An evidence-based review of primary spontaneous pneumothorax in the adolescent population

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Abstract

Primary spontaneous pneumothorax (PSP) is a relatively common problem in emergency medicine. The incidence of PSP peaks in adolescence and is most common in tall, thin males. Recent advances in the care of patients with PSP have called into question traditional approaches to management. This clinical review highlights the changing management strategies for PSP and concludes with a proposed evidence-based pathway to guide the care of adolescents with PSP.

KEYWORDS
adolescent, chest tube, evidence-based, needle thoracostomy, spontaneous pneumothorax, tube thoracostomy

1 INTRODUCTION

Primary spontaneous pneumothorax (PSP) is the accumulation of air in the pleural space in patients without clinically apparent lung disease.1 Secondary pneumothorax is associated with an underlying lung disease, including infection and cystic fibrosis, and is outside the scope of this review.1,2

PSP peaks in adolescence and early adulthood, making this condition of importance to both pediatric and adult-trained physicians. The management of PSP has traditionally been tube thoracostomy, but several recent studies call into question this approach, advocating for more conservative care, including observation and simple aspiration. Moreover, no current review has been published since 2012.3

Given the lack of a broadly accepted approach to management,4 the purpose of this review is to provide a current, evidence-based update on PSP with a focus on recent studies of alternative approaches to treatment. After reviewing the evidence, we conclude by presenting an evidence-based approach to PSP management.

2 EPIDEMIOLOGY

PSP is diagnosed predominately in adolescent males. Across 7 recent international case series, 84% of patients were male and the mean age was 16.3 years (Table 1).5–11
The incidence of PSP varies based on patient age, whether secondary pneumothoraces are included, and geographic location. In a 2012 study, the estimated annual incidence of all pneumothoraces among children in the United States was 34 cases per 100,000. A retrospective, longitudinal cohort study from Taiwan estimated the annual incidence of PSP at 52 cases per 100,000 persons (children and adults). By the age of 23 years, the annual incidence steadily decreased to 20 cases per 100,000 persons and continued to decline throughout adulthood. A similar pattern was reported from researchers in Denmark, who examined the incidence of first PSP using a national registry. The peak annual incidence was 16 cases per 100,000 persons between 16 and 20 years of age. All 3 of these studies were of hospitalized patients, so the true incidence may be higher if patients managed in the outpatient setting were included.

### 3 | PATHOPHYSIOLOGY

The mechanisms leading to a communication between the alveolar and pleural spaces are likely multifactorial, involving a complex interplay between age, sex, body habitus, and environmental and genetic factors. Of patients with PSP, >80% demonstrate apical subpleural blebs or parenchymal bullae on chest computed tomography (CT). Investigators have identified specific ultrastructural abnormalities in the elastin fibers found in the apical regions of the lungs of individuals undergoing blebectomy/bullectomy, supporting the concept that localized connective tissue abnormalities lead to blebs and bullae development.

Spontaneous rupture of blebs or bullae is commonly believed to be the primary mechanism leading to pneumothorax. However, several observations challenge this idea. First, it is unclear how often these lesions are pre-existing at the specific site of air leakage, with sites of lung rupture difficult to demonstrate during surgery or from resected lung tissue. Second, up to a quarter of patients with PSP do not demonstrate blebs or bullae on chest CT or during thoracoscopy. Third, blebs and bullae are detected in asymptomatic individuals on CT scan and thoracoscopy at rates ranging from 4% to 33%.

There are alternative theories for the pathophysiology of PSP. “Pleural porosity” is the concept that mesothelial cells on the visceral pleura are thought to be replaced by a more porous inflammatory layer that allows air leakage into the pleural space. In addition, as adolescents with PSP frequently have tall, asthenic body types, investigators have speculated that rapid longitudinal growth during adolescence generates greater distending pressure in the lung apex. Whether greater porosity or greater distending pressures subsequently lead to the formation of blebs or bullae, or contribute to the development of a pneumothorax in individuals who already have localized ultrastructural defects, is unclear.

Environmental factors, such as smoke exposure, may increase the risk for PSP. Compared with non-smokers, the relative risk of a pneumothorax is 4 to 7 times higher in light smokers (1–12 cigarettes/day) and up to 100 times higher in heavy smokers (>22 cigarettes/day). There also are reported associations between cannabis smoking and/or vaping and PSP, but they are confounded by concomitant tobacco smoking. Several reports identified increased spontaneous pneumothoraces after days with large changes in atmospheric pressure, but there are conflicting findings in recent investigations.

Approximately 10% of patients with PSP have a positive family history of pneumothorax, although no specific genetic mutations have been associated with sporadic PSP. Moreover, familial PSP comprises several genetic disorders and can be subdivided between those caused by defects of extracellular matrix proteins (ie, connective tissue disorders) and those caused by mutations of tumor suppressors. Connective tissue disorders associated with pneumothoraces include Marfan syndrome, vascular Ehlers-Danlos syndrome, and Loeys-Dietz syndrome. In these syndromes, pneumothorax is believed to result from the lower tensile strength of the visceral pleural.

Mutations affecting tumor suppressor pathways can cause both the formation of pulmonary cysts and intrinsic defects in the composition and integrity of the extracellular matrix in alveoli. A heterozygous mutation in the tumor suppressor folliculin gene (FLCN) predisposes patients to Birt-Hogg-Dube syndrome (BHD). BHD is the most common mutation in individuals with familial PSP, with a prevalence ranging from 17% to 50%.

Identifying heritable causes of PSP is important as pneumothorax may be an early presentation of disorders that may subsequently have severe extra-pulmonary manifestations, including...
life-threatening arterial rupture in connective tissue disorders and renal cell carcinomas in BHD.60,41

4 | PRESENTATION AND RADIOGRAPHIC DIAGNOSIS

4.1 | Presentation

The primary symptom associated with the development of PSP is chest pain (Table 1).5–11,25 Chest pain typically has an acute onset and is localized to the side of the pneumothorax. Bilateral pneumothoraces are unusual and reported in only 1.3% of cases.6 Less common symptoms include dyspnea (43%) and cough (13%). PSP usually develops while the patient is at rest in children (76%) and adults (87%).3,42

The evidence for associations between specific physical examination findings and the size of the pneumothorax is limited. Small pneumothoraces often are clinically silent, whereas larger pneumothoraces are thought to produce more classically described signs and symptoms, including ipsilateral hyper-resonant percussion, decreased or absent breath sounds, and decreased vocal fremitus.1,43 Expanding pneumothoraces, generally considered to encompass >50% of the lung volume, may progress to tension physiology and shock.1 The vast majority of pneumothoraces, however, do not develop tension physiology, that is, the patient has signs or symptoms of tension pneumothorax and not radiographic evidence alone.44

4.2 | Radiographic diagnosis

The diagnosis of PSP is almost always confirmed on a standing posterior-anterior chest X-ray (CXR).17 Classic findings are radiographic displacement of the pleural line and the absence of lung markings between the visceral pleural line and the chest wall. Expiratory CXRs have no additional diagnostic benefit—studies comparing paired inspiratory and expiratory CXR demonstrate that pneumothoraces can reliably be demonstrated with inspiratory radiographs alone.45,46

Although CT of the chest is more sensitive for small pneumothoraces, CXR is the preferred initial approach. Any pneumothoraces large enough to be symptomatic should be detected by CXR. Moreover, because of the cost and concerns of relative radiation dosage, chest CT is unnecessary for the majority of uncomplicated PSP cases already identified on CXR.47,48 Several studies have shown that point-of-care ultrasonography (POCUS) has both high sensitivity and specificity for pneumothorax.49 The routine use of POCUS in pediatric PSP, however, has not been clearly established.50,51

The extent of a pneumothorax is usually expressed in 1 of 2 ways—as either an estimated percentage of lung collapsed or on an ordinal scale: small, moderate, or large. Several investigators and international societies have developed approaches to estimate the extent of the pneumothorax based on specific measurements obtained from the CXR. However, the clinical utility of these approaches in children has proven problematic. First, there are no equations for estimating the size of a pneumothorax in the pediatric population, where the thoracic volume varies with age. Second, there is high variability between raters, approaches, and centers.52–54 Of the 7 recent international pediatric PSP case series, 5 reported unique methods to differentiate small versus large pneumothoraces.5–11 Therefore, physicians should be aware that size estimations may not be reliable and, more important, may not correlate well with the clinical findings.

5 | ACUTE MANAGEMENT

5.1 | Oxygen

The inhalation of higher than ambient concentrations of oxygen creates a diffusion gradient of nitrogen from the pleural space into the alveoli, which experimentally increases the absorption of gas from the pleural cavity.55 In animal models, oxygen therapy has been demonstrated to increase the rate of resolution of pneumothoraces.56 Small clinical studies of older adult patients with secondary pneumothoraces have demonstrated mixed results with oxygen treatment, ranging from no effect to up to a 5-fold increase in the rate of absorption.57,58

For PSP, the efficacy of oxygen therapy was examined in a retrospective study of 175 pediatric and adult patients. Patients were treated with either room air or 2–4 L/minute nasal cannula oxygen. Patients receiving oxygen had a radiographic resolution rate twice that of those receiving room air (4.3%/day vs 2.1%/day).59 Although the administration of oxygen may hasten absorption of air from the pleural space, there remains uncertainty regarding the optimal fraction of inspired oxygen, especially the amount that speeds recovery without prolonging hospitalization.

5.2 | Observation versus intervention

There is general agreement among guidelines that observation is the accepted treatment in minimally symptomatic, clinically stable patients with PSP.60 With the increasing ease of radiographically assisted thoracentesis and tube placement for direct air evacuation; however, the rates of intervention in adults with PSP has steadily increased during the past several decades.61,62 Management in children has followed suit, with almost 80% of pediatric patients undergoing some form of intervention—aspiration, chest tube drainage, or video-assisted thoracoscopic surgery (VATS; Table 2).5–11

The notion that immediate intervention is needed in PSP has been challenged by several studies. Retrospective cohort studies in adults suggest that observation is safe and effective in patients with PSP who do not have a substantial risk of developing tension physiology.61,63,64 Recently, in 2020, Brown et al published a multicenter randomized controlled trial (RCT) of observation versus tube thoracostomy in PSP.65 The study enrolled clinically stable patients 14–50 years of age who had moderate to large PSP. Observation was found to be non-inferior to thoracostomy for radiographic resolution of the pneumothorax within 8 weeks. Observation-only patients
TABLE 2  Approach to treatment and overall frequency of recurrence from 7 case series of pediatric patients with primary spontaneous pneumothorax

| Study (year) | No. patients | Observation, % | Oxygen, % | Aspiration, % | Chest tube, % | VATS, % | Recurrence, % |
|--------------|--------------|----------------|-----------|---------------|--------------|--------|--------------|
| Lee et al (2010) | 77 | 15 | 0 | 30 | 47 | 8 | 25 |
| Shih et al (2011) | 78 | 15 | 27 | 0 | 50 | 8 | 42 |
| Seguier-Lipszyc et al (2011) | 46 | 0 | 39 | 0 | 39 | 22 | 43 |
| Robinson et al (2015) | 41 | 0 | 0 | 20 | 80 | 0 | 41 |
| Kuo et al (2013) | 171 | 0 | 19 | 0 | 32 | 49 | 21 |
| Chiu et al (2014) | 120 | 9 | 45 | 19 | 37 | 19 | 31 |
| Soccorso et al (2015) | 50 | 0 | 2 | 34 | 64 | 0 | 36 |

VATS, video-assisted thoracoscopic surgery.

5.3 Needle aspiration versus tube thoracostomy

For patients in whom intervention is indicated, the 2 primary approaches to removal of pleural air are needle aspiration or tube thoracostomy. In adults, recent RCTs and a Cochrane review comparing both methods found no differences in recurrence rates, whereas needle aspiration resulted in shorter duration of hospitalization and fewer adverse events.68–71

In contrast to adults, tube thoracostomy is favored over needle aspiration in pediatric patients. Retrospective and prospective studies examining needle aspiration in pediatric patients with PSP report success rates of approximately 50%, which is lower than cited rates in adults.5,8,72,73 Among 618 patients included among 7 pediatric case series, 12% underwent aspiration compared with 44% tube thoracostomy (Table 2). The lower rates of needle aspiration use may reflect either less familiarity with the procedure in pediatric practitioners, less evidence of relative efficacy, or both. The recent increase in use of POCUS in pediatric settings may facilitate greater use of needle aspiration.74 POCUS can help practitioners in identification of the “lung point,” which correlates with the size of the pneumothorax and in determination of resolution after aspiration.75

5.4 Small-bore versus large-bore chest tubes

Despite the advantages of smaller tubes, large-bore tubes continue to be inserted in pediatric patients with PSP.48 Studies in adults and adolescents report that small-bore chest tubes (<14 French)76 are associated with less pain, shorter hospital length of stay, and fewer complications than large-bore catheters, with the equivalent ability to evacuate air from the pleural space.10,77–83 In a prospective cohort study of adults with large pneumothoraces in the ambulatory setting, small-bore chest tubes connected to a 1-way valve demonstrated a successful resolution rate of 78% by day 4, with added cost savings and a 1-year recurrence rate of 26%.84

5.5 Suction

The role of suction with tube thoracostomy in pediatric PSP is uncertain. This practice is used in cases of ongoing air leak to promote healing by the theoretical apposition of the visceral and parietal pleura. Several guidelines suggest that there is no role for the immediate use of suction in PSP, citing a lack of supportive data and concerns for both re-expansion pulmonary edema19,47,60,85,86 and potentially increased risk of recurrence.61,65 Two adult studies demonstrated the rate of lung re-expansion in PSP is similar with or without suction.87,88

6 Recurrence

The risk of recurrence after a spontaneous pneumothorax is high in pediatric patients, ranging from 21% to 43% (Table 2). This range correlates closely with the non-interventional arms of RCT in adults, where...
TABLE 3  Findings of computed tomography of the chest in 4 studies of pediatric patients with primary spontaneous pneumothorax

| Study (year)       | No. patients | Abnormal CT, n | Recurrence, n | Normal CT, n | Recurrence, n |
|--------------------|--------------|----------------|---------------|--------------|---------------|
| Nathan et al (2010) | 25           | 14             | 3             | 11           | 3             |
| Seguier-Lipszyc et al (2011) | 29         | 13             | 5             | 16           | 8             |
| Choi et al (2014)  | 114          | 63             | 38            | 51           | 16            |
| Chiu et al (2014)  | 56           | 26             | 7             | 30           | 13            |

CT, computed tomography.

the risk of recurrence ranged from 21% to 54%. A recent single-center retrospective cohort study of pediatric patients with PSP found a recurrence rate of 23.4% within 2 years of the initial presentation. The risk for repeated recurrences (ie, more than 1 recurrence) among patients with PSP treated non-surgically is also believed to be high, ranging from 40% to 83%. However, the referenced literature on the risk of repeated recurrences is based on an adult series that included elderly patients, with a smoking rate of 61% to 72%.

6.1 Predictors of recurrence

Several investigators have examined risk factors for recurrence of PSP that could be used to determine which patients would benefit from more aggressive treatment at initial presentation. Unfortunately, the current pediatric literature is too limited to determine which patients are at higher risk of recurrent PSP. A study of 918 adults with PSP in France could not identify clinical factors associated with recurrence. A Taiwanese study found evidence that younger age was a risk factor in pediatric patients, with a 34% risk of recurrence in 14-year-old patients compared with 22% in 18-year-old patients. Other studies have identified a larger pneumothorax at initial presentation and a low body mass index as additional risk factors, although not all studies consistently identify either factor. A study from 2020 identified smaller sized pneumothoraces with a higher rate of recurrence, but recurrence was not significantly affected by treatment modality.

Several investigators have examined the association of blebs or bullae detected on CT after a first episode of PSP with pneumothorax recurrence. Across 4 retrospective studies of pediatric patients with an initial PSP, 52% had a bleb or bullae on chest CT (Table 3). Although 43% of those with abnormal CT findings had a PSP recurrence, 37% of patients with a normal CT also developed recurrence. This finding is similar to 3 adult studies where recurrences in the absence of CT abnormalities ranged from 27% to 33% of patients.

6.2 Prevention of recurrence: VATS and pleurodesis

Since the 1990s, VATS with a wedge resection of a bleb or bullous lesion has been the preferred intervention to prevent recurrence of PSP in the pediatric population. The efficacy and role of VATS for preventing pneumothorax recurrence, however, are somewhat unclear. Among 10 recent retrospective studies, including >2000 pediatric and adult patients, recurrence after VATS averaged 13% (range, 7%–21%), suggesting a significant reduction compared with non-surgically treated patients (Table 4). Younger age at the time of VATS was a consistent risk factor for post-VATS recurrence among studies performing multivariate analyses. The high rate of contralateral recurrences in younger patients suggests that the underlying pathogenesis leading to a pneumothorax may progress independent of surgical interventions in developing lungs.

To reduce ipsilateral recurrence rates, pleurodesis is often recommended for patients undergoing VATS. Pleurodesis is performed to create an adhesion between the visceral and parietal pleural membranes, theoretically preventing recurrence by removing the pleural space in the area of a previous bleb or bullae. There are several potential approaches to pleurodesis: partial pleurectomy, chemical pleurodesis, mechanical pleurodesis using pleural abrasion, and wide staple line coverage with absorbable material. The benefit and optimal approach to pleurodesis in PSP remains unclear. Retrospective studies show lower recurrence rates post-VATS in patients undergoing mechanical and chemical pleurodesis. However, an RCT of adolescents and adults with PSP found no difference in 18-month recurrence rates between thoracoscopic wedge resection with or without pleural abrasion. RCTs comparing mechanical pleural abrasion with either apical pleurectomy, chemical pleurodesis with minocycline, or staple line coverage with cellulose mesh and fibrin glue have not demonstrated any approach to be more effective in preventing recurrences.

7 PATIENT TRANSPORT AND RESTRICTIONS ON FUTURE ACTIVITIES

Patients with a spontaneous pneumothorax requiring transport for definitive management should not have routine tube thoracostomy performed before transport. Previous literature suggesting tube thoracostomy to be performed on the pre-hospital/community setting was based on a single case series of trauma patients and expert opinion. Patients being transported via air medical transport should...
TABLE 4  Recurrence of primary spontaneous pneumothorax after video-assisted thoracoscopic surgery in 10 studies that included adolescent patients

| Study (year)       | No. patients | Mean age (year) | Recurrence, % | Contralateral recurrence |
|--------------------|--------------|-----------------|---------------|--------------------------|
| Choi et al (2013)  | 281          | 19.2            | 7             | NR                       |
| Chiu et al (2014)  | 84           | 17.8            | 21            | 15/18                    |
| Chang et al (2015) | 149          | 20.0            | 11            | 4/17                     |
| Robinson et al (2015) | 59     | 15.3            | 20            | 3/12                     |
| Huang et al (2015) | 248          | 19.0            | 5             | NR                       |
| Noh et al (2015)   | 285          | NR              | 18            | NR                       |
| Chen et al (2016)  | 425          | 20.2            | 17            | 32/72                    |
| Nakayama et al (2017) | 167  | 23.0            | 10            | NR                       |
| Tan et al (2017)   | 176          | 19.8            | 14            | NR                       |
| Dagnegard et al (2017) | 234 | 30.0            | 13            | NR                       |

NR, not recorded.

be monitored closely for worsening of their clinical symptoms, with needle aspiration advised if deterioration is observed.123

Consensus recommendations vary for non-urgent air travel by patients with an active or recent pneumothorax. Guidelines recommend waiting from 7 to up to 21 days from the date of radiographic resolution.125–127 The Aerospace Medical Association notes that the presence of lung cysts or bullae is not a contraindication to flying.128

A history of PSP has consistently been a contraindication of compressed-air diving because a recurrence under water could theoretically increase the risk of rapid expansion and tension physiology. A recent review examining the risk of PSP recurrence with diving supported this conclusion and noted that the available evidence does not support a specific waiting period after pneumothorax resolution or intervention.96

8  | AN EVIDENCE-BASED APPROACH TO MANAGEMENT

Although treatment patterns in pediatric centers favor interventional approaches, we recommend patients presenting with a PSP without hemodynamic or respiratory compromise be observed for 6 hours off oxygen in the ED, followed by a repeat CXR. If the patient remains clinically stable with no pneumothorax enlargement, the patient may be safely discharged with strict return precautions and follow-up by a primary care physician. In the absence of hypoxemia, we do not recommend oxygen administration to hasten pneumothorax resolution.

For patients with PSP and evidence of tension physiology, including sustained tachycardia, tachypnea,129 or hypotension,130 we recommend air evacuation with either needle aspiration or tube thoracostomy. If an initial attempt at needle aspiration is not successful, we suggest a second attempt to be performed, as studies in adults suggest a high success rate for lung expansion with a second attempt.69,70 We recommended small-bore chest tubes (<14 French) be inserted via the Seldinger technique76 due to equivalent efficacy compared with larger tubes and lower adverse effects.10,77–80 We recommend against the immediate use of suction.

If patients require needle aspiration or tube thoracostomy, we recommend local anesthesia via an intercostal nerve block followed by either intravenous anxiolysis/analgesia or conscious sedation. Anxiolysis with nitrous oxide is discouraged as it has been noted to enter the pleural space, potentially worsening the extent of the pneumothorax.131

We recommend surgical treatment, specifically VATS, for patients with an air leak beyond 4 days after initial intervention. As there are no reliable predictors of recurrence in adolescents, including the presence of blebs or bullae on chest CT, we do not recommend surgery for otherwise uncomplicated first occurrences. Clinicians should inform patients that VATS will likely reduce the rate of ipsilateral recurrence, but the decision to proceed with surgery should be balanced by the uncertainty about the degree of risk reduction and the risks of operative complications.132,133

There is increasing recognition that a pneumothorax may be the initial presentation of an underlying pulmonary or connective tissue disorder. For patients with a first PSP, we recommend hospital follow-up with a pulmonologist. The focus of pulmonology evaluation should be a thorough review of past medical and family histories, evaluating risk factors for connective tissue disease and respiratory disorders that predispose to PSP. Patients may require pulmonary function testing (PFT) investigating for occult reactive airways disease or other respiratory disorders (Table 5). An outpatient chest CT should be performed in patients with restrictive or moderate obstructive patterns on PFTs and for all patients with a history of familial PSP or a family history of blebs, bullae, or cysts.

Clinicians should be especially concerned for an underlying disorder in a preadolescent child with pneumothorax, including asthma, foreign body aspiration, congenital malformations, and connective tissue disorders. In addition to patients with positive PFT, chest CT is recommended for all preadolescent children, in patients with more than 1 recurrence, and in biological females, as the mutationa
burden to cause pneumothorax in women appears to be higher. Genetic sequencing for FLCN or referral to a geneticist are recommended for patients with familial PSP if physical exam findings suggest a pneumothorax-associated syndrome or chest CT findings are suggestive of an underlying cystic lung disease.

9 | AREAS FOR FUTURE RESEARCH

We anticipate several areas of research during the ensuing decade will further improve our understanding of the pathogenesis and management of PSP. Continued efforts to identify novel genetic mutations associated with both sporadic and familial pneumothorax are essential, both to understanding the mechanism of pneumothorax formation and to guide management and prognostication. Future studies are needed examining the costs and benefits of routine chest CT to detect diffuse cystic lung disease in patients with a first-time PSP. This practice has recently been advocated for all adults as a cost-effective means of earlier detection of underlying cystic lung disease.134 Studies with larger numbers of adolescents with PSP are needed to confirm the safety and efficacy of the observation-only approach. If pediatric centers adopt more conservative, observation-based approaches, prospective cohort studies combined with genetic analyses for pneumothorax-associated mutations may provide a more personalized approach for selecting patients most likely to benefit from surgery.

For patients needing evacuation of their pneumothorax, prospective studies are needed to assess the efficacy and safety of needle aspiration compared with tube thoracostomy. Prospective studies in adolescents are also needed to determine both the additional utility of pleurodesis to prevent postsurgical recurrence and the frequency of operative complications. Should pleurodesis prove to be superior, investigations into the optimal pleurodesis techniques are also necessary.

10 | CONCLUSIONS

PSP is a relatively common condition in adolescents in the ED, and recent research suggests that several changes to traditional management are indicated, with a focus on more conservative approaches such as observation or need aspiration. More research is needed to determine the ideal surgical approach in pediatric patients.

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CONFLICTS OF INTEREST
The authors have no conflicts of interest to disclose.

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