direct fistula closure [2, 25, 81–84]. The procedure resulted in recurrences of fistulization and prolonged hospitalization and significant mortality. This technique is rarely

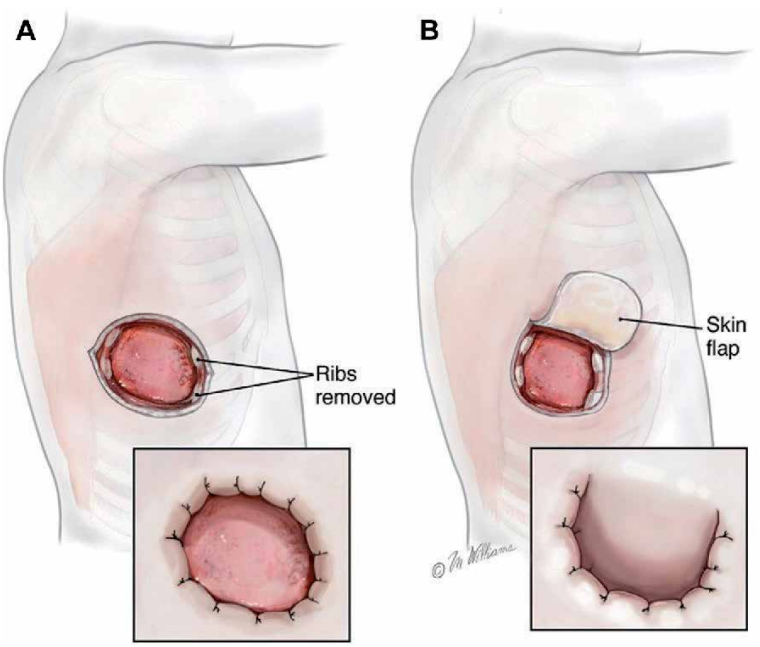

Figure 4.
(A) Clagett window and (B) Eloesser flap. (Sugarbaker D, Bueno R, Colson Y, et al, editors. Adult chest surgery. 2nd edition. New York: McGraw-Hill Education; 2015; with permission).

used and has been modified with initial bronchial stump closure with muscle transposition described earlier [2, 25, 80–84].

Once the BPF is closed and buttressed with muscle transposition, diluted wet povidone-iodine (Betadine) dressings are placed in the thorax and changed every 48 hours in the operating room [81, 83, 84]. This is done for approximately 4 to 6 days until the muscle flap is adherent to the bronchial stump and adjacent mediastinum [81, 83, 84]. Then the pack is changed in the patient's room 3 to 4 times a day. When health granulation is present in the pleural space, the entire cavity is filled with antibiotic solution selected to tailor culture and sensitivity results [25, 81, 83, 84]. In multiple layers to avoid leakage of fluid, the chest is then closed [25, 81, 83, 84].

The modified Clagett procedure involves daily intracavitary dressing changes, lasting for a long period of time and may not allow chest closure. Other ways to accelerate wound healing process were investigated [85]. Wound vacuum-assisted closure (VAC) therapy has recently been evaluated and used in patients with complex infected wounds without the OWT [86]. Bacterial proteinases are microorganisms and play a pathogenic role in an infected wound by consuming oxygen and nutrients that are required for tissue repair [87]. Reducing the bacterial proteinase load in a wound would allow the body to heal [87]. The VAC allows topical solutions to be cyclically flushed into the foam dressing before removal under negative pressure that irrigates, cleans, and removes infectious material from the pleural space [85, 87]. This is done without OWT, decreasing postoperative pain [88]. Recent studies show that as an adjunct to standard therapy, the VAC can decrease pain, hospital length of stay and morbidity in patients with complicated postoperative empyema [85, 88].

5.3.2 Eloesser flap

The Eloesser Flap OWT continues to evolve. A "H" or "U" shaped incision is made above the previous incision over the dependent portion of the space [25, 80]. A segmentary resection of one or two ribs are removed to obtain a window and limit the tendency of the opening to contract and close [25, 79, 80]. Necrotic tissue is debrided and edges of the flap are sutured directly to the parietal pleura with absorbable interrupted sutures to create an epithelized tract which encourages healing and maintains window patency [25, 79, 80]. The window should be not too far inferiorly which may interfere with the diaphragm and not too posterior that would be difficult for the patient to manage [25, 79, 80]. Using moistened gauze, dressing changes are performed until the cavity is decontaminated. Care is taken to prevent cardiac tamponade by excessive gauze inserted in the cavity [25, 79, 80]. The thoracostomy is closed with a thoracomyoplasty when clinical conditions suggest correct timing. In the chest cavity, healthy granulation tissue, improved clinical condition, closure of the bronchial stump and negative cultures of the chest cavity all suggest proper timing [25, 79, 80].

6. Endoscopic treatment of bronchopleural fistula

6.1 Biological glue

Many different biological glues for endoscopic BPF closure are available. Fibrin-based, albumin-glutaraldehyde tissue adhesive, and cyanoacrylate-based glues are the most common [2, 83]. Application technique is performed by a catheter inserted through the flexible bronchoscope and placed above the fistula [2, 83]. The glue is injected into the fistula and creates a plug after a few seconds that occludes the

fistula with instantaneous cessation of air leak expected [2, 83]. Some prefer glue injection with a 21G needle due to less glue displacement and more effective closing of the BPF. This procedure may need to be repeated and endoscopic surveillance and close clinical monitoring is important for signs of failure [2, 83].

Cardillo et al. 2015, reported patients with BPF sized 1 cm or less with a viable bronchial stump were treated endoscopically [89]. The cure rate with endoscopic treatment was 92.3% in very small fistulas <2 mm with mechanical abrasion of the fistula. Cure rate was 71.4% in small fistulas >2 mm and < 3 mm with submucosal injection of 0.5 to 2 mL polidocanolhydroxypolyethoxydodecane at the fistula. This liquid surfactant causes endothelial cell lysis. It induces sclerosis and acts on the venous endothelium via interferences with cell membrane lipids. Cure rate with intermediate fistulas >3 mm and < 6 mm was 80%. Treatment was with n-butyl cyanoacrylate glue injected into the fistula. This mechanically occludes the fistula causing proliferation of the bronchial mucosa and a local inflammatory reaction. Morbidity and mortality rates were 5.8% [89].

6.2 Endobronchial valves

Endobronchial valves (EBV) have been available since 2003 and were originally developed for the reduction of lung volume in patients with emphysema [90, 91]. They were first described by Snell et al., 2005 for BPF [92]. Introduced through a flexible bronchoscope, EBV have a unidirectional valve to prevent airflow into the fistula and will result in atelectasis and collapse of the fistula [90, 91, 93]. This results in decreased or absent air leak. The process of recovery would lead to resolution of the shunt, fibrosis, and eventual extraction of the EBV [90, 91, 93]. Complete elimination of air flow through the BPF does not always occur and does not mean the EBV is unsuccessful. Decreased flows may bring the rate below critical rate flows and allow for fistula healing [91].

6.3 Amplatzer device closure

Many small fistulas (<3 mm) spontaneously heal or heal with glue placed endoscopically [94, 95]. Treatment for BPF endoscopically can bridge to control infection until a patient is able to able to undergo surgical repair [90, 92] (**Figure 5**). Amplatzer

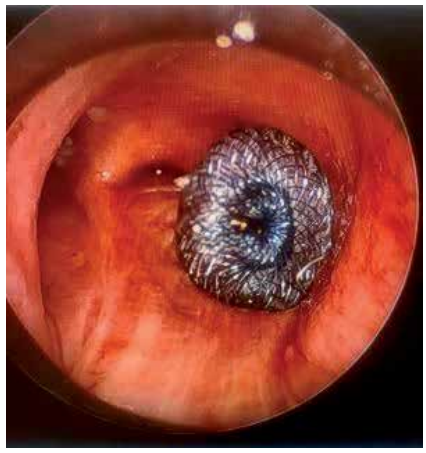

Figure 5.
Amplatzer Muscular VSD Occluder 8mm x 7mm placed to occlude the right mainstem bronchopleural fistula. Image courtesy of Dr. Tarek Dammad, Orlando, Florida.

device is normally used for transcatheter closure of atrial septal defects. This device can contribute to intrabronchial granulation tissue and has good biocompatibility [94, 95]. The tissue growth reduces the risk of displacement. The waist of the Amplatzer device is placed inside the fistula and the two discs are placed at the distal and proximal ends of the fistula [94, 95]. Fruehter et al. 2011 treated nine patients with Amplazter device with BPF and the fistula was successfully closed [96]. After nine months, the results were maintained [96].

7. Conclusion

Improvements in thoracic surgery have decreased the incidence of BPF but mortality remains high. Proactive approaches to risk management and mitigating potential causes for increased chance for BPF preoperatively and intraoperatively are essential to improved outcomes. Expeditious surgical repair for acute BPF, along with new therapies with wound vacuum-assisted closure (VAC) therapy and endoscopic options for small fistulas may all expedite closure of BPF and improve survival.

Conflict of interest

The author declares no conflict of interest.

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Chapter 6

Surgical Challenges of Chronic Empyema and Bronchopleural Fistula

Yu-Hui Yang

Abstract

Chronic empyema has always been a clinical challenge for physicians. There is no standard procedure or treatment to deal with the situation, and multi-modality approach is often necessary. Surgical intervention plays a very crucial role in the treatment of chronic empyema. Since bronchopleural fistula is often seen in chronic empyema patients, therefore it should also be mentioned. In this chapter, the focus will be on the different treatment options, various surgical approaches, and the rationale behind every single modality. Certain specific entity will be included as well, such as tuberculosis infection, post lung resection empyema, and intrathoracic vacuum assisted closure system application. Even with the advancement of technology and techniques, chronic empyema management is still evolving, and we look forward to less traumatic ways of approach with better outcome in the future.

Keywords: Empyema, bronchopleural fistula, open window thoracostomy, VAC, Clagett procedure, thoracoplasty, muscle flap transposition

1. Introduction

Empyema is a common clinical problem to both pulmonary physicians and thoracic surgeons. It affected 65,000 patients annually in the US [1]. Thanks to the advent of antibiotics and continuous advancement of minimally invasive procedures, most acute empyema patients can now receive tube thoracostomy and/or video-assisted thoracoscopic surgeries (VATS) to alleviate the infection with good recovery [2]. Empyema, also known to be pleural empyema or thoracic empyema, is defined as infection in the pleural cavity. The most common scenario is that the patient has a prior or ongoing pneumonia which the infection has extended to the lung surface, causing a series of inflammation and infection response on the visceral pleura and therefore parietal pleura. The products of the infection then accumulate in the pleural space resulting in empyema. Some patients would develop pleuritic pain which they easily mistake it as muscle strains or sprains, so they tend to overlook the real problem and lead to delay diagnosis. There are also a lot of other reasons that can eventually cause empyema, such as trauma, invasive procedures (including thoracic operation), liver abscess, spinal abscess, mediastinitis (because in the vicinity of an infection source) or being transmitted through hematogenous route.

2. Stages of empyema

According to American Thoracic Society classification, empyema is divided into three stages (**Table 1**) [3, 4]. In the early stage of pleural cavity infection, some fibrin would develop in this avascular space along with some body fluid. It is often recognized as parapneumonic pleural effusion. At this exudative phase, most fluid in the pleural cavity can be drained by a chest tube. If the infectious process continues and the fluid accumulates, the fluid will become thicker with more fibrin deposition. This second stage is often characterized by loculated pleural effusion which makes it difficult to drain all effusion in different areas with a single chest tube. Patients with this true empyema stage often require surgical intervention to deloculate the effusion for complete drainage. Fibrinolytic agent is another option for non-surgical candidate. When the disease progresses, more and more fibrin pile up and the fluid becomes denser and denser. A thick peel will form to cover all contact surfaces, including lung, inner chest wall, diaphragm, and mediastinum. This final stage of empyema, organizing phase, will restrict lung expansion and hence reduce lung compliance. More aggressive treatment modalities should always be considered to avoid long-term lung function impairment.

Stage	Phase	Characteristics	Status of Lung Parenchyma	Treatment
I	Exudative (Acute)	Pleural membrane thickening Fibrin deposition Presence of exudative fluid	Compliant Reexpansion possible with evacuation of fluid	Thoracentesis Closed-tube thoracostomy
II	Fibrinopurulent	Extensive fibrin deposition Pleural fluid becomes turbid or purulent Presence of loculated empyema	Partial compliance Lung entrapment due to fibrin deposition	Closed-tube thoracostomy with/ without fibrinolytics VATS Thoracotomy
III	Organized (Chronic)	Fibroblast in growth Thickened pus Granulation tissue replacement of the pleural space	No compliance Lung completely entrapped by fibrous peel	VATS (decortication) Thoracotomy (decortication) Open window thoracostomy

(Modified from Taylor and Kozower [3].)

Table 1.
Stages of empyema.

3. Treatment principles

Since empyema equals to infected pleural cavity, the primary goal is to treat the infection. There are a few recognized treatment principles to such disease. First, sterilization of the pleural space. Second, adequate drainage. Third, optimizing lung expansion and reducing potential pleural space. These principles will be explained in detail below.

3.1 Sterilization of the pleural space

Just like treating other infectious disease, removal of pus or necrotic tissue and antibiotics therapy are the two key components to successful treatment. In

empyema, sterilization targets not only the pleural space but also the original infection source, such as pneumonia or liver abscess. To select effective antibiotics, obtaining cultures are important so that adjustment can be made according to susceptibility test after empirical antibiotics. Other effective ways to lower the pathogen colonization in the pleural cavity are removal of the infectious debri and irrigation. These procedures, debridement and irrigation, are often carried out during the surgery, either through VATS or thoracotomy. Although some doctors believe irrigation may result in unstable hemodynamics as capillary permeability increases due to transient bacteremia, the author thinks it is reasonable to do so as it is easier and faster to achieve sterilization. If the patient's blood pressure drops during the surgery, it is suggested to irrigate the pleural cavity with some diluted epinephrine with cautious monitoring. Since the patient's capillary permeability may increase, it is possible that the patient would develop tachycardia and hypertension if the medication is well-absorbed by the pleura.

3.2 Adequate drainage

Unlike airway, pleural cavity is a closed space. The fluid should be drained adequately to avoid further or repeated infection. A chest tube is sufficient for simple parapneumonic pleural effusion (stage I empyema) while complicated pleural effusion (stage II empyema) or organizing empyema (stage III empyema) often requires surgical intervention and a chest tube(s) after the surgery for adequate drainage.

3.3 Optimizing lung expansion and reducing potential pleural space

When the empyema reaches to its final stage --- organizing stage, the lung would become completely trapped and therefore poorly expanded. This not only leads to restrictive lung (impaired lung function), but also leaves a potential dead space in the pleural cavity. This space would possibly result in repeated infection. Therefore, the initial treatment goal of empyema should also include best pleural apposition to prevent chronicity. To achieve this, remove "peels" from the lung and other pleural surfaces. This surgical procedure is known as "Decortication." As long as it is feasible, removing all debri and resuming patients' optimal pulmonary function are always recommended. However, there could be exceptions that the lung fails to fill the pleural cavity. If this is the case, other measures should be taken to reduce the potential pleural space.

From a thoracic surgeon's point of view towards managing empyema, it is always "the earlier the easier." In an acute setting of empyema (stage I or II), most patients can be cured by tube thoracostomy or VATS [2]. This further emphasizes the fact that early diagnosis and early aggressive treatment to prevent chronicity are crucial. In addition, the choice of first intervention is important as well. According to the literature, failure of the first attempted procedure was an independent predictor of death [5]. As a result, operation is the most successful initial procedure in this study. More and more studies demonstrated good outcomes of early surgical intervention treating complex empyema [5, 6]. Furthermore, VATS decortication is found to be superior to open surgery in the management of primary empyema [7]. In the author's hospital, empyema is a surgical disease. Once the diagnosis is made, almost all patients need surgical consult for further treatment planning. All surgeons tacitly agree that VATS is the gold standard procedure to treat acute empyema in the author's institution.

There are still certain patients who will eventually continue to have the infection and enter to a chronic phase. Several causes of chronic empyema include delayed

diagnosis, retained hematoma in the pleural cavity, bronchopleural fistula with continuous airway secretion spillage, a large potential pleural space (e.g. post lung resectional empyema) which is prone to have repeated infection, and the patient is too ill to receive definite treatment at the initial acute phase. Among all the causes, the author thinks that retained hematoma in the pleural cavity is the most preventable cause of chronic empyema. Blood clots are perfect culture medium for bacteria, so it is important to avoid too much oozing when one performs VATS debridement and decortication on empyema patients, especially those who have liver cirrhosis, end stage renal disease, or other bleeding tendency. Adequate hemostasis and diluted epinephrine irrigation are helpful to prevent retained hematoma. If retained hematoma still happens, at least it is detectable from the drainage fluid. The drained fluid would be bloody initially then turned to dark brown and remained in this color without turning to light yellow. As one recognizes the sign of retained hematoma in the pleural cavity, it is often required to do another operation to remove all the blood clots to prevent chronic empyema.

4. Treatment options

In this section, the focus will be solely on the treatment options of chronic empyema and to which treatment principles that each option fits in.

When dealing with empyema, following the above mentioned three treatment principles is the key to success. Although the principles are the same in different stages, treatment strategies may vary, especially in the chronic stage. Treating chronic empyema is more complicated, more unpredictable, and therefore more challenging. It may require staged operations, different surgical approaches, and there is no standardized option. Before establishing treatment plan for chronic empyema patients, comprehensive understanding between each option is necessary.

4.1 Optimizing lung expansion by decortication

Decortication can be done either through VATS or thoracotomy. It is basically surgeon's preference. During the same surgery, debridement is also done so that non-viable tissue and debri are removed to achieve "cleaning" in the pleural cavity. In stage III empyema, the lung is always restricted by thickened "cortex," so freeing the lung by decortication can optimize lung expansion and reduce the potential pleural space. Choosing proper surgical instruments accelerates the procedure. In the author's experience, Roberts artery forceps or long Kelly forceps are best tools to separate the lung from the overlying "cortex." This separation process can be done sometimes with the operated lung ventilating so that the correct pleural plane is evident. If pleural apposition still cannot be achieved after decortication, make sure to check the lung surface again. There may be some remnant peel from the multilayered peel that restricts lung expansion. Sometimes the peel is extremely thick and firm. Using a scalpel cautiously to slit through the peel will aid in removal.

*Fitting in the treatment principles sterilization of the pleural cavity and reducing potential pleural space by optimizing lung expansion.

4.2 Optimizing lung expansion by other means

To optimize lung expansion, there are several other ways, but none are as effective as decortication.

4.2.1 Positive airway pressure

Some of these patients are ventilator dependent while others are not. If they still require ventilator support, it is acceptable to increase positive end-expiratory pressure (PEEP) a little, by 1 or 2 cmH2O, to further expand the lung. If patients can be weaned off from ventilator successfully after the operation, a strategical management option is to delay extubation time by 0.5 to 1 day. This may also allow the lung to further expand.

*Fitting in the treatment principle reducing potential pleural space by optimizing lung expansion.

4.2.2 Negative pleural pressure

Positive airway pressure expands the lung from internal while negative pleural pressure provides a tractive force externally. A suction pressure of −20 cmH2O is usually recommended with a traditional chest drainage system. Other modality that can create negative pressure in the pleural cavity is Vacuum-assisted closure (VAC) therapy. (see 4.4).

*Fitting in the treatment principles drainage and reducing potential pleural space by optimizing lung expansion.

4.3 Open window thoracostomy (OWT)

4.3.1 History of OWT

OWT was first described by Robinson in 1916 and then revised by Leo Eloesser in 1935 which was also called Eloesser flap thoracostomy window [8]. However, the most adopted OWT is modified by Symbas and coworkers in 1971 as modified Eloesser flap [9].

4.3.2 Rationale, advantage, and disadvantage of OWT

This procedure, an open drainage method, is often saved as the last resort to treat chronic empyema, especially when the pleural infection is difficult to be managed by debridement and decortication. It is also a treatment option for critically ill patients who are too weak to receive decortication. As the name presents itself, OWT is to create a window through the patient's chest so serial dressing changes are feasible to clean the infected pleural cavity and therefore alleviate the septic condition. The advantage of OWT is that it is proved to be safe and effective [10]. On the other hand, it affects the patient's appearance and may cause chronic pain after chest wall resection. Some of the patients will need another surgery to close up the wound.

*Fitting in the treatment principles sterilization of the pleural cavity and drainage.

4.3.3 Surgical techniques and special considerations of OWT

The most common use of OWT is modified Eloesser flap [11]. The window is usually created at the basal part of the hemithorax where most of the infected material accumulates (**Figure 1**). After confirming the chest CT image, an inverted U-shaped incision is made at this area. Electrocautery is used for dissection till the rib cage. In order to create a sufficient window, two or three

ribs need to be resected. Then, the tongue-shaped muscular-cutaneous flap is folded inward and sutured to the diaphragm (**Figure 2**). The remaining wound edge is sutured to the pleura so that the window can be maintained for a period of time without spontaneous closure. It is also imperative that the window is large enough for the convenience of frequent wet packings. Another key point that must be mentioned is the timing of OWT creation. From the Massera et al. study [12], immediate OWT requires lesser time for the resolution of empyema comparing to the delayed OWT after prolonged chest tube drainage. As a result, the median OWT closure time (between performing and closing of OWT) of immediate OWT was 8 months shorter than that of delayed OWT. The timing of attempted closure should be carefully decided by the surgeon after a thorough evaluation of the empyema patient's condition. This includes free from recurrent disease, good recovery of the pleural cavity with coverage by healthy granulation tissue, the patient's general condition, and to a lesser degree by the normalization of inflammatory parameters [12, 13]. Methods of OWT closure please see 4.6.2 below.

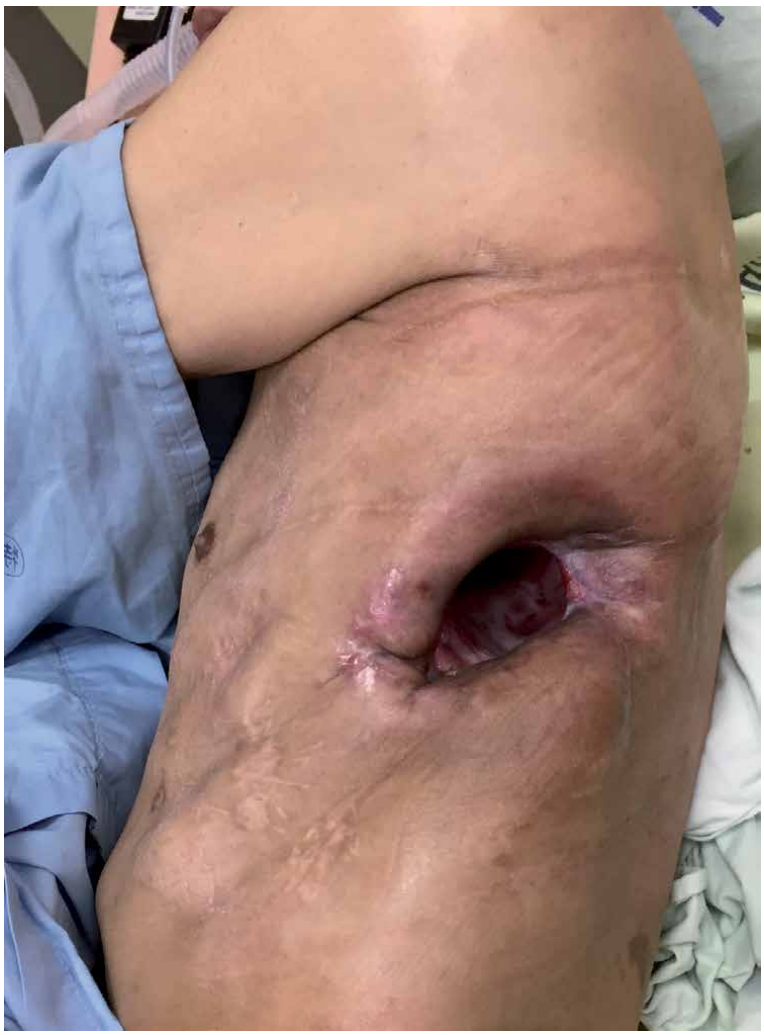

Figure 1.
OWT. An OWT on the patient's left-side chest wall.

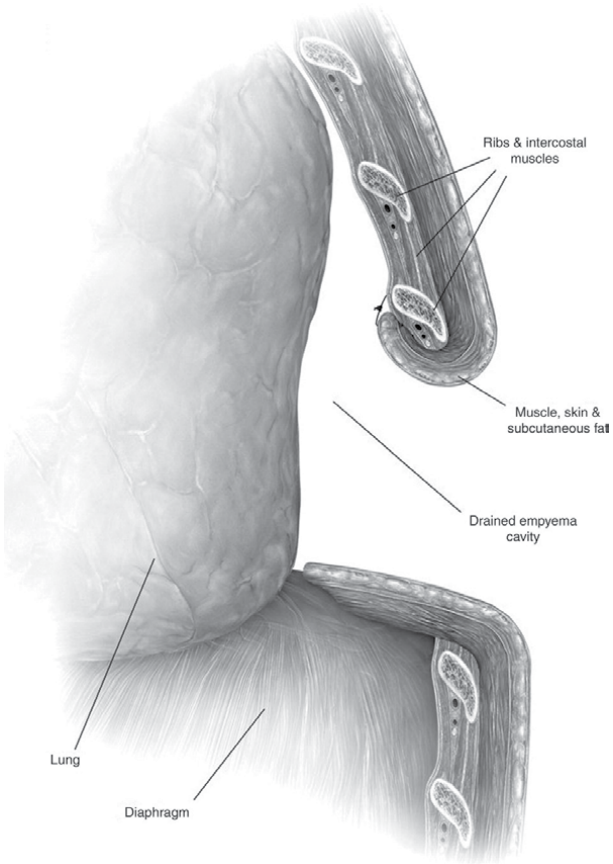

Figure 2.
Coronal view of the Eloesser flap window. Demonstrating the supposition of the skin surface of the inferiorly based soft tissue flap to the diaphragmatic surface. (Adapted from Denlinger [11].)

4.4 Vacuum-assisted closure (VAC) therapy

4.4.1 History of VAC therapy

VAC is a negative pressure wound therapy that is widely used in acute and extended open wounds. The first case report of intrathoracic VAC therapy was published in 2006 [14]. Varker et al. managed a postlobectomy empyema patient with VAC device successfully after open debridement of the empyema cavity. In the next following decade, with the popularity of VAC therapy, it was proved that it is safe and efficient to fight against all kinds of intrathoracic infections [13, 15–17].

4.4.2 Rationale, advantage, and disadvantage of VAC therapy

VAC device is able to create a negative pressure wound environment that promotes wound healing by reducing edema, promoting granulation tissue formation and perfusion, and removing exudate and infectious material. As to treating chronic empyema, it is a useful tool to apply on an open wound such as an OWT after debridement of the pleural cavity (**Figure 3**). In the setting of intrathoracic VAC usage, it may reduce the duration and frequency of dressing changes necessary for spontaneous chest closure or a space filling procedure, reducing patient's

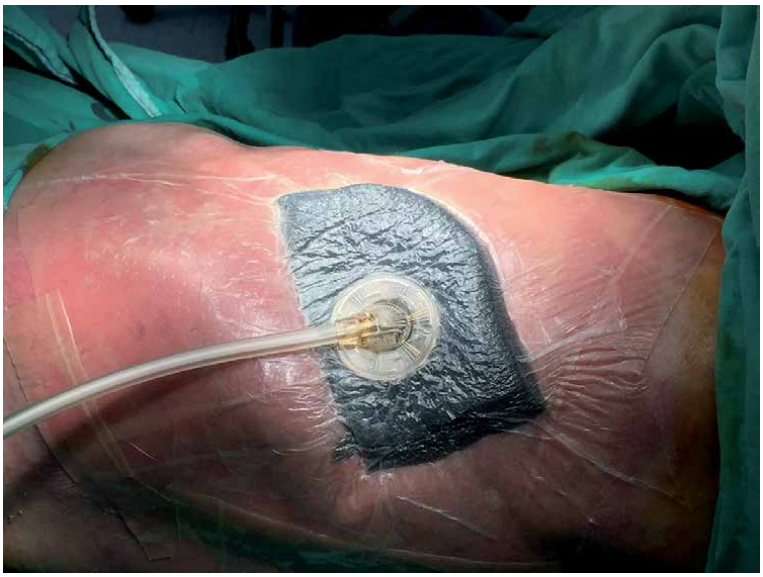

Figure 3.
Intrathoracic VAC therapy. VAC therapy is applied through the patient's OWT.

discomfort, and resolving the infectious process faster [18]. When compared with conventional management of OWT, VAC therapy accelerates wound healing and helps re-expansion of residual lung parenchyma in patients with OWT [19]. In selected patients, applying Mini-VAC procedure can even avoid OWT by insertion of the ALEXIS (Applied Medical, Rancho Santa Margarita, CA, USA) wound retractor to create a similar window effect without resecting the ribs which preserves the chest wall integrity and avoids the consequences that OWT can cause (**Figure 4**) [20]. However, the biggest disadvantage of this device is that it is not suitable for everyone. VAC device should be used cautiously or be avoided on patients with bleeding tendency, presence of malignancy, or unstable hemodynamics. Because VAC creates a negative pressure environment, it may lead to continuous bleeding, promote cancer growth, or deteriorate hypotension. The reason why

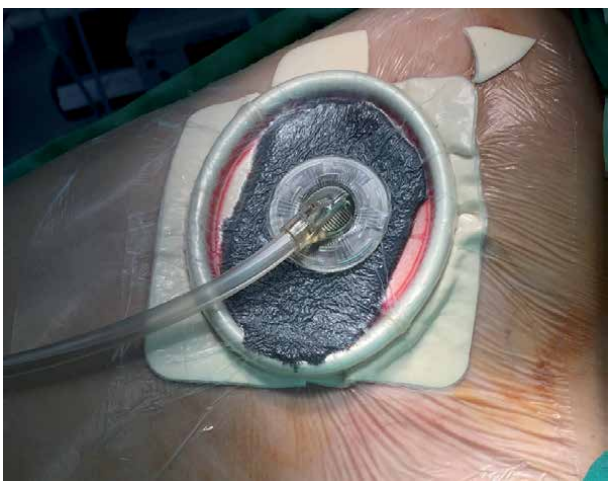

Figure 4.
Mini-VAC procedure. VAC therapy is applied through the ALEXIS wound retractor which creates a similar window effect without resecting the ribs.

hypotension may develop is probably due to the negative pressure effect intrathoracically causing decreased cardiac output. Thus, intrathoracic application in older patients must be monitored closely and should be avoided on patients with poor cardiac function.

*Fitting in the treatment principles drainage and reducing potential pleural space by optimizing lung expansion.

4.4.3 Surgical techniques and special considerations of VAC therapy

VAC therapy is designed to be applied on open wounds. To treat chronic empyema with VAC, an open chest wound or an OWT must be created during the surgical intervention. Some authors advocate leaving the thoracotomy wound open directly after the operation [13, 14] while others create an OWT to make dressing changes easier [17–19]. It is reasonable to decide on an individual basis depending on the size and depth of the residual pleural space. A large and deep residual pleural space is preferred for OWT. The advantage of OWT is that the chest will stay open for a longer period because of the inverted skin flap compared to just leaving the thoracotomy wound open. OWT would avoid the skin from healing before complete eradication of the infected pleural cavity. It is contraindicated to apply VAC on a dirty wound with necrotic tissue that has yet to be debrided. After adequate debridement in the pleural cavity, VAC sponges (GranuFoam) are inserted in the residual pleural space to fill the entire cavity. Placing the sponges directly in contact with exposed blood vessels, anastomotic sites, organs, or nerves are prohibited, except for the lungs. According to the literature [13, 21] and the author's personal experiences, VAC dressing can be safely applied directly on the visceral pleura or lung parenchyma without any complications. The negative pressure can be set at -50 mmHg from the start, and gradually increased to -125 mmHg if the patient does not have any discomfort. The dressing change should be done at least twice a week, and it can be performed at the bedside. During the VAC therapy period, the skin covered by the dressing should be well protected to prevent skin maceration problems. If negative pressure fails to be maintained due to significant air leak caused by bronchopleural fistula (BPF), combining a one-way valve may solve this issue [21].

When dealing with postpneumonectomy empyema (PPE), VAC therapy should be used carefully, especially for patients who develop the complication shortly after the initial surgery. This is because negative pressure would shift the mediastinum which may cause heart or great vessels herniation leading to obstructive shock or even cardiac arrest. On the contrary, if PPE is developed at a later stage, such events will not happen as the mediastinal shift has already completed and the patient's body has compensated it well.

4.5 Empyema tube --- rationale, advantage, and disadvantage

There are two scenarios where chronic empyema patients would need an empyema tube for long-term drainage. One is that the patient is too unstable and fragile to receive general anesthesia and adequate surgical intervention. To alleviate the septic condition, empyema tube (tube thoracostomy) can be placed to decrease the burden of infection until definite treatment can be initiated. Another scenario is that the chronic empyema is somehow localized in a small area without systemic infection. It is either a tube thoracostomy left after previous surgical intervention or a new chest tube inserted into this localized area for drainage if the patient is not a surgical candidate.

In the author's opinion, this treatment option is only reserved for those who are not able to receive other definite treatment because of the low success rate, and not

all infected materials can be drained adequately. However, if adequate drainage can be achieved, the tube may be slowly retracted over a period of weeks to months while the infected space heals behind it [3].

*Fitting in the treatment principle drainage.

4.6 Filling the potential pleural space with different measures

4.6.1 Clagett procedure

4.6.1.1 History, rationale, advantage, and disadvantage of Clagett procedure

Clagett procedure was first described by Clagett and Geraci in 1963 [22]. It is a method that obliterate the pleural cavity with antibiotic solution. As a precondition of the procedure, there must be no BPF and the pleural cavity should be sterilized by debridement and irrigation. In other words, if the patient has BPF and primary repair is impossible, Clagett procedure is not suitable for the patient. Nonetheless, this procedure has a good overall success rate in selected patients (no BPF at the time of the procedure), range from 81–100% [12, 23–25]. Those who fail from the procedure are mainly due to persistent or recurrent BPF.

*Fitting in the treatment principle reducing potential pleural space.

4.6.1.2 Surgical techniques and special considerations of Clagett procedure

After confirming that there is no active BPF in the pleural cavity or it is firmly closed, antibiotic fluid can be instilled to fill the remaining pleural cavity after it is fully cleansed. DAB solution (gentamicin 80 mg/L, neomycin 500 mg/L, and polymyxin B 100 mg/L) is one of the antibiotic solution choices [23]. The combination of the fluid can be chosen according to the microbiological findings [26].

4.6.2 Tissue flap transposition

4.6.2.1 Rationale, advantage, and disadvantage of tissue flap transposition

Tissue flap transposition technique is frequently used in chronic empyema patients for the purpose of either closure of the BPF or OWT, and/or obliteration of the residual pleural space. It can also be used for the prophylactic reinforcement of a bronchial stump after major lung resection to avoid BPF formation. Because the flap tissue is full of mesenchymal cells, it can promote granulation tissue growing under good circulation and secure the bronchial stump as a backup layer. A bulky muscle flap is extremely helpful to reduce the residual pleural space while a smaller residual space only requires a smaller tissue flap. However, not every patient is medically fit for long-hour flap surgery especially the critically ill. A successful flap reconstructive surgery is determined by a well-perfused flap which is highly dependent on patients' stable hemodynamics.

*Fitting in the treatment principle reducing potential pleural space.

4.6.2.2 Surgical techniques and special considerations of tissue flap transposition

Tissue flaps commonly used in chronic empyema are latissimus dorsi (LD) muscle flap (**Figure 5**), serratus anterior (SA) muscle flap, pectoralis major (PM) muscle flap, intercostal muscle flap, pedicled omental flap, and other free flaps. LD is the largest muscle among all chest wall muscles. Therefore, it is an ideal option for pleural cavity obliteration. However, if the patient has received a standard

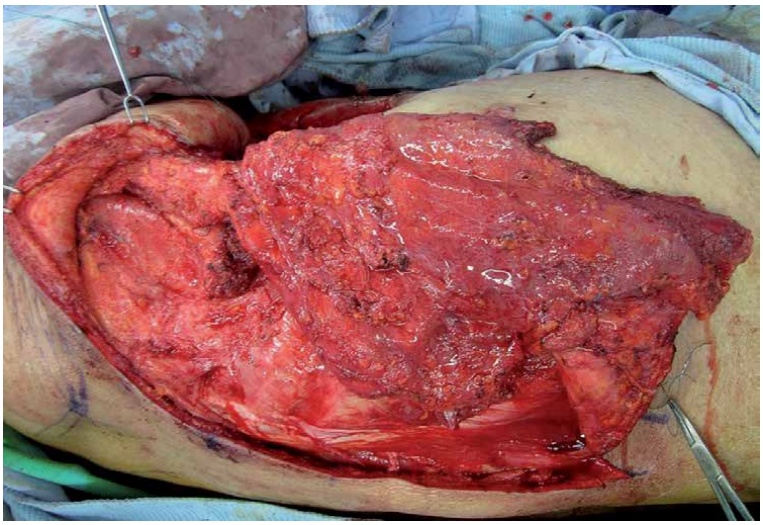

Figure 5.
LD muscle flap. Harvest of the LD muscle flap to reinforce the PPE BPF closure.

posterolateral thoracotomy previously, this muscle may have been compromised and hence not suitable. PM flap is another good alternative for it is the second largest chest wall muscles. Because of its anatomy and orientation, PM flap is particularly useful to obliterate the apical residual pleural space [3, 27]. Although SA flap and intercostal muscle flap are relatively small compared to LD and PM flaps, they can be sufficient to help accelerate BPF healing as long as the pedicle is healthy. Omental flap is another option if no chest wall muscle is available [28]. However, entering the peritoneal cavity may potentially spread the infection and complicate the situation. Sometimes the remaining pleural space is too big that only by combining two flaps will fill the space [27]. Free flap may also be considered in highly selected patients.

4.6.3 Thoracoplasty

4.6.3.1 History, rationale, advantage, and disadvantage of thoracoplasty

Thoracoplasty has a long history in the field of thoracic surgery. It was first described by Estlander in the late 19th century when tuberculosis was a troublesome pandemic without medical cure [29]. The original concept of this surgery is to collapse the chest wall to minimize the cavitary pleural space caused by mycobacterium. To achieve this goal, multiple ribs are resected resulting in loss of rigid chest wall configuration and therefore obliteration of the infected pleural space. Although it is an effective way to fill the potential pleural space, this procedure can cause significant morbidity, including chronic pain, chest wall deformity, thoracic spine scoliosis, limited ipsilateral shoulder range of motion, and finally resulting in poor quality of life.

*Fitting in the treatment principle reducing potential pleural space.

4.6.3.2 Surgical techniques and special considerations of thoracoplasty

Thoracoplasty can be classified into three types, full, extended, and tailored thoracoplasty. Full thoracoplasty is defined as removing first 11 ribs to collapse the whole hemithorax. Extended thoracoplasty, on the other hand, is removing 7

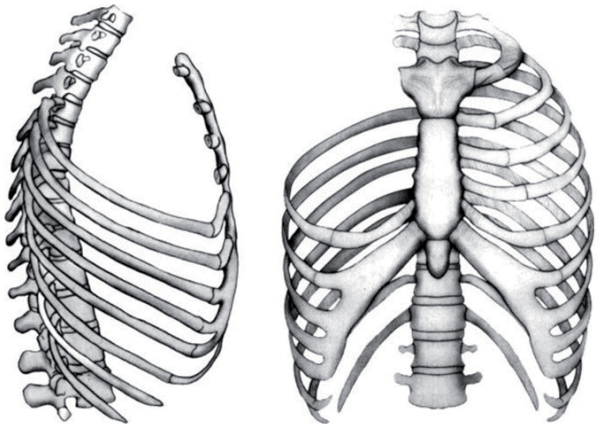

Figure 6.
Thoracoplasty. Complete resection of the 4 right upper ribs. (Adapted from Lewis and Wolfe [31].)

to 9 ribs while tailored thoracoplasty is removing fewer than 5 ribs at certain area [30]. Resection of 7 ribs can lead to approximately 50% reduction of the pleural space, and resection of 5 ribs results in 25% reduction (**Figure 6**) [31]. The key to a successful thoracoplasty is complete resection of the targeted ribs which means from the transverse process of the thoracic spine posteriorly to the costosternal joint anteriorly. In the modern era, this procedure is seldom conducted alone. Combining with muscle flap transposition is an effective alternative so that chest wall deformity can be less significant [32, 33].

Managing chronic empyema is art. There is no standardized option. Knowing the different measures in depth and applying each principle with these measures will certainly increase the success rate of treatment. Making a customized treatment plan according to the patient's physical condition, complications, and special requirements cannot be emphasized enough. There are special circumstances which will be introduced below for better understanding of how to put the different treatment options in use.

5. Special circumstances

5.1 Post-resectional empyema

The main issue contributed by post-resectional empyema is that the residual pleural space is often large. The treatment strategy therefore should be emphasized on how to fill the space. If post-lobectomy empyema occurs in a delayed setting, the size of the residual pleural space would not be a concern because the pleural cavity should have been remodeled by diaphragm elevation, mediastinum shifting, and narrowing of the intercostal space over time. However, if post-resectional empyema happens in an acute phase when the remodeling has not been completed yet, different filling procedures should always be considered. For instance, if a patient who is medically fit for surgery develops a post-lobectomy empyema in a delayed phase, VATS or thoracotomy debridement and decortication are usually amenable to solving the problem.

Post-pneumonectomy empyema (PPE) is notorious for its high morbidity and mortality rate [12]. It is a challenging situation clinically, especially when BPF is present (**Figure 7**). According to the literature [12, 25, 30], approximately 65 to 84% PPE patients have BPF. Closure of the BPF is imperative or else spillage from

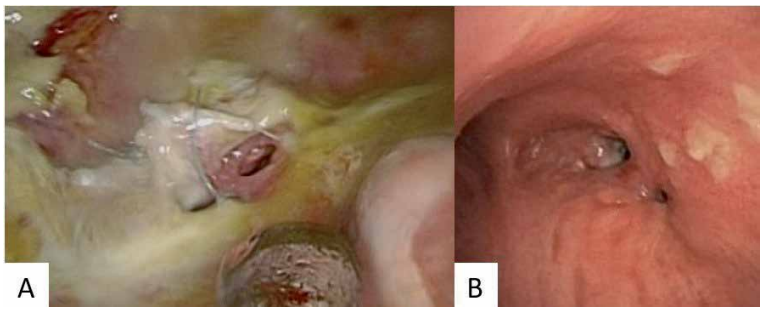

Figure 7.
PPE with BPFs. (A) from the thoracoscopic view of the BPFs (B) from the bronchoscopic view of the BPFs.

the infected cavity into the airway can cause pneumonia or even acute respiratory distress syndrome (ARDS). On the other hand, the secretion from the airway would also leak into the pleural space continuously and contaminate the cavity. After closing the BPF, as per treatment of other empyema, sterilization of the cavity with debridement, irrigation, parenteral antibiotics, and adequate drainage, the most important is effective obliteration of the remaining pleural space. Since the BPF is often failed by primary suture alone, covering the stump with pedicled muscle flap ensures secondary healing as well and obliteration the pleural space at the same time. For example, if a debilitated patient suffers from severe sepsis caused by late onset right-sided PPE with BPF, it is reasonable to lay out a staged surgical plan. First, do a tube thoracostomy and forbid the patient to lie in a left decubitus position to protect the contralateral lung. This first stage is for drainage and lung protection. Second, perform simple debridement, OWT, and primary BPF repair added on a buttressed intercostal muscle flap. Instead of frequent dressing changes after OWT, VAC therapy can be initiated under the circumstance without any contraindication. VAC dressings can be changed at least twice a week. After a period of aggressive treatment plus appropriate nutritional support, successful BPF closure, a clean pleural cavity covered with healthy granulation tissue, and improved physical status of the patient can be expected. The second stage is for sterilization of the pleural space and open drainage. The third stage is purely for filling. Choose an appropriate procedure, such as Clagett procedure, to obliterate the pleural cavity.

5.2 Bronchopleural fistula (BPF)

As mentioned in the last paragraph, BPF connects the bronchus to the pleural cavity leading to infection burden and possible respiratory distress. Life threatening events, such as ARDS or septic shock, must be managed as top priority. Successful closure of the BPF may prevent those critical situations from happening. As long as the patient's physical condition is suitable for intervention, attempts to close the BPF should be carried out as early as possible.

There are several ways to manage BPF, either bronchoscopically or surgically. Treatment choices mainly depend on patients' clinical status, duration before the development of BPF, and number and size of the BPF [30]. An algorithm for treatment of BPF at the European Oncologic Institute [34] (**Figure 8**) was created according to these principles. If the BPF occurs in an early setting (<14 days after surgery), surgical repair of the bronchial stump is always encouraged. In a delayed setting (>14 days after surgery), bronchoscopic application with sealants, fibrin glue, silver nitrate, coils, endobronchial stents, Endobronchial Watanabe Spigot, or atrial septal defect occluder device [35–38] can be used for small BPF size <8 mm or for patients who are physically unfit for surgery. As for BPF size >8 mm, patients

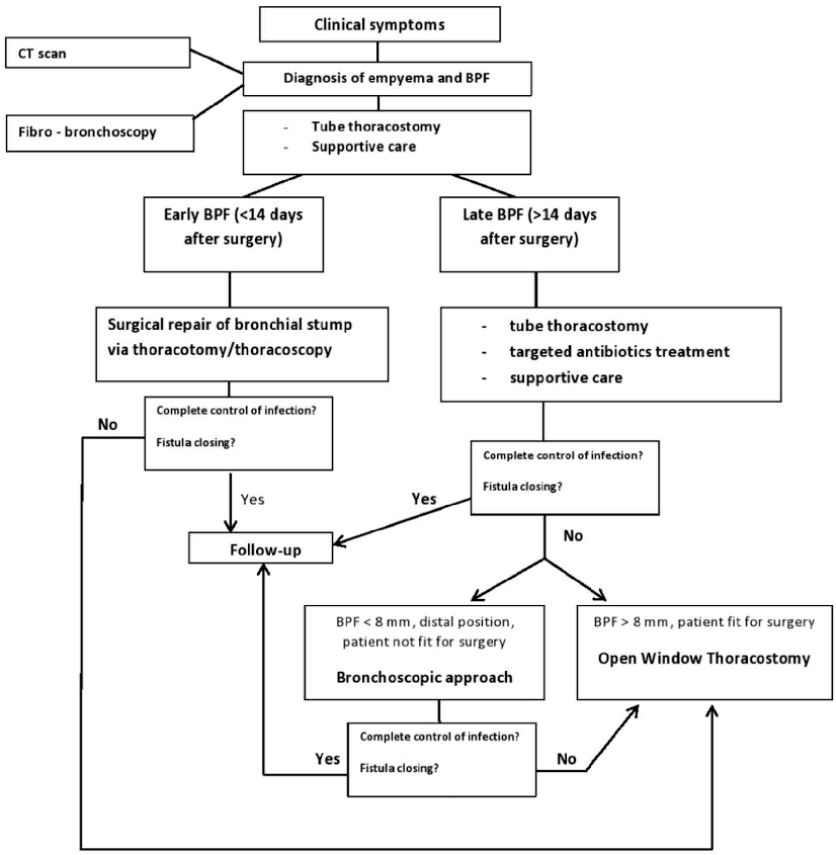

Figure 8.
Management of PPE BPF: EOI algorithm. (Adapted from Mazzella et al. [34].)

who are fit for surgery, patients who had failure from other treatment strategies, surgical intervention is unavoidable. In addition to primary closure of the bronchial stump, muscle flap transposition to cover the sutured stump provides a good environment for secondary healing which may increase the success rate of closure. If the BPF is deemed to be closed during the operation, Clagett procedure may be considered after thorough cleansing of the infected pleural cavity. Since continuous spillage from the BPF may occur, therefore OWT is often a treatment option to enable frequent dressing changes to eliminate the infection.

5.3 Malignant pleural empyema

At times, malignant pleural effusion can be infected either through hematogenous or direct inoculation by invasive procedures. The treatment principles are essentially the same. Sterilization of the pleural cavity and adequate drainage are not difficult to achieve. Since the pleura tumor cells cannot be eradicated immediately by surgical procedures or medical treatment, it is almost impossible to fully expand the lung via decortication and therefore a possible residual pleural space which can cause repeated infection. Under this circumstance, a thorough decortication is not practical because tumor cells are prone to bleed and cause the underneath lung tissue to be more fragile. Too much "peeling" will lead to excessive bleeding resulting in hematoma retention and causing the lung to tear. To weigh the benefits and risks of surgical intervention is crucial since the patient's life expectancy may

be limited. From the author's personal experience, debridement, irrigation, and limited decortication followed by a tube thoracostomy are sufficient to treat the infected pleural cavity.

5.4 Tuberculous empyema

Although some surgical measures for chronic empyema originated from treating tuberculous (TB) empyema [8, 29], such as Eloesser flap thoracostomy window and thoracoplasty, these intensive procedures are now rarely used to treat TB empyema. It is not that TB empyema patients do not need invasive procedures, but it is that most of these patients can be managed by tube thoracostomy or VATS debridement with decortication. When it comes to uncontrolled TB empyema with initial treatment attempt failure, more aggressive modalities should be considered which are the same as treating other bacterial chronic empyema.

5.5 Application of double lumen endotracheal tube

Double lumen endotracheal tube intubation is frequently seen in thoracic surgery for lung isolation. It can be an adjunct to help with BPF treatment after pneumonectomy if the patient still requires ventilator support or to protect the remaining lung from fistular spillage. Application of this device would help ventilate the remaining side of the lung and leave the fistular side of the hemithorax unventilated to accelerate fistular healing. However, the diameter of the double lumen tube is certainly greater than the single lumen tube which would make the patient feel uncomfortable if not sedated. Another frequently encountered issue is that the left-sided tube tip would slide outward easily, and this malposition may cause failure of lung isolation. Although the whole diameter of the double lumen is greater than the single lumen tube, each individual double lumen tube diameter is smaller. This would make it difficult to clean the airway by suction as the suction tip may not always reach to the proper depth. As a result, airway hygiene may become a serious issue if the tube is placed in the bronchus for a long time.

6. Future directions

With the development of modern medicine and minimally invasive technology, the role of both bronchoscopic and thoracoscopic (VATS) procedures have become increasingly important replacing some of the traditional surgeries in treating chronic empyema. More studies should focus on solving existing issues like, Mini-VAC replacing OWT completely, customized device to help repairing BPF, and 3D bioprinting assisting BPF closure. The author believes that chronic empyema management is still evolving, and look forward to less traumatic ways of approach with better outcome in the future.

7. Conclusions

Treating chronic empyema and BPF are certainly clinical challenges that thoracic surgeons would encounter from time to time. It is necessary to thoroughly comprehend each treatment option and some management key points of different situations. With the development of modern technology, more treatment modalities can be anticipated.

Notes/Thanks/Other declarations

The author has nothing to declare.

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Section 5

Pneumothorax

Chapter 7

Pneumothorax: A Concise Review and Surgical Perspective

Shilpi Karmakar

Abstract

Pneumothorax is the collection of air in pleural cavity, which is commonly due to development of a communication between pleural space and alveolar space (or bronchus) or the atmosphere. In this chapter, we will discuss the various aetiologies of pneumothorax, the differences in their pathophysiology and the implications on the management of the disease. The chapter focusses on the surgical aspects in the management, the revolution brought in by video-assisted thoracoscopic surgery (VATS) and the advancement of the field by introduction of uniportal VATS and robotic-assisted thoracic surgery. The principles of management of catamenial pneumothorax are revisited. The chapter also throws light on the nuances of anaesthesia techniques and the latest developments are outlined. Lastly, a section is dedicated to COVID-19 associated pneumothorax and the approach to its management.

Keywords: pneumothorax, tube thoracostomy, VATS, pleurodesis, bullectomy, chest X-ray, flap, COVID-19, intercostal tube

1. Introduction

The term "pneumothorax" was coined by a French physician Itard, in 1803 [1]. Pneumothorax is defined as the presence of air in the pleural space. Even though intrapleural pressures are negative throughout the respiratory cycle, air does not enter the pleural space, as the net movement of gases from capillary blood into pleural space requires pleural pressures to be lower than −54 mmHg, which does not occur in normal circumstances. Hence, for air to be present in pleural space, one of the three events must occur: communication between pleural space and alveolar space (or bronchus), or communication between pleural space and the atmosphere, or presence of gas-producing organism in the pleural space [2].

Clinically, pneumothorax is classified as spontaneous (no obvious precipitating factor present) and non spontaneous (consequence of any thoracic injury). Spontaneous pneumothorax may be primary (no apparent underlying lung disease) or secondary (associated with clinically apparent underlying disease, like chronic obstructive pulmonary disease, cystic fibrosis), or catamenial (associated with menstruation). Pneumothorax can be of varying clinical severity, ranging from a small pneumothorax, which is likely to resolve spontaneously, to those with large pleural defects and collapse of entire lung and compromised ventilation.

Pneumothorax ranks second to rib fracture, as the most common manifestation of traumatic chest injury and is noted in 40–50% of patients with chest trauma [3]. Weissberg et al. in a study of 1199 cases of pneumothoraces found secondary

spontaneous pneumothorax (505 patients) to be most common, followed by primary spontaneous pneumothorax (218 patients), traumatic pneumothorax (403 patients), and iatrogenic pneumothorax (73 patients) [4].

2. Pathophysiology

Normally, the pressure in pleural space is negative compared to the alveolar pressure during the entire respiratory cycle, due to the inherent elastic recoil of the lung. The pleural pressure is also negative with respect to atmospheric pressure. Development of communication between alveolus or atmosphere and the pleural space allows air to flow into the pleural space until there is no longer a pressure difference or until the communication is sealed [5].

Tension pneumothorax is a condition where there is continuous increase in the air trapped in the pleural space, due to formation of a one-way valve by the injured tissues. This trapped air builds up pressure on the affected side, causing collapse of the ipsilateral lung and shift of mediastinum into the contralateral hemithorax. This causes respiratory distress. Also, there is reduced venous return and thus decreased cardiac output. Further, hypoxia leads to increased pulmonary vascular resistance via vasoconstriction. Cardiopulmonary arrest becomes imminent. Tension pneumothorax, thus, culminates in a life-threatening condition.

Spontaneous rupture of blebs may result in pneumothorax. The rupture may be a consequence of pressure change, as seen in airplane crew members or scuba divers [6]. The volume of given mass of gas at a constant temperature is inversely proportional to its pressure. A given volume of air at an altitude of 3050 m, saturated at body temperature, expands to 1.5 times the volume at sea level. Scuba divers breathe the compressed air delivered by a regulator and during ascent, as ambient pressure falls rapidly, gas in the lungs expands and may rupture blebs [7].

Secondary spontaneous pneumothorax may be due to rupture of pre-existing blebs or due to areas of increased porosity. These are areas of disrupted mesothelial cells on the visceral pleura, replaced by an inflammatory elastofibrotic layer with increased porosity, allowing air leak into the pleural space [8]. Pneumothorax has, also, been reported to be the presenting sign of peripheral necrotic tumour or centrally located tumour.

Catamenial pneumothorax is defined as two episodes of pneumothorax temporally related to the onset of menses, usually within 72 hours. Catamenial pneumothorax is the presentation of thoracic endometriosis and thorax is the most common site of extra pelvic endometriosis. An older age at diagnosis (34.2 ± 6.9 years), and right sided lesions predominate the clinical picture. Thirty-nine percent of patients have associated diaphragmatic lesions. Diverse hypothesis have been advanced to explain the pathogenesis of endometriosis related pneumothorax: spontaneous rupture of blebs, shedding of endometrial implants of visceral pleura, and the transdiaphragmatic crossing of air from the genital tract during menses. Known risk factors associated with thoracic endometriosis include previous gynaecologic surgery (such as curettage for miscarriage, hysteroscopy for endometrial biopsy, or revision of the uterine cavity after caesarean section), primary or secondary infertility, and the history of pelvic endometriosis.

Iatrogenic pneumothorax may be caused during transthoracic needle aspiration or biopsy, subclavian or jugular vein catheterization, thoracocentesis, mechanical ventilation, cardiopulmonary resuscitation, tracheobronchial biopsy, among the commonly reported causes. Rarer reported causes are liposuction of axilla fat, liver biopsy, colonoscopy and gastroscopy [9]. Surgeries with operative fields far removed from thorax, have been reported to be associated with pneumothorax,

such as orthognathic surgery [10]. Iatrogenic pneumothorax related to mechanical ventilation has been reported in up to 15% of ventilated patients [11].

Communication between a bronchus (main stem, lobar or sublobar bronchus) and pleural space, called bronchopleural fistula, usually results as a complication of lung-resection surgery. The incidence of bronchopleural fistula is up to 1% after lobectomy and about 4–20% after pneumonectomy [12].

3. Diagnosis

3.1 Clinical examination

On inspection, tachypnea, increased work of breathing and respiratory distress may be seen. Cyanosis, drowsiness and decreased oxygen saturation may be found in tension pneumothorax. On palpation, tachycardia, chest wall tenderness, subcutaneous emphysema, decreased chest wall expansion, decreased tactile fremitus and tracheal shift are noted.

Hyper-resonant notes on percussion over the affected lung fields and decreased air entry perceived on auscultation are indicative of pneumothorax. There may be absent breath sounds on the ipsilateral side with contralateral reduced air entry in tension pneumothorax. Iatrogenic pneumothorax should be suspected in any patient who becomes more dyspneic after a medical or a surgical procedure that is known to be associated with the development of the pneumothorax. Sudden increase in peak airway pressure and sudden decline in oxygen saturation in a patient on mechanical ventilation should ring warning bells for the intensivist.

3.2 Investigation

A chest X-ray may reveal free air around the periphery of the lung fields and decreased lung volume. It may demonstrate the aetiology of the pneumothorax, such as rib or sternal fractures or presence of emphysematous lungs. Films should be taken in erect position, because in supine position, air spreads out in whole of pleural cavity, and films may appear normal, even in the presence of significant air. In patients who cannot be positioned erect and need to be supine, a deep sulcus sign (deep lateral costophrenic angle) should be looked for [13].

Methods to determine the size of pneumothorax on chest X-ray give approximate idea only. There are currently two methods described in adults. If the lateral edge of the lung is >2 cm from the thoracic cage, then, it implies air is occupying at least 50% of thoracic volume and hence, pneumothorax is large in size. Another method is measuring the fractional change in linear dimension of lung, and that multiplied by a factor of three, gives the fractional volume of pneumothorax [14].

Computed tomography (CT) chest provides more accurate information regarding volume of pneumothorax and associated pathology. Obtaining X-ray or CT images may be problematic and time-consuming in poly-trauma patients. Nowadays, in many trauma centres, pneumothorax is detected by sonography and has been included as a part of focused abdominal sonography for trauma (FAST) examination [15]. Ultrasound plays a important role in patients who are not stable enough for chest X-ray and CT. Also, ultrasound is not invasive and the patient is not exposed to radiation. According to a study of Blaivas et al., chest X-ray and ultrasound have a sensitivity of 75.5 and 98.1%, respectively and a specificity of 100 and 99.2%, respectively [16].

Bronchopleural fistula should be suspected in a lung resection patient with large continuous air leak and signs of empyema (leukocytosis, fever, purulent fluid on

thoracocentesis, and pleural fluid on chest X-ray or CT scan). Large pneumothorax developing days or weeks after resection is strongly indicative of a bronchopleural fistula. There is often a persistent and worsening cough. Since these patients have high mortality rates, of 11–18% for early fistula (within 30 days of surgery) and 0–7% for late fistula (beyond 30 days of surgery), they should be evaluated thoroughly by CT scan and flexible bronchoscopy. Bronchopleural fistula is separately discussed thoroughly elsewhere.

4. Management

4.1 Initial management

Initial management of pneumothorax patients involves ensuring adequate airway, providing supplemental oxygen, securing an intravenous line, looking for signs of compromised breathing and deciding on the need of tube thoracostomy. Tension pneumothorax should be diagnosed by clinical assessment and a tube thoracostomy/needle thoracocentesis should be performed immediately. Scant data exists in literature proving the efficacy of needle thoracocentesis procedure. However, when tube thoracostomy is anticipated to take time, a needle thoracocentesis may be done immediately, to save life.

Tube thoracostomy is an emergency procedure and is mandatory where pneumothorax is large, or patient has respiratory compromise. Some centres practice drainage of all traumatic pneumothoraces irrespective of symptoms [11]. This line of management in simple pneumothorax is considered invasive by other centres, who recommend observation and oxygen supplementation for small pneumothoraces.

Sucking chest wounds require immediate sealed-cover with an occlusive, air-tight, clean plastic sheet. The sterile inside of gloves-packet can be used in an emergency situation. No patient with penetrating chest wound should be neglected, as tension pneumothorax or life-threatening respiratory emergency can arise.

Upright positioning is beneficial unless contraindicated, like in spinal injury. In a patient with pneumothorax who requires air transport, it is essential that an intercostal tube with Heimlich valve be placed prior to transfer, as pressure changes during flight will cause progression in the severity of the injury and may potentially lead to development of tension pneumothorax.

Pain impairs the ability of the person to breathe, further compromising lung mechanics, in inflammed and contused lungs. In addition, it causes the retention of pulmonary secretions which further suppresses the patient's cough reflex, finally leading to atelectasis and increasing morbidity, Nonsteroidal anti-inflammatory drugs, systemic opioids or regional analgesia methods such as epidural analgesia, intrapleural analgesia, intercostal nerve block, and thoracic paravertebral block have been used for pain control.

Supplemental oxygen therapy, instead of room air, accelerates the resorption of air in pleural cavity by four-fold. By breathing 100% oxygen instead of air, alveolar pressure of nitrogen falls, and nitrogen is gradually washed out of tissue and oxygen is taken up by vascular system. This builds substantial gradient of nitrogen between tissue capillary and the pneumothorax space, resulting in multifold increase in absorption from pleural space. About 1.25% of the volume of pleural air is absorbed in 1 day; hence 25% of the volume is absorbed in 20 days [17]. Small pneumothoraces are often managed with oxygen administration and monitoring via chest X-rays.

4.2 Tube thoracostomy

Correct placement of the tube is seen as the stream of the bubbles during expiration and coughing and the rise on the level of fluid in the underwater seal during inspiration. Complications of tube thoracostomy include injury to lung or mediastinum, haemorrhage (usually from intercostal artery injury), neurovascular bundle injury, infection, bronchopleural fistula, and subcutaneous or intraperitoneal tube placement.

Heimlich valve or the Vycon self-sucking chest drainage valve are applied directly to the chest tube and reduce or eliminate the underwater drainage period. The Heimlich flutter valve is quite inconspicuous under clothes and makes ambulatory treatment possible. The valve is made of latex rubber that acts as one-way valve, letting air out and preventing reentry. The Vycon device is a double self-sucking valve. It has a soft plastic casing that allows application of manual pressure to aspirate air or fluid [18].

If the lung remains unexpanded or if there is a persistent air leak 72 hours after tube thoracostomy, thoracoscopy or thoracotomy should be considered. Presence of hemopneumothorax, bilateral pneumothorax, first contralateral pneumothorax and pregnancy may be considered for early invasive treatment [19].

Tube thoracostomy is usually sufficient to treat primary spontaneous pneumothorax. However, Schramel et al. reviewed 11 studies over 32 years, involving 1242 patients with primary spontaneous pneumothorax, treated with needle aspiration or tube drainage, and concluded that about 30% patients have recurrence of pneumothorax [20]. Risk factors for recurrence are radiographic evidence of pulmonary fibrosis, smoking, asthenic habitus and younger age [21]. Presence of blebs or bullae was not found to be significantly associated with recurrence [21]. Of patients with recurrent pneumothorax after initial spontaneous pneumothorax, 72% will develop a subsequent pneumothorax within a 2-year period [21]. Recurrent spontaneous pneumothorax or persistent air leaks at initial presentation are indications for operative treatment. Patients in occupations with excessive pressure changes (pilots and divers) or those residing in remote areas, are candidates for operative intervention after a single episode of spontaneous pneumothorax to prevent a potentially life-threatening recurrence.

Clinical picture in secondary spontaneous pneumothorax (SSP) is complicated by the presence of underlying diffuse lung disease, such as chronic obstructive pulmonary disease (COPD), cystic fibrosis, tuberculosis, fibrotic lung diseases such as idiopathic pulmonary fibrosis, and autoimmune diseases involving pleura such as rheumatoid arthritis, ankylosing spondylitis, systemic sclerosis, and Sjogren's syndrome. Observation without evacuation of the pneumothorax, is usually not possible because these patients usually are very symptomatic. Simple aspiration is less likely to be successful in SSP than in primary pneumothorax [22]. It is attempted as an initial treatment in small (air space <2 cm) pneumothoraces in minimally breathless patients under the age of 50 years. If the patient with SSP is 50 years or older, and if the rim of intrathoracic air is larger than 2 cm on a chest X-ray, intercostal tube drainage is advocated. Clinically unstable patients should have a chest tube inserted, notwithstanding the size of the pneumothorax. Sixty-one to seventy percent of leaks resolve by day seven of tube drainage. Further drainage is unlikely to improve success. If air leak does not stop after 48 hours of continuous drainage, consultation for surgical intervention is recommended because of significantly lower healing rate of pleura in cases of SSP compared with primary spontaneous pneumothorax [23].

Indications for operative treatment include persistent air leak, recurrent pneumothorax, pneumothorax after pneumonectomy or intolerance of the prolonged effects of pneumothorax, not relieved by more conservative approaches.

4.3 Surgical method

Prevention of persistent air leak or future recurrence requires initial identification of the source of the air leak, that is, macroscopic blebs or bullae. Bullae are air filled spaces within the lung parenchyma resulting from the progressive destruction of alveolar tissue. Typically they have relatively thick fibrous walls, grow progressively larger, and are poorly ventilated and with poor perfusion. A giant bulla is defined as one which occupies more than one third of the chest cavity. Complete intrathoracic inspection requires division of all pleural adhesions since these often conceal the culprit lesion. The source of air leak is then controlled by stapling, or suturing.

After completion of the bleb resection, pleurodesis is performed to decrease risk of recurrence. Horio et al. has shown, in a comparative study, that recurrence rate diminished from 16 to 1.9%, when pleurodesis is added to bullectomy [24]. Areas of pleural porosity are potential sources of recurrence, and may be too widespread to be resected. Hence, pleural symphysis is important.

There are three basic approaches to achieve the principles above: thoracostomy, thoracoscopy or thoracotomy. Video-assisted thoracoscopic surgery (VATS) is enabled by the insertion of a 5- to 10-mm videothoracoscope via a 1- to 2-cm incision in the lateral sixth intercostal space. Two more similar incisions are placed anteriorly and inferiorly in the fourth and seventh intercostal space (**Figure 1**). Instruments are introduced via rigid or flexible ports. Adhesions are taken down with sharp dissection. Bleb excision or bullectomy is carried out with an endoscopic linear cutter. The bullae are deliberately opened by cautery or scissors and allowed to deflate. An endoscopic lung clamp is used to grasp the bulla and is then rotated repeatedly as if winding a clock. This action collapses the bulla onto itself and the demarcation between bulla and normal lung parenchyma is revealed. Small ventilated breaths to the ipsilateral lung can also highlight this transition zone. The endoscopic linear cutter stapler is then used to amputate the base of the bulla (**Figure 2**). Alternatively, bleb may be ligated using a pre-tied Roeder slip knot, introduced by an external applicator.

When excising the emphysematous bulla, the staple lines must be reinforced to reduce chance of postoperative air leak. Application of buttress material in the staple line distributes tension throughout the staple line, seals off the staple holes and narrows the spaces between each staple, thus reducing tearing at the staple line. Additionally, the buttress provides a broader pressure profile around each

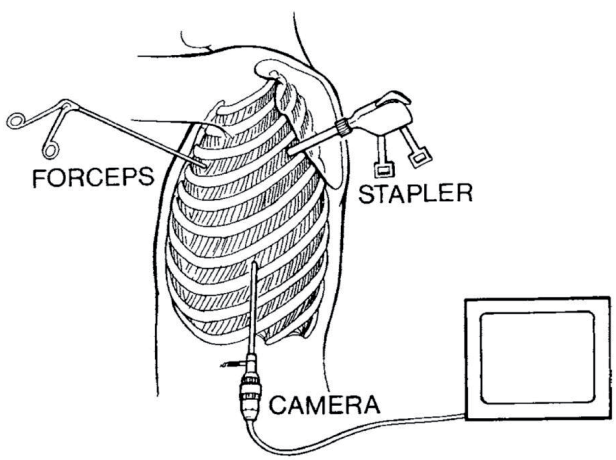

Figure 1.
Port placement for blebectomy [25].

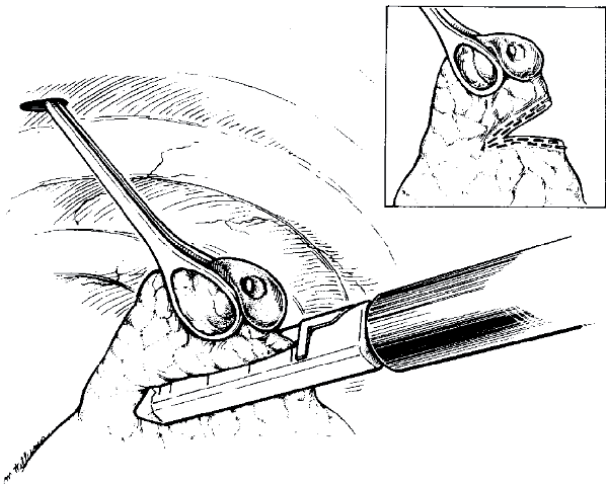

Figure 2.
Apical bullectomy using ring forceps and endoscopic stapler [25].

individual staple across the staple line, leading to potentially improved haemostasis. Material such as fibrin glue, bovine pericardium, poly-glycolic acid, polydioxane ribbon, Teflon felt, collagen patches and polytetrafluoroethylene (PTFE) sheets have been used to reinforce staple line. Nonabsorbable synthetic materials carry the potential hazard of inflammation and/or bacterial colonisation. Biomaterials originating from animal tissues have a risk of cross-species transmission of infection.

Accessory ports are removed under direct thoracoscopic guidance and the sites inspected for haemostasis. A 24 or 28 F drain is placed to the apex of the hemithorax. This is brought out of one of the port sites and connected to underwater seal drainage and suction. The lung is inflated under direct vision by the scope to verify complete inflation, locate additional blebs, and insure proper placement of the chest tube to the apex of the hemithorax. An inflated lung can displace a tube 2–3 cm caudally. If not corrected, this will frequently lead to a loculated pneumothorax at the apex and thwart the pleurodesis. The sites are closed in two layers with an absorbable suture.

Open surgery is usually performed via muscle-sparing thoracotomy. A lateral or axillary thoracotomy via the fourth intercostal space preserving the fibres of latissimus dorsi and with minimal rib retraction is the approach of choice. Bullae are opened, bronchial edges are oversewed, edges of the bullae are unfolded and stapled. Exogenous materials are buttressed to minimise postoperative air leak.

Randomised prospective study comparing VATS with axillary thoracotomy found no significant difference in postoperative blood loss, lung function, postoperative pain, use of analgesics, postoperative complications, duration of hospital stay and resumption of normal activities. However, with a minimum follow-up of 2 years the recurrence rate after VATS was 4.3% and after a limited thoracotomy, was 0% [26].

However, for recurrent pneumothorax, a randomised study found significantly longer operative time with VATS. Complication rate, chest tube duration, hospital stay, and incidence of chronic pain were not significantly different [27].

In multiple studies, VATS was found to be associated with higher recurrence rate compared to open thoracotomy [28–30]. Barker and colleagues performed a meta-analysis by comparing the reported recurrence rates in patients undergoing VATS with those having open surgery. Results showed a four-fold increase when a similar pleurodesis procedure is performed with a video-assisted approach compared with an open approach [28]. One of the reasons attributed to it was insufficient visualisation of bullae or blebs on the lung by thoracoscopy. Another reason quoted

was less adhesion between the lungs and the chest wall postoperatively when VATS is performed compared with open thoracotomy. Inspite of this, many thoracic surgeons prefer the VATS approach as it is less invasive, less painful, and associated with a shorter hospital stay [31]. VATS is, thus, now considered approach of choice for elderly patients or those with multiple comorbidities [32, 33].

Migliore et al. approached pneumothorax through single port, using hand-crafted 20 mm flexible trocar [31]. Jutley et al. compared the standard three-port VATS and uniVATS for surgical management of spontaneous pneumothorax and demonstrated safety and effectiveness with the latter technique [34]. Reduction of intraoperative blood loss and postoperative pain with a higher patient's satisfaction score in uniVATS emerged from a propensity matched comparative analysis by Dai et al. [35]. However, retrospective comparison of uniport versus multiport VATS lobectomies by Chang et al. revealed no difference in operative time, postoperative 30-day mortality, chest tube permanence, hospital stay and reoperation rates [36].

More recent advance in the field of thoracic surgery is robotic-assisted surgery. The surgeon sits at a console, away from the patient in operating room and controls the instruments, including camera, on the robotic surgical system. A small 3D high-definition camera is placed through one of the incisions to provide a good view of the chest cavity, while wristed robotic instruments are inserted through the other small incisions.

For bilateral bullous disease, staging the operations is preferred, to minimise morbidity as well as to allow the ipsilateral lung to re-expand completely, optimising the patient's functional status before tackling the contralateral lesion.

Catamenial pneumothorax with mild symptoms is usually managed with simple rest and thoracocentesis or chest tube for symptomatic relief. The surgical aspects include removal of blebs and bullae, wedge resection, and pleurodesis (abrasion or talc). Most surgical treatment is performed by thoracoscopy, and pleurodesis has been advocated to reduce recurrences. Endometrial deposits on diaphragm are removed as conservatively as possible to spare the diaphragmatic function. Multiple small defects are repaired by titanium clips. The diaphragm is finally reinforced by Prolene or Gore-Tex® mesh. Spiral clips are placed radially at the border of the prosthesis [37]. There is still no agreement regarding whether a prosthetic repair should be recommended. Bagan et al. reported fewer recurrences after diaphragm reinforcement with polyglactin mesh [38]. Concern exists about the use of VATS for large diaphragm defects. Minimally invasive approach is not fully supported by evidence. Both sides of the diaphragm need to be evaluated if one side is noted to have endometrial implants. Superficial diaphragmatic endometriosis can be treated with cold scissors, monopolar energy, bipolar energy, CO_2 laser, or a plasma energy source [39]. Bagan et al. suggested application of surgical treatment during menses, for better visualisation of the endometriotic lesions [38].

Postoperative treatment with GnRH agonists or oral contraceptives for 6–12 months is suggested for all patients with proven catamenial pneumothorax for symptomatic relief and to reduce recurrences. The goal of early GnRH analogues administration is to prevent cyclic hormonal changes and induce suppression of ectopic endometrium activity, until accomplishment of effective pleurodesis, since formation of effective pleural adhesions require time [40]. Longer period of hormonal treatment (median 17.5 months) has been required after reoperations for catamenial pneumothorax. Recurrence rate varied from 14.3 to 55%.

4.4 Pleurodesis (mechanical and chemical) and parietal pleurectomy

Pleural symphysis is used to obliterate the potential space between pleural surfaces to prevent recurrent pneumothorax. This is accomplished by inducing an

inflammatory reaction between the visceral and parietal surfaces with a chemical agent, mechanical abrasion or by stripping the parietal pleura which results in fusion of the visceral surface to the denuded thoracic wall. Chemical agents include talc, doxycycline, tetracycline, bleomycin, iodopovidone, Corynebacterium parvum and silver nitrate. Mechanical pleurodesis is done by vigorously abrading the parietal pleural surface with tightly rolled gauze, held by ringed forceps or a Bovie scratch pad (**Figure 3**).

Parietal pleurectomy involves sacrifice of the parietal pleura. With the help of saline infusion in sub-pleural space, the parietal pleura can be bluntly dissected with a end-forceps. Alternatively, electrocautery can be used. Ayed and Chandrasekran suggested that in apical region, pleurectomy might be a more effective procedure than pleural abrasion [41].

In a randomised prospective study of 96 patients, pleurodesis by talc slurry resulted in the lowest recurrence rate of 8%, compared to 13% with tetracycline and 36% with simple tube drainage [42]. Talc is insufflated into the chest so that complete dispersion throughout the hemithorax is accomplished. This is typically accomplished with an atomizer. Alternatively, talc can be blown into the chest from a LUKI tube in front of a 6 L/minute oxygen flow rate. Alternatively, talc slurry can be instilled through a chest tube in patients who are not surgical candidates.

Talc is cheap. Talc instillation carries a low risk. However, complications such as pulmonary edema, acute respiratory distress syndrome, and hypotension have been reported [43, 44]. In an experimental study in rats, rapid absorption of talc from the pleural space was seen and systemic distribution might explain the complications [45]. Thus, size of the talc particles seems important, smaller particles inducing more systemic complications. In a recent prospective European multicentre study, thoracoscopic pleurodesis with 2 g of graded talc consisting of large particles, was found to be safe after a 30 day observation period [46].

Talc induces a painful inflammatory reaction on the pleural surfaces, which requires adequate analgesia. Aggressive pleurodesis methods should be avoided in chronic obstructive pulmonary disease patients who are suitable for lung transplantation, to reduce graft implantation complications.

In a comparative, randomised study including 73 patients with pleural effusion or spontaneous pneumothorax, talc and iodopovidone were found to be equally efficient and safe [47]. Pleurodesis by autologous blood has been initially used by Robinson, for treatment of persistent air leak in spontaneous

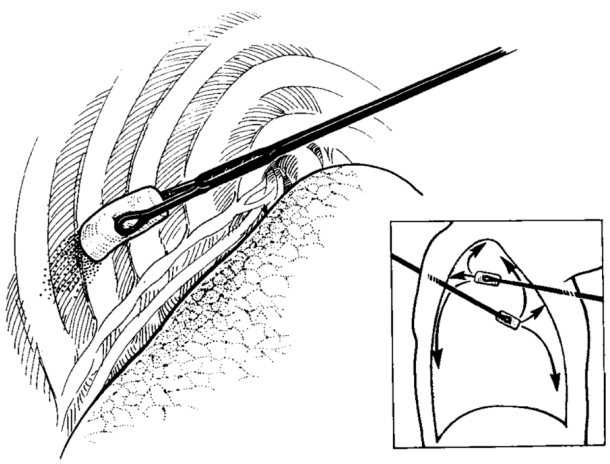

Figure 3.
Method of mechanical pleurodesis [25].

pneumothorax patients [48]. This method is being widely used as a treatment of choice for air leaks, since pain and fever, which have been reported with other chemical pleurodesis agents, are rarely encountered with this agent [49, 50]. Development of empyema and tension pneumothorax have been reported, which had occurred due to clotting of the blood in the chest tube and care must be taken to prevent it [50].

In children, the management protocols of pneumothorax remain almost the same. In children too, surgery reduces ipsilateral primary spontaneous pneumothorax recurrence. But, surgery is shown to be predictive for contralateral recurrence in them [51]. Perhaps the positive pressure ventilation required during surgery leads to formation of new blebs contralaterally, or to over-distension of already existing contralateral blebs [52].

5. Anaesthesia

VATS is commonly performed under general anaesthesia with split-lung ventilation. The COPD patient's baseline pulmonary functions are often suboptimal and they may represent a relative contraindication to split-lung ventilation, thus conferring axillary thoracotomy an advantage over VATS. However, postoperative exacerbation of respiratory function or postoperative chest pain has been more effectively avoided with thoracoscopic surgery [53, 54]. To prevent hypoxemia during one-lung ventilation for thoracoscopic surgery, application of continuous positive airway pressure to the non-ventilated lung is performed [55]. More sophisticated techniques using fiberoptic bronchoscopic segmental oxygen insufflation and recruitment have been reported [56].

Awake surgery under epidural anaesthesia might be advocated in case with several thoracic diseases [57, 58]. Though the efficacy and safety of awake surgery are still controversial, and definitive criteria for indications for awake surgery do not exist, studies have shown that the mean time for chest tube drainage, hospital stay, and operative time were shorter in epidural anaesthesia group than in general anaesthesia group. The postoperative pain score was significantly lower in the epidural anaesthesia group. The study proved that well-maintained breathing and hemodynamics during the awake thoracoscopic surgery attenuated the surgical stress responses and had a smaller impact on the postoperative lymphocyte responses when compared with conventional thoracoscopic surgery under general anaesthesia with single-lung ventilation [59, 60].

Another alternative to general anaesthesia with split-lung ventilation is total intravenous anaesthesia, using propofol and sufentanil, with local anaesthesia, using lignocaine, at incision sites and pleural surface. This has been described to have comparable results, while doing away with the adverse effects of epidural anaesthesia, such as epidural hematoma, spinal cord injury and phrenic nerve palsy. Total intravenous anaesthesia is technically demanding, and anaesthesia-related phenomena, such as hypotension and bradycardia, may arise. Anaesthetists have used laryngeal masks to secure the patients' airway during the procedure, and provided deep sedation without compromising patient safety [61].

In contrast to secondary spontaneous pneumothorax due to COPD, that caused by lung fibrotic disease shows different characteristics—lungs with fibrotic disease are very fragile and shrunken. The postoperative mortality rate is high (three of 14 patients in one study) due to the exacerbation of basic lung disease and also because full expansion of lung is not achieved by applying negative intrathoracic pressure due to low respiratory compliance [62]. Such a pulmonary fibrotic disease that has taken the centre stage among all diseases, is the COVID-19 disease.

6. Pneumothorax in COVID-19 patients

Lungs of patients with COVID-19 who have significant interstitial involvement seem physiologically small, with low compliance and reduced elastance. The thickened, stiff tissue makes it difficult for lungs to expand properly, and sustained-pressure ventilation may be necessary to obtain acceptable gas exchanges. In this setting, fibrotic parenchyma and preexisting emphysematous blebs are prone to rupture, with consequent risk of pneumothorax. Overinflation and high positive end-expiratory pressure in such fibrotic and hypoelastic lungs may cause alveolar or preexisting bleb rupture.

Furthermore, pneumothorax and bulla have been reported in COVID-19 patients who did not have any risk factors for pneumothorax, including mechanical ventilation, history of smoking, or pulmonary comorbidities [63]. The alveolar damage, and bronchiolar distortion and narrowing, caused by fibrosis following resolution of COVID-19 pneumonia, led to pulmonary bullae formation. Moreover, the severe cough associated with viral infections increases the intrapulmonary pressure. This, in turn, may precipitate bullae rupture and pneumothorax formation [64].

Chest tube placement should be considered first-line treatment. Persistence of air leak may constitute an indication for low-tidal volume two-lung ventilation thoracoscopy. Because of stiffer parenchyma, black cartridge staplers are needed for bulla resection. Ideal timing for surgical procedure is unclear. It may be better to do the procedures early in the disease when the interstitial tissues are less traumatised, less fibrotic, and less inflamed [65].

Extra-corporeal membrane oxygenation (ECMO) as a treatment option for pneumothorax with severe ventilator settings has been tried successfully, to reduce ventilator settings and thus, allowing the lungs to rest. This reduced the lung inflation, and avoided over distension of the lungs, while reducing the air leak and allowing the pleura to heal [66, 67].

7. Conclusion

Pneumothorax is a relatively common malady, both in traumatic and non-traumatic setting. The management is initiated by tube thoracostomy and other supportive measures. Presence of underlying lung disease warrants a more aggressive approach. Prevention of recurrence is also crucial, as recurrences are associated with poorer outcome. VATS is an attractive surgical option due to smaller incision and faster recovery. Innovative procedures continue to be described and many will achieve wide acceptability.

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Chapter 8

Secondary Pneumothorax from a Surgical Perspective

Simona Sobrero, Francesco Leo and Alberto Sandri

Abstract

Although less frequent than the primary spontaneous pneumothorax (PSP), secondary pneumothoraces (SP) are a common clinical problem with a wide range of severity, depending on the triggering cause(s) and patient clinical condition. By definition, an SP occurs in those patients with an underlying condition that alters the normal lung parenchyma and/or the visceral pleura and determines air entry in the pleural space (e.g., COPD) or, eventually, following trauma or invasive procedures (i.e., iatrogenic pneumothorax). Less frequent, yet described, is SP occurring in neoplastic patients or infectious ones. The gravity of an SP is directly correlated to the underlying cause and patients' clinical conditions. For example, it may be a life-threatening condition in an end-stage COPD but less severe in a catamenial related syndrome. In this chapter, we are providing a surgical overview of the most relevant and updated information on etiology, incidence, pathophysiology, and management of secondary pneumothoraces.

Keywords: secondary pneumothorax, COPD, malignant pneumothorax, post-traumatic pneumothorax, iatrogenic pneumothorax, catamenial pneumothorax

1. Introduction

Pneumothorax (PNX) is an abnormal collection of air in the pleural space. It is defined as primary spontaneous pneumothorax (PSP) or secondary, based on age, causes, and the requirement of different management [1].

A PSP usually occurs following the rupture of subvisceral pleural blebs and its cause is unknown. Most frequently, patients are males, healthy teenagers or young adults, and smokers [2].

Instead, a spontaneous secondary pneumothorax (SPS) is often associated with a known lung disease and the main cause is a chronic obstructive pulmonary disease (COPD). Other causes are, for instance, idiopathic fibrosis, acquired immunodeficiency syndrome (AIDS), and neoplastic disease. Secondary pneumothorax (SP) could also occur after a chest trauma (post-traumatic pneumothorax) or after invasive procedures (iatrogenic). A specific subgroup is represented by the catamenial pneumothorax, as discussed further on.

The annual incidence of SPS is in general 26 cases per 100.000 and it is more common in men with a 3:1 ratio. It is mainly observed in patients aged 50–60 years old [3, 4].

In general, symptoms include chest pain and shortness of breath, but symptoms could differ according to the cause of pneumothorax [5].

In the following chapter, all the aspects related to a secondary pneumothorax are described.

2. Secondary pneumothorax

The annual incidence of an SP is approximately 6.3 cases per 100.000 in men and 2 cases per 100.000 in women, every year [3].

A SP may occur:

- in the presence of pre-existing lung diseases, like COPD, infections (e.g., tuberculosis, necrotizing pneumonia, and pneumocystis carinii), inflammatory disease (e.g., rheumatoid arthritis, polymyositis and dermatomyositis, and systemic sclerosis);
- in the presence of neoplastic disease (e.g., primary lung cancer, sarcoma metastases, and malignant pleural mesothelioma);
- as a consequence of a chest trauma;
- as a complication of medical or surgical procedures (iatrogenic pneumothorax); or
- concomitant to other pre-existing pathologies (e.g., catamenial pneumothorax) [6].

Moreover, compared to a primary pneumothorax, SP afflicts patients with a known history of lung disease. For such reasons, an SP:

- is less tolerated by patients because of a co-existing lung disease;
- is generally characterized by the presence of a persistent air leak that does not tend to resolve spontaneously, requiring an active intervention; and
- oxygen could be required to promote air reabsorption, especially in the case of subcutaneous emphysema.

Generally, the management of such patients is complex and the treatment requires a chest tube insertion, prolonged hospitalization, and consideration for a surgical procedure to induce pleurodesis.

2.1 Secondary pneumothorax in nonneoplastic lung disease

2.1.1 Definition and incidence

The main cause of SP is COPD, with an incidence of 26 cases per 100.000 patients per year [7]; COPD is one of the three main causes of death in the world and one of the main causes of chronic disease [8].

Based on computed tomography (CT) images, COPD may be divided into:

- emphysema- and airway-dominant COPD: SP generally occurs as a consequence of bullae disruptions (**Figure 1**);
- nonemphysematous COPD.

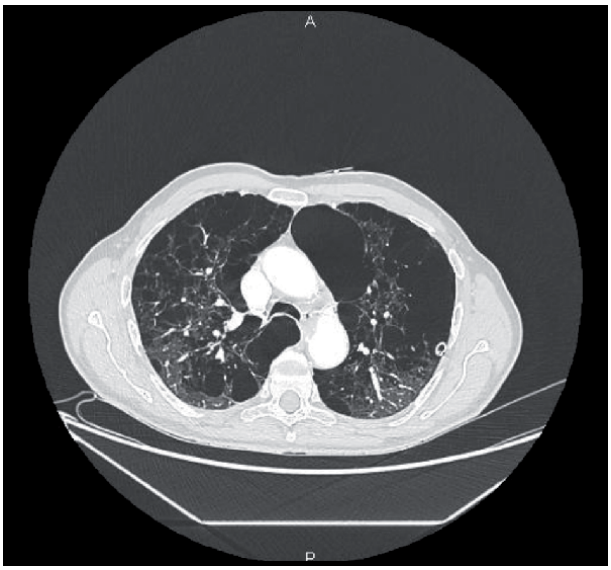

Figure 1.
Emphysema dominant COPD.

According to the GOLD guideline [9], COPD severity depends on pulmonary function, evaluated by means of a spirometry. The risk of an SP is higher in patients affected by severe COPD. Patients with FEV1 < 1 L and/or a FEV1/FVC < 40% are deemed at high-risk [10], with a common observance of severe hypoxemia associated with hypercapnia in case of pneumothorax [8].

The development of a secondary pneumothorax in COPD patients is a parameter of high mortality and, in fact, it has been demonstrated that each SP event increases fourfold the chances of death in such patients [11].

2.1.2 Pathophysiology and clinical features

When a pneumothorax occurs in a COPD patient with a low respiratory function, it is common to observe severe hypoxemia caused by a lower ventilation-perfusion (V/Q) rate, which is capable to determine an incremented shunt that is directly proportional to the PNX size. Compensatory hypercapnia is often associated [8].

For such reasons, an SP onset in COPD patients is generally associated with a rapidly progressive dyspnea and pleuritic chest pain where a prompt management is mandatory.

2.1.3 Diagnosis

Generally, COPD patients present with hyperinflated lungs and abnormal lung auscultation. A reduced or absent vesicular murmur associated with symptoms such as shortness of breath, low saturation, and hyperventilation should easily guide to diagnose a PNX.

A chest X-ray is mandatory to assess the presence of a PNX, which usually appears as a complete collapse of the lung. Seldomly, a subcutaneous emphysema may occur, concealing the PNX at the chest X-ray (**Figure 2**).

Generally, at chest X-ray, bullous lesions have a concave appearance while a pneumothorax has a concave profile (**Figure 3**).

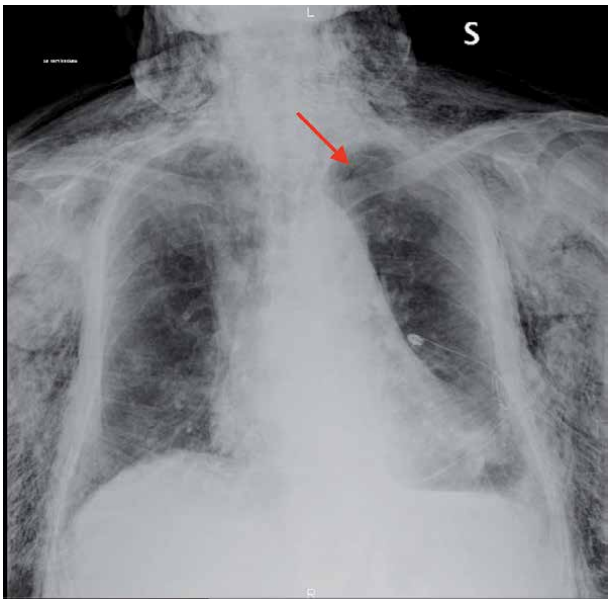

Figure 2.
Massive subcutaneous emphysema. Red arrow to indicate the small size SP.

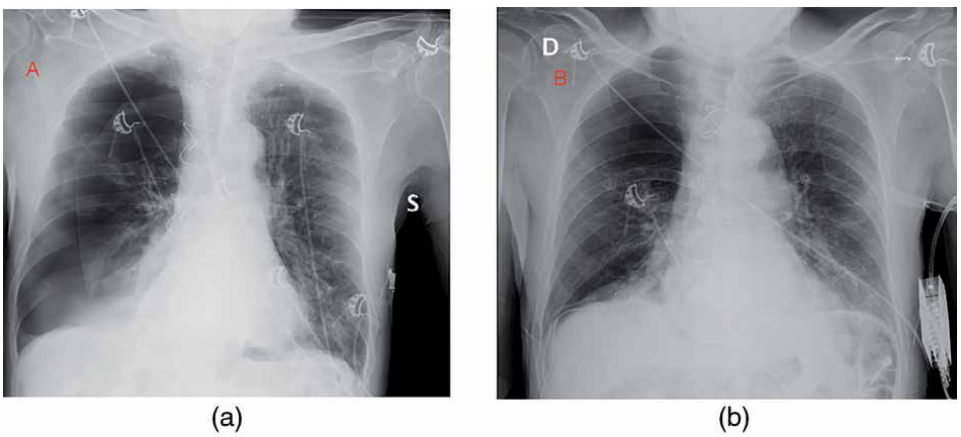

Figure 3.
The different appearance between an SP and bullae. Image a: a secondary pneumothorax in a COPD patient. At the chest X-ray, a pneumothorax has a concave profile. Image b: bulls lesion has a concave appearance.

In COPD patients, however, a CT scan is useful to better analyze the pneumothorax size and the severity of the lung disease. Moreover, The CT scan can help in distinguishing a big bulla from a true PNX. This may not be an easy task; however, if a bulla is detected, a chest tube is not always indicated, or if it is, it should be carefully placed under CT guidance, in order to avoid an iatrogenic rupture of the bulla determining a complex PNX, which potentially requires a surgical treatment.

It is important to remember that due to the underlying pathology and the low functional reserve, these patients could become suddenly critical in case of a PNX and should therefore be treated accordingly. For the same reason, even if the PNX is correctly treated by means of a chest drain, these patients still remain at a higher risk of death. Death causes are, in fact, associated with the onset of an acute or late

respiratory failure [12, 13], or with a higher risk of developing sepsis as a consequence of pneumonia or empyema due to the pneumothorax management (i.e., chest tube and/or pleurodesis) [14].

2.1.4 Other causes of SP in non-COPD patients

Any noxa capable to affect the integrity of the visceral pleura and reduce the lung elasticity could be a cause of a secondary pneumothorax and therefore, a secondary pneumothorax may be diagnosed in the process of:

1. Infection: tuberculosis, necrotizing pneumonia, and *Pneumocystis carinii* (it determines an infection capable of recalling macrophages in the lung parenchyma with consequent tissue destruction and fibrosis), viral or mycotic infection (**Figure 4**). In these cases, a medical treatment is mandatory before considering surgery as an option to resolve the SP.

2. Interstitial diseases: cystic fibrosis, acute severe asthma. Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and fibrosing lung disease of unknown etiology. The rates of pneumothorax range from 2 to 20% in patients with IPF, becoming the second cause of SP after chronic obstructive pulmonary disease (COPD) [15].

3. Inflammatory or connective-related diseases: such as rheumatoid arthritis, polymyositis, dermatomyositis, systemic sclerosis, Marfan's syndrome, and Ehlers-Danlos syndrome.

Acquired immunodeficiency syndrome (AIDS) could be another cause of SP, likely related to an increased risk of developing cystic lesions in the sub-pleural space [16].

2.1.5 Management

As in the case of primary pneumothorax, the treatment goals should aim at:

- evacuating the pleural cavity from the air to restore the normal intrapleural negative pressure;

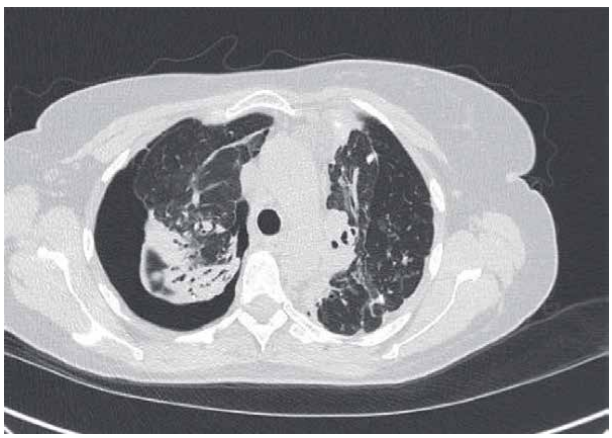

Figure 4.
Pneumothorax caused by tubercular infection.

• obtaining lung re-expansion and pleural apposition;

• reducing the risk of recurrence.

According to the BTS guidelines, a secondary pneumothorax that occurred in a known diseased lung requires the insertion of a small-bore chest tube to drain the air in the pleural space [17].

Pneumothorax aspiration, which finds a treatment indication in the primary spontaneous pneumothorax, has a high-risk of failure, but it may be taken into account in the case of symptomatic patients with a small pneumothorax. A persistent air leak can be managed conservatively obtaining a complete resolution [17].

A talc slurry pleurodesis could be a nonsurgical therapeutic management option to be considered for persistent air leak in patients deemed unfit for surgery. According to the American College of Chest Physicians (ACCP) consensus, a talc slurry pleurodesis through the chest tube is indicated to avoid recurrence after the first episode [14].

By contrast, the BTS guidelines suggest pleurodesis in case of a recurrent SP or in case of a persistent air leak, which in COPD patients may resolve in a long time compared to non-COPD patients [18]. Surgery is an option in SP, but COPD patients may not be deemed fit enough for surgery because of their clinical status. A prerequisite for talc pleurodesis is a complete or major re-expansion of the lung. In case of partially expanded or nonexpandable lungs, other options should be advocated, such as permanent drains connected to a Heimlich valve. Furthermore, prior to proceeding to talc pleurodesis, the increased risk of a pulmonary restrictive dysfunction secondary to talc insufflation should be well pondered and discussed interdisciplinary.

Contrarily to the ACCP guidelines that suggest medical thoracoscopy or VATS as the first choice to perform talc pleurodesis, because of their lower morbidity, the BTS guidelines consider an open approach (thoracotomy) as the procedure of choice, limiting VATS procedures to unfit patients [17].

Furthermore, in nonsurgical patients with a persistent air leak a talc slurry via chest tube should be taken into consideration.

2.1.5.1 Focus on: management of emphysema-dominant COPD lung volume reduction surgery (LVRS)

The 2021 GOLD guidelines consider as the main surgical option in high-grade COPD [9]:

Emphysema at CT scan	**Pre-operative exercise capacity**	**LVRS risk of death**	**Survival**	**Post-operative exercise tolerance**	**Symptoms control**
Upper lobe-predominant emphysema	Low	Lower than medical therapy	Improved	Improved within 3 years from surgery	Improved
	High		Not improved	Improved (years 1–3)	Improved (years 1–4)
Non-upper lobe-predominant emphysema	Low	No effects	Not improved	No effects	
	High	Increased	Not improved	No effects	No effects

Table 1.
Results in the four groups studied in the NETT trial.

- lung volume reduction surgery (LVRS);

- bullectomy/blebectomy, which are associated with an improvement of dyspnea and lung function;

- lung transplantation: in very high-risk patients, with progressive COPD. Inclusion criteria are exacerbations associated with hypercapnia ($pCO2 \geq 50$ mmHg), pulmonary hypertension, FEV1 < 20%, and/or a diffusing capacity for carbon monoxide (Dlco <20%) [9].

LVRS can improve survival in severe lung emphysema, mainly in the upper lobes localized emphysema, and low-ability exercise patients [17]. The National Emphysema Treatment Trial (NETT) identified four groups of patients [19] on the basis of their postoperative exercise tolerance and their emphysema pattern at the CT scan (**Table 1**).

The NETT demonstrated that the effects of LVRS are durable and that it is strongly recommended in upper lobe-predominant emphysema with low exercise capacity and should be considered for palliation in patients with upper lobe emphysema and high exercise capacity (**Figure 5**).

2.1.5.2 Endobronchial valves

Predominantly, the following endobronchial procedures find an indication in reducing the end-expiratory lung volume and to improve exercise tolerance:

- endobronchial lung volume reduction with one-way valves (BLVR);

- endobronchial coils filling;

- thermal ablation.

Endobronchial valves are placed in segmental or lobar bronchi through rigid bronchoscopy, allowing peripheral lung deflation, lung volume reduction, and improvement of symptoms with an accepted mortality rate equal to 5–10% [20]. The valve mechanism does not permit air to go through the segmental or lobar bronchus during the inspiration but, instead, it allows it passage during the expiratory phase. The valves are available in multiple diameters, ranging from 4 to 8.5 mm.

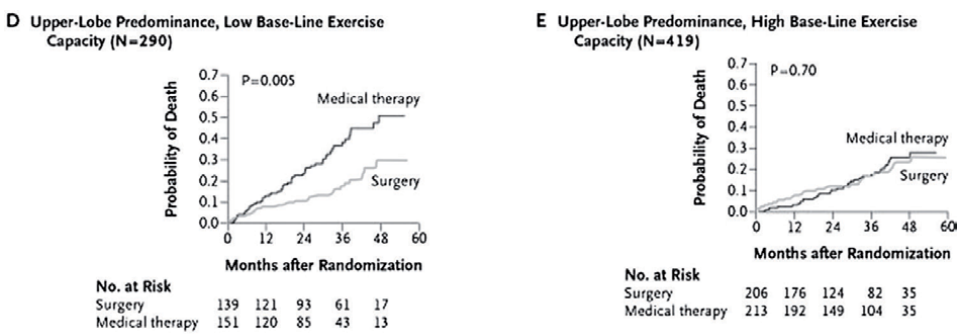

Figure 5.
Results of NETT. Image D: Upper lobe–predominant emphysema with low exercise capacity group. The surgical group has a lower probability of death than the medical group.

In general, two main devices are available:

- the "aspiration umbrella", which is an implantable Intra-Bronchial Valve (IBV) that can be positioned via flexible bronchoscopy, leaving the umbrella shape adherent to the airway wall and limiting the airflow distally;

- the Emphasis Bronchial Valve (EBV), which is able to prevent air entering in the lung during inspiration but allows outflow of air and secretion. A flexible aspiration valve is present in the endobronchial valve structure from which exhaled air and secretions can be cleared out or aspirated because of the unidirectional valve.

Both devices are inserted in the operating theater with the patient sedated and in spontaneous assisted (jet-) ventilation [21].

The VENT trial (Endobronchial Valve for Emphysema Palliation Trial) [22] is a two-arm, randomized, controlled, multi-center trial that showed a 4.3% FEV1 increase in the EBV group compared to the 2.5% in the control medical group.

However, the study shows that complications following the procedure may counterbalance the advantages of the procedure itself. In fact, on the one hand, patients may obtain an improvement in their respiratory function, and on the other hand, it may be associated with hemoptysis, pneumothorax with persistent air leak, and COPD exacerbations, which may occur more frequently in advanced, hyper-inflated emphysema patients. Moreover, as evidenced in the VENT trial, the 2-yrs mortality rate in the EBV group was 2.8% compared to no deaths in the control group, but the difference wasn't statistically significant ($p = 0.19$).

2.2 Secondary pneumothorax in concomitant neoplastic disease

Although rare findings, the main causes of SP from malignant diseases are primary cancers of the lung and pleura (e.g., mesothelioma) followed by infiltrative/metastatic pleural diseases, such as in the case of germ cell tumors, breast cancer, or osteogenic and soft tissue sarcomas metastasis [21–23].

2.2.1 Incidence

The occurrence of an SP as the first manifestation of a lung cancer ranges between 0.03% and 0.05% and usually allows to detect the unknown presence of a lung tumor or metastasis [24] without affecting the prognosis [25, 26].

By contrast, a review published in 2010 analyzed data available in the literature concerning pneumothorax secondary to sarcoma, highlighting increased mortality in such patients compared to those without such complications [26].

2.2.2 Pathophysiology

Several hypotheses have been taken into account to explain the pathogenesis of pneumothorax secondary to malignant disease, which include (i) an alteration of the pleural surface following tumoral pleural infiltration; (ii) rupture of a necrotic tumoral nodule; and (iii) necrosis of subpleural metastases [27].

Moreover, adjuvant or neoadjuvant chemotherapy and/or radiotherapy treatments may alter the lung parenchymal structure. In these cases, the high-risk of infection associated with a reduced functional repair mechanism could enhance the risk of pleural alterations, possibly leading to a secondary pneumothorax. Also, a

tumoral invasion of the small airways could be responsible for a distal alveolar space dilatation determining air-trapping, which may lead to rupture and pneumothorax.

2.2.3 Clinical features and diagnosis

The clinical presentation depends on the patients' performance status according to their functional status and disease stage. Usually, clinical signs and symptoms are chest pain and shortness of breath.

A chest X-ray is mandatory to assess the presence of a pneumothorax, which usually appears as a complete collapse of the normal areas of the lung. A CT scan is useful to better analyze the pneumothorax size and to investigate a possible progression of disease.

Pneumothorax can be the first sign of neoplastic disease, especially when it assumes a recurrent nature in high-risk patients (heavy smokers, COPD), who will therefore undergo further investigations, which will lead to eventually diagnose the tumor.

2.2.4 Management

Diagnosis and management of a secondary pneumothorax concomitant to a pulmonary neoplastic disease are the same for a pneumothorax happening in a pre-existing neoplastic condition. A chest tube is recommended according to its size and the clinical features of patients.

In case of a persistent air leak or in a recurrent pneumothorax, surgery is an option in order to investigate the causes and proceed to talc pleurodesis in case of nonoperable tumors or unfit for surgery patients. If surgery is contemplated, the surgeon may proceed to obtain a diagnosis in case this was not achieved previously, by means of pleural biopsy/wedge resection/lymph node sampling. Cases of recurrent pneumothorax as the first sign of pleural mesothelioma or sarcoma metastasis have been reported, identifying the thoracoscopic bullectomy as the key to the best diagnosis and treatment [28, 29].

2.3 Secondary pneumothorax in chest trauma

2.3.1 Incidence

Thoracic trauma is the third leading cause of death following abdominal injury and head trauma in polytrauma patients [30]. Management of chest trauma patients is complex and requires an interdisciplinary team with experience in anesthesia, critical care, and surgical disciplines, especially neurosurgery, trauma surgery, abdominal surgery, and thoracic surgery.

Blunt and penetrating chest traumas can be the cause of pneumothorax and trauma should be taken into account when discussing secondary pneumothoraces.

2.3.2 Definition

Thoracic trauma can be differentiated into blunt or penetrating.

Penetrating injuries, such as blade wounds and firearm injuries, are disruptive to tissue integrity. Gunshot and stabbing account for 10% and 9.5% of penetrating chest injuries, making these the most common etiology of penetrating trauma.

A blunt trauma (**Figure 6**) is a nonpenetrating injury of the chest. Blunt thoracic injuries are more common than penetrating injuries [30].

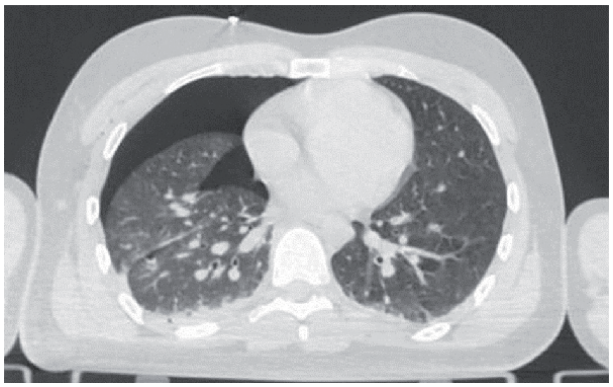

Figure 6.
Pneumothorax after a barotrauma.

Blunt injuries can cause damage to organs and structures without disrupting the integrity of the tissue. Falls from a great height, motor vehicle accidents, and occupational accidents are the main mechanisms of blunt injuries [31–33].

2.3.3 Diagnosis

Depending on the mechanism of injury (e.g., acceleration-deceleration and direct impacts on the chest) an SP may be detected and should be treated and investigated on the cause of its onset (rib fractures, tracheal/bronchial or esophageal disruptions, lung contusion, and lung laceration).

Particular attention is reserved for a tension pneumothorax, in which air enters the pleural space at each inspiration, while the air in the pleural space cannot escape from the pleural space due to the one-way valve mechanism. The continuous accumulation of air in the pleural space determines a lung collapse, hypoxia, tachypnea, and tachycardia, a mediastinal shift with compression of the contralateral lung and the superior vena cava (SVC), leading to respiratory distress and rapidly to respiratory failure with cardiovascular collapse.

2.3.4 Management

Management of patients following major trauma should follow the standardized protocol of emergency and resuscitation advanced trauma life support guidelines (ATLS), and a primary survey of the airway, breathing, circulation, disability, and exposure (ABCDE approach) should be performed.

Particular attention is required in a tension pneumothorax because, if a prompt intervention is not carried out, can rapidly lead to death [34]. Immediate evacuation through a chest tube is mandatory as recommended by the ATLS [35].

In general, a chest tube has to be positioned in a post-traumatic pneumothorax, in order to stabilize the patient.

Once the patient is stabilized, radiological investigations, such as chest X-ray and chest CT scan are mandatory to identify the cause of pneumothorax and eventually determine the need for further treatments (surgery).

At the same time, minor blunt traumas may be cause of small pneumothoraces, which may not require a chest tube and can be treated conservatively with high flow oxygen, pain control, and repeated CXR [36].

Penetrating injuries are disruptive to tissue integrity, with direct communication between the pleural space and the external environment and they can be acutely life-threatening.

It is mandatory to know the mechanism of injury as the management may vary. For example, stab versus gunshot injury to the chest can result in different patterns of injury.

Depending on the penetrating trauma, immediate surgery may be deemed necessary and a chest tube is required to stabilize the patient for surgery (e.g., during patient transportation from the trauma site to the hospital). Frequently, when a post-traumatic pneumothorax is present it can be associated with a hemothorax [37].

2.4 Secondary pneumothorax after invasive procedures (iatrogenic pneumothorax)

Iatrogenic pneumothorax is a possible complication of several invasive procedures, such as a central venous line insertion (0.5–5%), thoracentesis (1, 5–7%), and CT-guided lung biopsy (1–6%); at times they can be associated with hemothorax (1% of all procedures) [38, 39].

In some cases, it may occur as a complication following bronchoscopic positioning of unidirectional valves in emphysematous patients [21].

2.5 Catamenial pneumothorax

The term "catamenial" derives from two Greek words meaning "pertaining to" and "monthly."

Catamenial pneumothorax is defined as a recurrent accumulation of air in the pleural cavity in reproductive-age women.

2.5.1 Incidence and etiology

A catamenial pneumothorax (CP) arises within 48–72 h from menstruation. It occurs in 3–6% of spontaneous pneumothoraces and most frequently involves the right side [40].

This kind of pneumothorax is, mainly, included in two syndromes:

- the thoracic endometriosis syndrome (TES), which is associated with hemothorax and lung nodules. It is a rare clinical disease that sometimes is secondary to the presence of endometrial gland tissue in the lungs, pleura, diaphragm, and tracheobronchial tree [41]. TES has been reported for the first time in 1953, in a case report of a young woman that developed hemothorax. In 1958, Mauerer described recurrent pneumothoraces in association with menstruation and pelvic endometriosis [42].

- the porous diaphragmatic syndrome: cases of CP without any evidence of endometrial implants, but secondary to the presence of diaphragmatic defects [43]. In rare cases, in fact, diaphragm fenestrations over the tendinous portion may be visualized during surgery and appear as orifices in the muscle, becoming the cause of pneumothorax.

2.5.2 Diagnosis

The cancer antigen 125 (CA-125), a gynecological serum marker, has assumed a role in the diagnostic work-up for TES. In fact, high levels of CA-125 have been associated with recurrent SP with evidence of thoracic endometriosis, such as focal thoracic endometrial implants, during VATS procedures. On the contrary, patients without thoracoscopic evidence of endometrial disease have normal CA-125 serum level [44].

The presence of a CP is not always related to pelvic endometriosis.

In a prospective study, 32 women had a CP diagnosis, but only 2 had pelvic endometriosis associated [41].

2.6 Pneumothorax and pregnancy

The occurrence of PSP in women of childbearing age is not unusual and there appears to be an increased risk of recurrence during pregnancy and during parturition with potential risks to the mother and fetus.

A more recent case series and literature review have recommended the use of more modern conservative management methods for which favorable outcomes have now been experienced [17, 45]. Pneumothorax in pregnancy can be managed by simple observation, if the mother is not symptomatic, there is no fetal distress and the pneumothorax is small (<2 cm). Otherwise, aspiration can be performed, chest drain insertion being reserved for those with a persistent air leak or a greater pneumothorax.

To avoid spontaneous delivery or cesarean section, both of which have been associated with an increased risk of recurrence, the safest approach will usually be that of elective assisted delivery at or near term. Less maternal effort is required with forceps delivery, which is therefore preferable. Because of the risk of recurrence in subsequent pregnancies, a minimally invasive VATS surgical procedure should be considered few weeks from delivery. Successful pregnancies and spontaneous deliveries without pneumothorax recurrence have been reported after a VATS procedure [17, 45].

3. Conclusions

In contrast to the benign clinical course of a PSP, SP is associated with pre-existing underlying lung disease, trauma, or invasive procedures and can be a life-threatening event. Patients with pre-existing lung disease tolerate a pneumothorax less well, and the distinction between PSP and SSP should be made at the time of diagnosis to guide appropriate management. The consequences of a pneumothorax in patients with a pre-existing lung disease are significantly greater, and the management is potentially more complex than in PSP patients. Furthermore, SP is correlated to a higher morbidity and mortality compared to PSP. Differently from a PSP, where the management is well defined by different international guidelines, SP treatment may vary because of the clinical conditions, previous episodes, severity and duration of symptoms, and the presence of an underlying pulmonary disease. Its treatment will therefore vary accordingly, from observation to needle aspiration or thoracostomy tube drainage with or without pleurodesis and potentially escalating to an open thoracotomy or VATS procedures, as described in this chapter. In case of surgery in high-risk patients (e.g., COPD patients, frail patients), the risk of proceeding to surgery with the aim of resolving the underlying cause and securing the lung with adequate pleurodesis should be well pondered both from the surgical and anesthesiological point of view based onto the patients' clinical status and consent.

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Chapter 9

Pneumothorax in Children

Hatice Sonay Yalçın Cömert

Abstract

Pneumothorax is a common pleural disease worldwide and is defined as the free accumulation of air between visceral and parietal pleura. Pneumothorax can be spontaneous, iatrogenic, and traumatic. Although it is less common than adults, it is seen in about 1.1–4 per 100,000 per year in the childhood age group. In patients presenting with variable clinic according to the cause of etiology, diagnosis is confirmed on a PA chest radiograph, sometimes a computed tomography may be required. The management of pneumothorax is varying from conservative, over intermediate (chest tube drainage) to invasive methods (video-assisted thoracoscopic surgery—VATS, thoracotomy). Here, we planned to write a chapter that includes a text containing general information about pediatric pneumothorax, algorithms, and visual and clinical cases of the causes of pneumothorax in children, including age, etiology, and treatment approach of pneumothorax in children.

Keywords: pneumothorax, children

1. Introduction

Although pneumothorax has been known in medical history since the times of Hippocrates and Galen, it was the first time that Itard named the term pneumothorax in 1803 [1]. Spontaneous pneumothorax due to bullae rupture was defined for the first time in 1926, and in 1932, Kjaergaard reported that pneumothorax may occur in completely healthy individuals due to isolated lung blebs [2]. In the treatment of pneumothorax, which was tried to be corrected with long bed rest, Noble has used a cannula, plastic drain, and underwater drainage system for the first time in 1873 [3]. The first thoracotomy and bulla resection was performed by Bigger in 1937, pleural abrasion by Churchill in 1941, subtotal parietal pleurectomy by Gaensler in 1956, and the first axillary thoracotomy and bulla excision and apical parietal pleurectomy by Deslauriers in 1980 [3].

2. Definition

Pneumothorax is defined as the free accumulation of air between visceral and parietal pleural space for various reasons. Pneumothorax can be spontaneous, iatrogenic, and traumatic in both neonatal and juvenile patients. Spontaneous pneumothorax is divided into two as primary and secondary. Primary spontaneous pneumothorax occurs secondary to apical blebs or bullae without evidence of other lung pathologies. Secondary spontaneous pneumothorax happens in the context of underlying lung diseases such as cystic fibrosis, asthma, connective tissue disorders, or pneumonia [4, 5].

Apart from these, if we define pneumothorax according to age, we should also mention neonatal and catamenial pneumothorax. Neonatal pneumothorax is the most common pneumothorax in childhood. It is reported that the cause is most likely the high transpulmonary pressure with the onset of breathing [6]. Catamenial pneumothorax is often associated with thoracic endometriosis syndrome.

3. Physiopathology of pneumothorax

Pressure in the pleural space is negative throughout the entire respiratory cycle, as the chest wall tends to expand and collapse in the lung. The pressure of −2 to −5 cm H_2O in expiration decreases to −25 to −30 cm H_2O in inspiration, and this pressure increases approximately 0.25 cm H_2O per cm from the lung basal to the apex [7]. Alveolar pressure is always greater than intrapleural pressure. Therefore, due to the high alveolar pressure and tension in the apical region, existing bleps and bullae in the apex may rupture. Thus, it causes air entry from the alveoli to the pleural space. Airflow continues until the pressure in the pleural space is equalized or until air leakage from the alveoli into the pleural space stops. This condition is called pneumothorax. Pneumothorax physiology includes a reduction in vital capacity and a decrease in oxygen partial pressure.

4. Types of pneumothoraces

Pneumothoraces can be classified as spontaneous (primary and secondary), iatrogenic, traumatic, neonatal, and catamenial pneumothorax. The types of pneumothoraces are shown in **Table 1**.

4.1 Spontaneous pneumothorax

Spontaneous pneumothorax (SP) is a comparatively rare condition in children. The peak age of occurrence in children is either in the neonatal period or in the late adolescent period [8]. Air enters the pleural space without any evident traumatic or iatrogenic mechanism. The incidence of pediatric SP is 4 per 100,000 in males and 1.1 per 100,000 in females with most occurring in patients 16–24 years of age [5, 9, 10]. SP is generally categorized into primary and secondary. In primary spontaneous pneumothorax (PSP), there is no underlying pathology and occurs unknown etiology. PSP refers to a pneumothorax from apical blebs or bullae [10]. However, secondary spontaneous pneumothoraces occur in children with underlying lung problems.

1. Spontaneous pneumothorax
a. Primary spontaneous pneumothorax
b. Secondary spontaneous pneumothorax
2. Iatrogenic pneumothorax
3. Traumatic pneumothorax
4. Neonatal pneumothorax
5. Catamenial pneumothorax

Table 1.
Types of pneumothoraces.

4.1.1 Primary spontaneous pneumothorax

A primary spontaneous pneumothorax (PSP) occurs without a precipitating event and in the absence of clinical lung disease and has an estimated incidence of 3.4 per 100,000 children with 4:1 male predilection [11]. In pediatric studies, the peak age of incidence occurs between 14 and 17 years of age, mainly in late teenagers [8]. The risk factors of PSP include tall and thin stature with low body weight [8]. Smoking is also the primary environmental risk factor for primary spontaneous pneumothorax, especially in teenage patients [12]. Some studies have shown that familial and genetic forms of PSP are related to mutations in the folliculin gene on chromosome 17 in the literatüre [5, 12].

It has been recommended that subpleural blebs and bullae are causally related to the development of primary SP and may be clarified by that these tall and slim children tend to have higher transpulmonary pressure at lung apex, and their rapid growth relative to pulmonary vasculature may result in ischemia and thus blebs evolution at these regions [5, 8].

Most patients are clinically stable on initial evaluation and small cases may present in fulminant distress [1]. Chest pain and shortness of breath are common presenting symptoms of PSP and may be developed at rest or accelerated by any maneuver that increases intrathoracic pressure (Valsalva) [5, 13]. Other clinical findings in patients with pneumothorax include cough, ipsilateral hypoventilation, and nonspecific respiratory distress [4, 5].

Sample chest X-ray and thorax-computed tomography of our patients admitted with primary spontaneous pneumothorax from our archive are shown in **Figures 1** and **2**.

4.1.2 Secondary spontaneous pneumothorax

Commonly known situations predisposing individuals to a secondary spontaneous pneumothorax (SSP) include primary lung disease as asthma, cystic fibrosis, interstitial emphysema, inflammatory/connective tissue diseases such as Marfan syndrome, Ehlers-Danlos syndrome, juvenile idiopathic arthritis, systemic lupus erythematosus, polymyositis, dermatomyositis, sarcoidosis, Langerhans cell histiocytosis, α_1-antitrypsin deficiency, Birt–Hogg–Dube syndrome, infections such

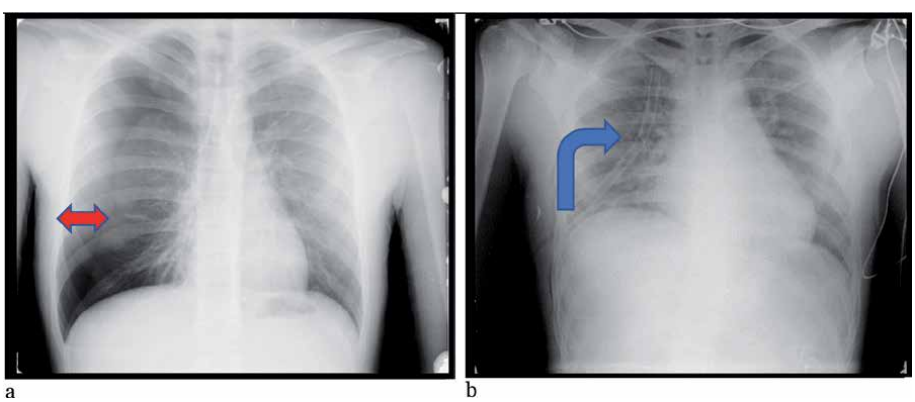

Figure 1.
(a) A 16-year-old male patient presented to the emergency department with a sudden onset of chest pain and was diagnosed with spontaneous pneumothorax on the right side of his chest X-ray (free air in the thorax marked with a red arrow). (b) Film of the same patient after right side chest tube placement (inserted chest tube marked with blue arrow).

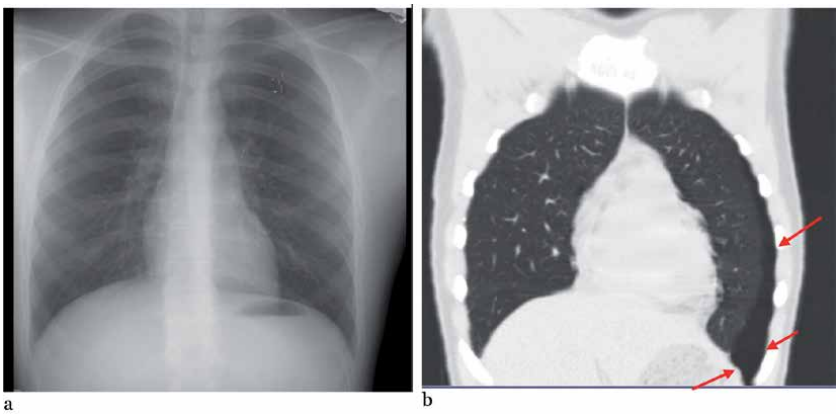

Figure 2.
A 17-year-old male patient presented to the emergency department with the complaint of sudden onset of chest pain. (a) There was no pneumothorax in the anterior–posterior chest X-ray of the patient. (b) Minimal pneumothorax image on the left side in the thorax-computed tomography of the patient (free air in the thorax marked with red arrows).

Primary lung disease: asthma, cystic fibrosis, interstitial emphysema	Infection: *Pneumocystis jirovecii*, tuberculosis, necrotizing pneumonia/abscess, measles, human immunodeficiency virus/acquired immunodeficiency syndrome, parasitic
Inflammatory/connective tissue disease: Marfan syndrome, Ehlers-Danlos syndrome, juvenile idiopathic arthritis, systemic lupus erythematosus, polymyositis, dermatomyositis, sarcoidosis, Langerhans cell histiocytosis, α_1-antitrypsin deficiency, Birt–Hogg–Dube syndrome	Malignancy—lymphoma, metastases
Foreign body aspiration	Congenital malformation: congenital cystic adenomatoid malformation, congenital lobar emphysema
Adapted from Dotson et al. [5].	

Table 2.
Causes of pediatric secondary spontaneous pneumothorax.

as *Pneumocystis jirovecii*, tuberculosis, necrotizing pneumonia/abscess, measles, human immunodeficiency virus/acquired immunodeficiency syndrome, parasitic, malignancy (lymphoma, metastases), foreign body aspiration, and congenital malformations such as congenital cystic adenomatoid malformation and congenital lobar emphysema [5, 14]. SSP causes are summarized in **Table 2** [5].

The theorized mechanism is chronic airway inflammation that causes small airway obstructions and creates the pressure needed for air to escape into the pleural space. These conditions can make the lung pleura more susceptible to rupture and subsequent development of pneumothorax [15]. The most important symptom of SSP is dyspnea, tachypnea, and tachycardia.

Cystic fibrosis (CF) is a severe obstructive airways disease and one of the most common causes of secondary spontaneous pneumothorax. Pneumothorax is seen approximately 3.4% of all patients will suffer from CF during their lifetime and mostly occurs in adult patients [16, 17]. Cysts, blebs, and bullae are all commonly found in the lungs of CF patients, and these cause gas to accumulate in the small airways, resulting in a cystic appearance. The typical presentation is acute onset of chest pain and

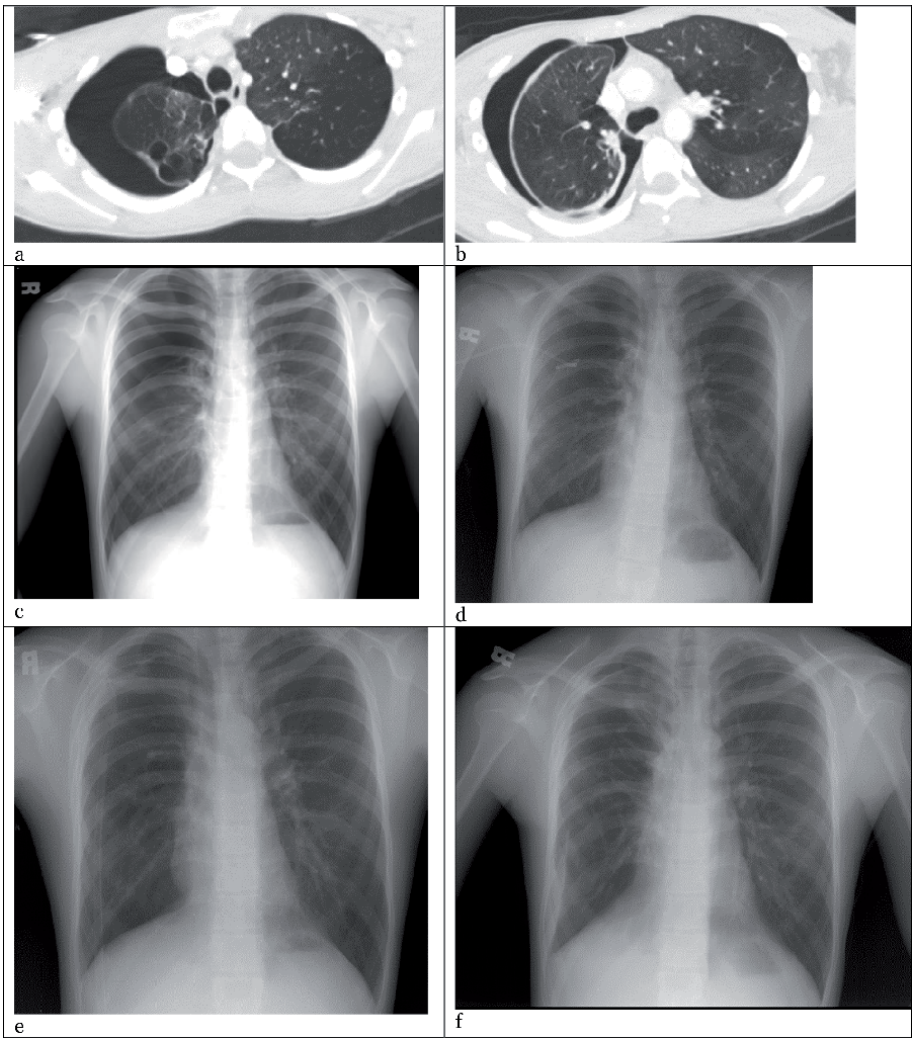

Figure 3.
A 13-year-old male patient followed up with the diagnosis of cystic fibrosis was admitted to the emergency department with respiratory distress. Upon the presence of pneumothorax in the right upper lobe in the thorax in computed tomography (a, b) and the chest X-ray (c), a pig-tail catheter was placed in the right thorax (d). The child's clinical condition did not improve and thoracotomy with pleurectomy was performed. The child was followed up with a chest tube after the operation (e), and has been covered and discharged (f).

breathlessness, and the treatment decisions include the size of the pneumothorax, severity of disease, stability of the patient, and whether this is the first or a recurrent pneumothorax [16]. Pneumothorax due to cystic fibrosis can also be seen in the childhood age group and invasive surgeries may be required. A spontaneous pneumothorax chest X-ray film of a CF patient from our archive is shown in **Figure 3a–f**.

4.2 Iatrogenic pneumothorax

The most frequent cause of iatrogenic pneumothorax is a transthoracic pulmonary biopsy, but it also may appear as a complication of many other procedures and caused by barotrauma secondary to mechanical ventilation [18, 19]. Iatrogenic pneumothorax is related to underlying lung disease along with high ventilatory settings [19]. The most common cause of iatrogenic pneumothorax is invasive diagnostic and therapeutic procedures, such as central venous access, thoracocentesis,

thoracic surgery, or intubation [1]. Iatrogenic pneumothorax may also develop during cardiopulmonary resuscitation and tracheostomy.

4.3 Traumatic pneumothorax

Although thoracic injuries occur less frequently in children than adults, thoracic trauma in children carries a 5% mortality [20, 21]. The most causes of trauma in pediatric patients are traffic accidents, followed by falling from heights, and bicycle accidents [22]. The greater flexibility of the thoracic cage in young children permits the anterior ribs to be compressed to meet the posterior ribs [23]. Because of the flexibility, pulmonary contusions are more common than rib fractures in children [23].

The most common injury in children with blunt thoracic trauma is pulmonary contusion and pneumothorax, which is observed as isolated injury in 30% of the cases [22].

Traumatic pneumothorax can be classified as small occult, tension, and open (**Table 3**). A small pneumothorax from blunt torso trauma is often asymptomatic, with more than half identified as being occult (defined as a pneumothorax observed on computed tomography scan of the chest, but not on chest radiograph) [22]. However, a large pneumothorax may cause clinical symptoms that overlap with those produced by lung parenchymal damage—tachypnea, distress, and decreased saturation [22]. A traumatic pneumothorax and contusion chest X-ray film of a patient from our archive is shown in **Figure 4**.

Open pneumothorax	Related to an open chest wall injury
Occult pneumothorax	Small pneumothorax without clinical significance, typically seen in trauma
Tension pneumothorax	Rapid accumulation of air within the thoracic cavity that leads to a reduction in central venous return as well as tamponade effect on cardiac output

Table 3.
Characteristics of traumatic pneumothorax [14].

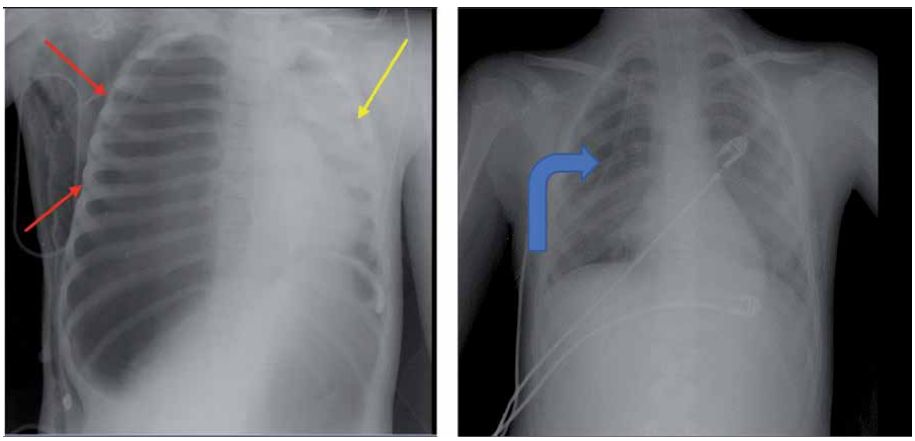

Figure 4.
An 8-year-old male patient applied to the emergency department due to a traffic accident. (a) Pneumothorax in the right thorax and contusion in the left lung were detected in the chest X-ray (free air in the right thorax marked with red arrows and contusion has shown with yellow arrow). (b) Chest X-ray after tube placement in the patient's right thorax (inserted chest tube marked with blue arrow).

When the mediastinum is displaced to the contralateral side with impairment of the venous return, the tension pneumothorax occurs and is more common in children [22]. The symptoms of tension pneumothorax are tachycardia, severe respiratory distress, and hypoxemia, with hypotension and tracheal deviation. Heartbeat is heard on the opposite side and the neck veins become dilated and severe cyanosis occurs. No chest X-ray is required to insert a chest tube in children with tension pneumothorax. The child's symptoms improve dramatically with chest tube insertion.

Open pneumothorax is usually seen after penetrating injuries. This causes a collapse in the lung on the side of the trauma and ventilation failure in the other lung. The patient who develops open pneumothorax is cyanosed and has serious respiratory distress is present. In the treatment, the defect should be closed with a sterile gas.

4.4 Neonatal pneumothorax

Neonatal pneumothorax, with an incidence of 1–2% in newborns, is symptomatic in 0.08% of all live births and is reported as 5–7% in those with a birth weight of less than 1500 g, although it can reach 30% in those with an underlying lung problem and those who need mechanical ventilation comes out [10, 11]. The most common cause of this condition is barotrauma [13]. In addition, male gender and cesarean delivery are also considered among risk factors [11].

In order to inflate the lungs of a newborn baby when he is not breathing himself, mechanical ventilation with an average pressure of 50–80 cm H_2O is required to overcome the high transpleural pressure. During this resuscitation, the air given into the lungs is distributed with an uneven pressure inside the lungs. As a result, some alveoli are ruptured and air passes from the peribronchial area to the mediastinum and pneumothorax develops [24]. A chest X-ray visualization from a newborn from our archive who needed resuscitation at 41-week postpartum and had pneumothorax on the right in the chest X-ray has been shown in **Figure 5**.

It most commonly occurs in the first three days and should be suspected in cases of sudden respiratory distress, decrease in oxygen saturation, inability to listen to breath sounds, or when ventilator parameters have to be increased.

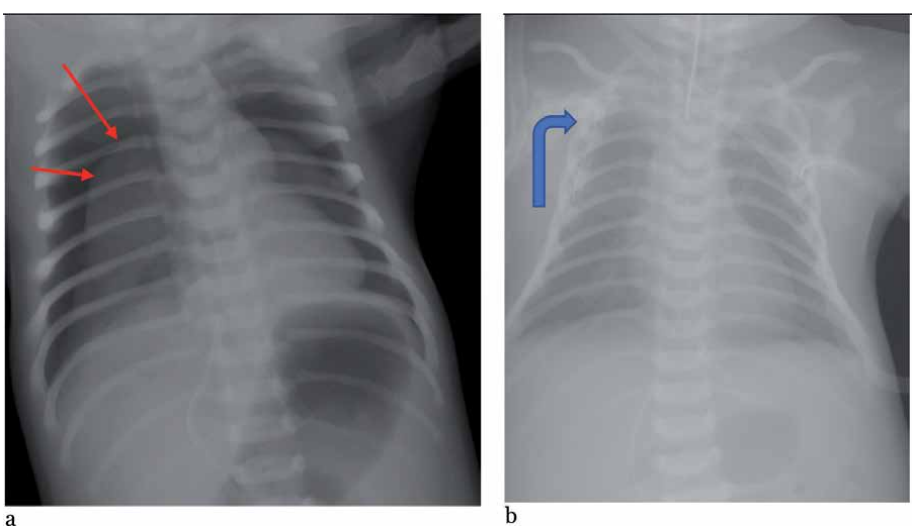

Figure 5.
(a) Film of newborn who needed resuscitation at 41-week postpartum and had pneumothorax on the right in the chest X-ray (free air in the thorax marked with red arrows). (b) Film of the same newborn after right-side chest tube placement (inserted chest tube marked with blue arrow).

It causes high mortality and morbidity, especially in premature babies and newborns with underlying lung parenchyma disease. Whatever the cause, neonatal pneumothorax needs to be treated very quickly because pneumothorax in neonates will lead to serious complications, including lung perforation, phrenic nerve palsy, chylothorax, and hemopericardium [11].

4.5 Catamenial pneumothorax

Catamenial pneumothorax (CP) is a form of thoracic endometriosis syndrome, which also includes catamenial hemothorax, catamenial hemoptysis, catamenial hemopneumothorax, and endometriosis lung nodules, as well as some exceptional presentations [25]. The most common extrapelvic manifestation of endometriosis is thoracic endometriosis and often presents as catamenial pneumothorax [10]. Most commonly occurs in women aged 30–40 years, but has been diagnosed in young girls as early as 10 years of age and postmenopausal women (exclusively in women of menstrual age) most with a history of pelvic endometriosis [25].

CP is a rare and important condition of recurrent pneumothoraces, which occurs within 48–72 h from the onset of menses [11]. The pathophysiology is not completely understood but it is treated with hormonal therapies [11].

5. Diagnosis

The diagnosis of pneumothorax can be made by physical examination or imaging studies including chest X-ray, ultrasonography, and computed tomography (CT) scan [19]. A conventional chest X-ray is a typical imaging examination used to confirm the diagnosis of pneumothorax and a CT scan may be validated to show smaller pneumothoraces. CT scan is commonly accepted as the gold standard in pneumothorax diagnosis [1]. Dotson et al. proposed that detection of blebs/bullae on the CT scan may be predictive of recurrence of PSP, especially bilaterally pneumothoraces [5]. There are multiple methods for calculating pneumothorax sizes like Light, Rhea, and Collins for adults, but these methods are not appropriate for the childhood age group [5, 26, 27].

Dahmarde et al. suggested that ultrasound is accurate and reliable for newborn pneumothoraces [28]. Ultrasound can result in timely diagnoses specifically in neonatal pneumothorax and facilitates the therapy process; lack of ionizing radiation and easy operation are the benefits of this imaging technique.

6. Treatment

The treatment options are changing by age, size, and the type of pneumothorax in childhood. There are no standardized guidelines for therapeutic interventions for children with pneumothorax; however, early identification and appropriate management can reduce morbidity and mortality.

While the size of the pneumothorax can be calculated by various methods in adults, there is no method that can be applied to children yet. Although minimal pneumothoraxes that do not cause clinical problems can be followed conservatively, most patients require drainage, and a thorax tube is inserted. Nonoperative treatment methods are monitoring with supplemental oxygen (100% high-flow) or needle aspiration. Surgical treatment methods range from the insertion of a chest tube to more invasive interventions such as video-assisted thoracoscopic surgery (VATS) or thoracotomy, including resections, pleurodesis, or bullectomy [10]. Surgical

Children weight (kg)	Tube size (French)
<3	8–10
3–8	10–12
8–15	12–16
16–40	16–20
>40	20–24

Table 4.
Guide for chest tube selection for pneumothorax [4].

indications for pneumothorax are resistant and prolonged air leak (>4 days), persistent and recurrent pneumothorax, large pneumothorax, first pneumothorax with a history of pneumothorax in the other lung, and bilateral pneumothorax [10, 11]. Chest tube placement should be the first choice in patients with surgical indication, and then, open or closed surgical techniques should be planned according to the child's clinic. Although the VATS procedure is easily used in the childhood age group, thoracotomy with resections, pleurodesis, or bullectomy may be preferred or needed in cases with severe air leak and recurrent pneumothorax [29].

Pleural catheters are tools that are placed in the fourth, fifth, or sixth intercostal space in generally anterior or midaxillary line with Seldinger technique and placed to water seal in children. In newborns, the catheters are usually placed from the second or third midclavicular line with again Seldinger technique and placed to water seal. The chest tube sizes are changing from the patient's size and age. The guide for chest tube selection for pneumothorax for children patients is summarized in **Table 4** [4].

The aim of surgical treatment is to resect of blebs and bullae and pleurodesis to prevent recurrences. VATS procedure is performed with good results in children with PSP and as the gold standard for surgical management of PSP by using various surgical instruments from 1 to 3 incisions of approximately 1.5–2 cm, which are opened on the chest with the help of a video [29, 30]. Blebs and bullae due to pneumothorax are removed with VATS with the help of staples. Pleurodesis ensures that the parietal and visceral pleura sheets stick together. Pleurodesis can be performed by using pleurectomy, pleural abrasion, or chemicals [31].

Lewit et al. suggested that nonoperative methods are not suitable for the treatment of pneumothorax and mentioned a decreased recurrence rate in those undergoing surgical treatment at initial presentation in the childhood age group [32]. Also, Lopez et al. have observed decreased median total length of stay and decreased recurrence rate in the surgical group compared with the initial non-VATS group in children [11].

On the other hand, Brown et al. discussed whether conservative management is an acceptable alternative to nonconservative procedures and found that conservative management of primary spontaneous pneumothorax was similar to interventional management, with a lower risk of significant adverse events [33].

The general approach is chest X-ray negative and CT scan positive pneumothoraces do not require invasive methods and they can be followed conservatively [23]. However, since childhood is a wide range, a pneumothorax that looks small may even be mortal for a newborn premature baby. Although thoracic tube insertion is a minor surgical procedure, every procedure has surgical stress, especially for neonatal intensive care patients. Therefore, every child with pneumothorax for whom a follow-up decision is made requires very special close follow-up. Likewise, close follow-up of a child patient with a chest tube placed should be very important in terms of possible complications.

7. Complications

The most common complications of pneumothorax seen in childhood are air leak, tension pneumothorax, pneumomediastinum, subcutaneous emphysema, hemothorax, and very rarely Horner's syndrome. If the air leak is continued within 48 hours of pneumothorax treatment, it may become resistant. Therefore, a second chest tube or even VATS or thoracotomy may be required for persistent air leakage, depending on the age of the child or the etiology of the pneumothorax [3].

8. Conclusion

In conclusion, the etiology and management vary according to age and type of pneumothorax in the childhood age group, and this is a life-threatening special condition that requires urgent intervention and special follow-up.

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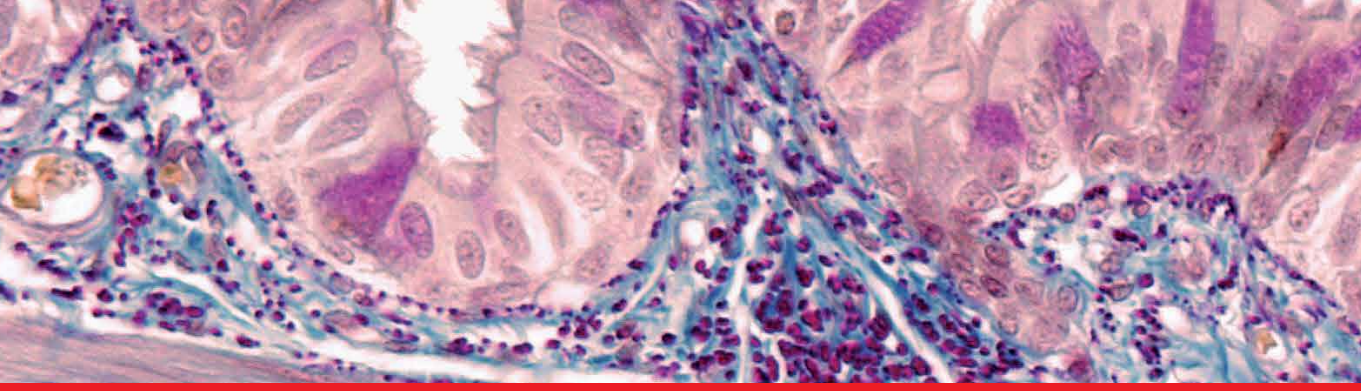

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