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# Fetal primary pleural effusions: Prenatal diagnosis and management

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A B S T R A C T

Fetal pleural effusions can be associated with significant perinatal morbidity and mortality. When diagnosed antenatally, referral to a tertiary fetal medicine center is recommended for a detailed ultrasound evaluation for additional structural abnormalities or features suggestive of congenital infections or fetal anemia. The effusions should be characterized as unilateral or bilateral, and presence of hydrops and/or mediastinal shift should be documented. Additional testing should include fetal echocardiography, maternal testing for blood group and screen, hemoglobinopathies, and congenital infections. Invasive genetic testing is recommended with infectious testing on amniotic or pleural fluid. Pleuroamniotic shunting is recommended for large primary pleural effusions with significant mediastinal shift or hydrops, as several large series have demonstrated improvement in perinatal survival, particularly in hydropic fetuses. Delivery should occur in a tertiary care center with neonatal expertise, and infants should be followed up long-term for respiratory and neurodevelopmental outcomes.



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## Introduction

Fetal pleural effusions affect 1 in 15,000 pregnancies [1], and affected fetuses are at significant risk of perinatal morbidity and mortality, which may improve with fetal intervention. Pleural effusions are either primary or secondary, depending on the underlying etiology. Primary effusions or hydrothorax, referred to as congenital *chylothorax* postnatally, usually arise from lymphatic malformations. Pleural effusions are considered to be secondary when associated with structural abnormalities and congenital infections or if there is generalized edema or hydrops due to causes other than the pleural effusions [1].

Prognosis is worse when associated with malformations [2] or diffuse hydrops [3,4]. In an older series describing the natural history of primary pleural effusions in 32 fetuses, overall mortality was 53%, with 100% survival in fetuses with spontaneous resolution of effusions or unilateral effusions without mediastinal shift or hydrops, compared to only 38% survival among hydropic fetuses [1].

The natural history of primary pleural effusions can be difficult to predict, as up to 22% can regress spontaneously, most commonly occurring in unilateral effusions without polyhydramnios or hydrops [3]; however, spontaneous resolution has rarely been reported even in the presence of hydrops [1]. A more typical clinical course involves progression of the effusion to involve the contralateral side. In the presence of large effusions, intrathoracic pressures can increase significantly, causing cardiac compression, compromised venous return [5], heart failure, and hydrops. Polyhydramnios, with its associated risks of preterm premature rupture of membranes (PPROM) and birth, may also result from esophageal compression and impaired fetal swallowing [6]. Large pleural effusions may behave as space-occupying lesions for the developing lungs, thereby causing pulmonary hypoplasia [1,7]. Fetal lungs are particularly susceptible to this mass effect during the canalicular phase, between 16 and 24 weeks of gestation, when airway differentiation begins [8]. Other factors that may contribute to delayed pulmonary maturation may include the severity and size of the effusions [1] and duration of exposure, particularly with diagnosis to delivery intervals of >2 weeks [9]. In one small series of primary pleural effusions, in 3 of 4 fetuses that died from pulmonary hypoplasia, there was ultrasound evidence of progressively enlarging bilateral effusions and hydrops for an 8- to 9-week interval [10].

## Investigations

### *Sonographic evaluation and maternal investigations*

Pleural effusions can develop throughout pregnancy but are most commonly detected in the second or early third trimester [11]. *Primary* pleural effusions are a diagnosis of exclusion, following extensive investigation to exclude other etiologies, similar to that for fetal hydrops.

Meticulous ultrasound evaluation is key, as associated malformations are present in 10–15% of cases [2,12]. Particularly, lung abnormalities should be excluded, including congenital cystic adenomatoid malformation (CCAM), bronchopulmonary sequestration (BPS), and right-sided congenital diaphragmatic hernia (CDH). BPSs can be associated with *ipsilateral* pleural effusions in 6–10% of cases and typically appear as solid, well-defined, triangular echogenic lung masses [13]. The pleural effusions associated with BPS have been speculated to arise from torsion of the sequestration with occlusion of venous and lymphatic vessels [14] or due to high output cardiac failure resulting from shunting of systemic blood through the sequestered lung to the pulmonary veins causing volume overload of the left ventricle [15]. Mediastinal tumors and congenital goiter are additional rare causes of pleural effusions. Sonographic evidence of congenital infections should also be sought after, including echogenic bowel, intra-abdominal, and intra-cranial calcifications. A fetal echocardiogram is also recommended, as up to 20% of cases of nonimmune hydrops (NIH) are secondary to cardiovascular abnormalities [16].

Fetal anemia should be excluded as part of the evaluation for pleural effusions; however, a pathognomonic feature of anemia is fetal ascites rather than pleural or pericardial effusions [17]. Investigations should include maternal blood type and antibody screen to exclude red blood cell alloimmunization, hemoglobin electrophoresis to evaluate for inherited hemoglobinopathies depending on ethnic background, Betke-Kleihauer test to exclude fetomaternal hemorrhage, and

Doppler evaluation of the peak systolic velocity (PSV) in the middle cerebral artery (MCA) to screen for fetal anemia. Maternal serology for infections associated with NIH should also be sent, including parvovirus $B_{19}$, cytomegalovirus, herpes simplex virus, and toxoplasmosis [18]. If invasive testing is performed, amniotic or pleural fluid should also be sent for infectious polymerase chain reaction (PCR).

### *Genetic testing*

Because of the increased risk of genetic abnormalities associated with pleural effusions, invasive genetic testing with amniocentesis, chorionic villus sampling, or pleural fluid aspiration should be offered. In one review of 246 fetuses with pleural effusions undergoing genetic analysis, 35% were aneuploid [19]. However, the aneuploidy rate was significantly higher when effusions were detected in the first trimester or when additional abnormalities were present, with aneuploidy occurring in 50% and 12% of fetuses with nonisolated and isolated effusions, respectively [19]. Other series have reported lower aneuploidy rates in primary pleural effusions in the range of 6–9.5% [2,20], and in our experience of 88 fetuses with primary effusions, 4.5% of fetuses were aneuploid [12]. The most commonly associated chromosomal abnormalities include trisomy 21 and 45,X [12,19], and among fetuses with pleural effusions, the risk of trisomy 21 has been estimated at 1.8% [20]. In a large series evaluating significant genomic abnormalities detectable by chromosome microarray analysis (CMA) for specific anomalies detected by ultrasound in nearly 3000 pregnancies with normal karyotypes, among the subset of 586 fetuses with isolated abnormalities of the neck and/or body fluid, including pleural effusions, significant abnormalities were detected in nearly 4% (23/544) and variations in unclear significance were seen in 3% (19/455) [21]. Thus, CMA should be strongly considered for additional diagnostic testing, and it is our practice to proceed directly to CMA if Quantitative Fluorescence (QF-) PCR is negative for common aneuploidies. In the absence of a karyotype or microarray abnormality, additional workup for Noonan syndrome is recommended, as this condition can present antenatally with pleural effusions and hydrops [22,23]. Pathogenic variants in individuals with Noonan syndrome are most commonly detected in the genes *PTPN11, SOS1, RAF1, and RIT1* and less frequently in the genes *KRAS*, *NRAS*, *BRAF*, and *MAP2K1* [24]. Analysis of additional candidate genes *VEGFR3, FOXC2, and ITGA9* implicated in congenital chylothorax may also be considered [25].

### *Diagnostic thoracocentesis*

Thoracocentesis performed at the time of amniocentesis may provide additional diagnostic information. In addition to rapid genetic analysis, pleural fluid can be sent for cell count. It was suggested that lymphocytosis >80% was pathognomonic for chylothorax [26], but this has not been consistently seen [27], and we have found that fetal pleural lymphocyte counts are commonly in this range, regardless of the underlying etiology. Mediastinal shift may also resolve or improve following thoracocentesis, thus improving visualization of intrathoracic structures and cardiac anatomy. Some authors have also reported an improvement in fetal heart rate abnormalities following thoracocentesis [28].

Recommended antenatal investigations in the evaluation of fetal pleural effusions are summarized in Table 1.

**Table 1**
Recommended investigations for fetal pleural effusions.

| Maternal | Fetal |
|---|---|
| CBC | Detailed anatomical survey |
| Group and screen | MCA PSV[b] |
| Betke-Kleihauer | Echocardiogram |
| TORCH[a], Parvovirus $B_{19}$ | Karyotype, chromosomal microarray, Noonan syndrome testing |
| | Thoracocentesis (pleural fluid cell count, TORCH[a] PCR[c]) |

[a] Toxoplasmosis, rubella, cytomegalovirus, herpes simplex.
[b] Middle cerebral artery peak systolic velocity.
[c] Polymerase chain reaction.

## Sonographic features of pleural effusions

When evaluating fetal pleural effusions sonographically, the effusions should be characterized as unilateral or bilateral, and the presence of mediastinal shift and associated hydrops (i.e., fluid accumulation in two or more compartments, including pleural effusion, pericardial effusion, skin edema, ascites, and polyhydramnios) should be specified.

Sonographically, pleural effusions appear as anechoic fluid surrounding one or both lungs (Fig. 1) and should be distinguished from pericardial effusion by the typical "bat wing" appearance of the freely floating lungs within the surrounding fluid [6]. Although the diagnosis of a primary pleural effusion is a diagnosis of exclusion, the presence of an isolated, unilateral, or asymmetric hydrothorax may be suggestive [3]. As 60–70% of fetuses are hydropic at presentation [3,12], determining whether the effusions are primary or part of a generalized hydropic picture can be challenging. Serial progression in pleural effusion size, presence of upper body edema, predominance of fluid within the thorax compared to other bodily compartments and absence of placental thickening or structural abnormalities, are suggestive that hydrops may be secondary to pleural effusions [3].

### *Antenatal sonographic prognostic indicators*

Perinatal morbidity and mortality in association with pleural effusions are predominantly related to prematurity, the presence of hydrops, and development of pulmonary hypoplasia [1]. Poor prognostic indicators include associated malformations [2], hydrops [1–4,11], diagnosis before 33 weeks [1], bilaterality of effusions [1,2], unilateral effusions with mediastinal shift [1], and prematurity [1,3,4]. Perinatal outcomes do not appear to be altered by sex [1,4], polyhydramnios [1,4], or mode of delivery [12]. In a review of 204 primary fetal hydrothroraces, 89 of which were not treated antenatally, overall mortality was 39%. Hydrops, the unilateral or bilateral nature of the effusion, spontaneous resolution, and gestational age at delivery were important determinants of outcome. However, following multivariate analysis, only hydrops remained a signifcant prognostic indicator among fetuses with untreated primary pleural effusions [3]. Other reported prognostic indicators in primary hydrothorax include effusion progression 1–2 weeks after initial diagnosis, with the development of hydrops and polyhydramnios [10], and the sonographic effusion ratio [5], determined by measuring the cross-sectional area of the effusion and the thoracic cavity on a standard two-dimensional (2D) four-chamber view of the heart. Thus, in summary, the majority of series suggest that large or rapidly progressive effusions with significant mediastinal shift, development of hydrops, and associated structural malformations carry a more guarded prognosis.

### *Prediction of pulmonary hypoplasia*

In a literature review of 198 fetuses with primary pleural effusions, overall mortality was 35% (69/198), with 75% of deaths occurring postnatally [3], related mostly to pulmonary hypoplasia

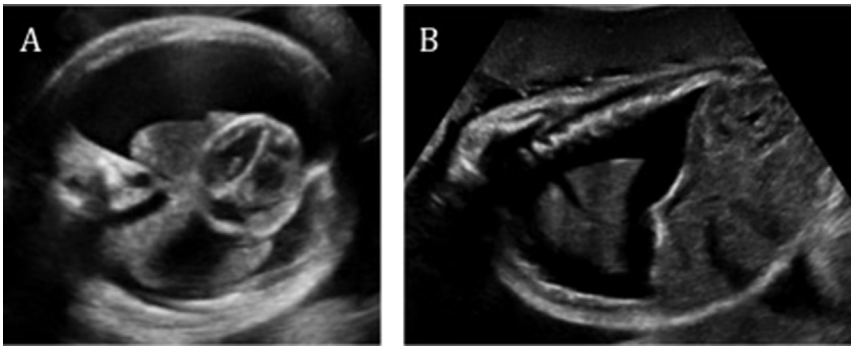


**Fig. 1.** Large left pleural effusion on axial (A) and sagittal views of the chest (B).

[1,7]. Thus, several attempts have been made to develop antenatal sonographic predictors of pulmonary hypoplasia, with limited success. Two-dimensional (2D) ultrasound parameters to estimate the risk of pulmonary hypoplasia have included thoracic circumference, thoracic circumference-to-abdominal circumference ratio, and lung area [29]. Overall, these parameters have inadequate negative and positive predictive values, and furthermore, thoracic circumference is of limited use in fetuses with pleural effusions, as chest size is generally normal [29]. Furthermore, visualization of lung parenchyma and accuracy of both 2D and 3D ultrasound may be limited by technical factors such as bone artifacts, oligohydramnios, fetal position, or maternal body habitus, and moreover, these parameters have yet to be validated prospectively [29]. With newer ultrafast gradient systems in magnetic resonance imaging (MRI), fetal MRI has been used to determine lung volume to predict lung hypoplasia [30]. However, the significant heterogeneity in imaging protocols and the wide reported range for normal lung volumes [31], limits the clinical applicability of this imaging modality for reliable prediction of pulmonary hypoplasia at this time [31,32].

## Management options for fetal primary pleural effusions in utero

Primary, small, nonhydropic effusions may be managed expectantly and may spontaneously regress [3]. In the presence of rapidly enlarging pleural effusions with associated mediastinal shift, hydrops, or significant polyhydramnios, drainage of pleural effusions is indicated. With thoracic decompression, the lungs may re-expand, possibly reducing the risk of pulmonary hypoplasia. Intrathoracic pressure may also decrease with improvement in venous return and potential hydrops reversal. Relief of esophageal compression may result in normalization of amniotic fluid volume, decreasing the risk of PPROM and preterm delivery. Response to pleural drainage may also provide prognostic and diagnostic information. Fetuses that do not demonstrate lung expansion following decompression may be at increased risk of pulmonary hypoplasia 33]. If hydrops does not resolve following drainage, this may also suggest an alternate underlying cause for hydrops other than pleural effusions [2].

Management options for fetal pleural decompression including thoracocentesis, pleuroamniotic shunting (PAS), and, more recently, pleurodesis with sclerosants are discussed below.

## Fetal intervention: thoracocentesis and pleuroamniotic shunting (PAS)

Thoracocentesis was first successfully performed in 1982 as a treatment for primary pleural effusion *in utero*; however, several repeat thoracocentesis procedures were required antenatally due to reaccumulation of fluid [34]. In a literature review of 29 fetuses with primary pleural effusions undergoing thoracocentesis, fluid reaccumulated in 75%, with a mortality of >50% among those cases [3]. Rapid reaccumulation of pleural fluid typically occurs within 24–48 h post decompression [2,6]. In an early series describing 5 cases undergoing fetal thoracocentesis, including 3 hydropic fetuses and 2 fetuses with massive unilateral effusions with mediastinal shift, all fetuses reaccumulated fluid, and there were no survivors except for one fetus that also underwent PAS following reaccumulation of pleural effusions with reversal of hydrops [1]. This early report recognized the potential life-saving nature of definitive thoracic decompression *in utero* with PAS.

Perinatal survival may be worse with thoracocentesis compared to PAS [3,11]. In a review of 203 fetuses with primary pleural effusions, overall survival was 60–66% with improved outcomes following PAS compared to thoracocentesis, although this did not reach statistical significance [11]. In this series, survival following thoracocentesis was 50% and 77% in fetuses with and without hydrops, respectively, compared to 62% and 82% in hydropic and nonhydropic fetuses, respectively, undergoing PAS [11]. When hemodynamic changes were evaluated following PAS in hydropic fetuses, the preload index and skin edema decreased significantly and the lung-to-thorax ratio improved significantly following shunt insertion [35], suggesting a therapeutic benefit of PAS in reversing hydrops. Furthermore, reversal of pre-eclampsia and maternal “mirror” syndrome have been reported with shunt insertion, which has reportedly occurs in 7% of cases of fetal pleural effusions and generally prompts delivery [12].

Although there are no randomized controlled trials comparing *in utero* treatment options for fetal pleural effusions, retrospective data from larger series support invasive therapy to improve perinatal

survival, and PAS appears superior to serial thoracocentesis particularly in hydropic fetuses [11,12,36–42].

Among 132 fetuses undergoing TAS for large pleural effusions in our institution, 70% of effusions were bilateral at presentation and 62% of fetuses were hydropic (12 and unpublished data). Overall survival was 65.2%, which was less in hydropic fetuses (38% if hydropic *vs.* 62% if nonhydropic) [12]. *In utero* demise occurred in 16 (12.1%) fetuses, and none had structural or chromosomal abnormalities. Among the 116 live born infants, 75% survived the neonatal period [12]. There were 30 (22.7%) neonatal demises (NND) with the majority related to pulmonary causes including pulmonary hypoplasia (n = 8), persistent pulmonary hypertension of the newborn (PPHN) (n = 4), and pulmonary lymphangiectasia (n = 4) as well as complications of prematurity [12]. The outcomes of the first 88 cases have been reported previously [12]. Gestational age at delivery was significantly later in both hydropic and nonhydropic survivors compared to neonates who died (34.9 vs. 31.6 and 37.8 vs. 32.6 weeks, respectively; $P = 0.0003$), emphasizing the significant impact of prematurity on overall prognosis [12]. Gestation at shunt insertion was not significantly different between survivors and nonsurvivors [12].

Perinatal outcomes from large single-center series for *in utero* PAS for pleural effusions are summarized in Table 2. Overall survival has been reported in the range of 48–68%, (60–100% *vs.* 33–66% in nonhydropic and hydropic fetuses, respectively) [11,12,36–39,43,44]. Hydrops resolution occurred in 46–89% of cases [12,37–41], and among those with persistent hydrops, alternative genetic or syndromic diagnoses have been reported, such as type 7 mucopolysaccharidosis [37], arthrogryposis [2], and akinesia deformation sequence [36]. In our series, hydrops resolved in nearly 50% of fetuses with PAS, and survival was significantly worse among persistently hydropic fetuses [12].

### *PAS shunt-related complications*

The most common shunt-related complication is preterm birth, with delivery occurring <37 weeks in 80% [12,37], as well as PPROM reported in 6–15% [12,37] and chorioamnionitis in 8.5% [37]. Catheter migration may be seen in up to 20% [45,46] with one reported NND related to intrathoracic migration and hilar strangulation [47] and one catheter migration into the maternal peritoneal cavity [48]. In our experience of 227 PAS shunt insertions for pleural effusions and macrocystic CCAMs, 16 (7%) dislodged *in utero* (unpublished data), and in 25% of cases, a repeat shunt insertion was required [12].

In our institution, the risk of procedure-related complications was 8.8% (10/113 shunt procedures), which included fetuses developing fetal distress necessitating cesarean section (n = 4), PPROM (n = 5), and fetal death (n = 1) [12]. *In utero* demise in association with shunt insertion has is rare and reported cases have been related to fetal hemorrhage and placental abruption with transplacental entry [36] or traumatic cord accidents [1,12]. Fetal hypoproteinemia [49], scars [50], and limb constriction bands [51] have also been rarely described. One case of uterine-peritoneal leakage following PAS with the development of maternal ascites and oligohydramnios, which ultimately resolved spontaneously has also been reported [52].

**Table 2**
Comparison of outcomes between large single-center pleural shunt series for primary pleural effusions.

| References | Number of cases | | GA at delivery (weeks) | Hydrops resolution % | Perinatal survival | | |
|---|---|---|---|---|---|---|---|
| | Total | Hydropic % | | | Overall % | Hydropic % | Nonhydropic % |
| Pettersen et al. (1997) [38] | 69 | 59 | 36 (23–41) | 46 | 68 | 46 | 100 |
| Picone et al. (2004) [37] | 47 | 100 | 34 (22–40) | 89 | 66 | 66 | – |
| Smith et al. (2005) [36] | 21 | 76 | 32 (22–40) | N/A | 48 | 44 | 60 |
| Rustico et al. (2007) [11] | 53 | 81 | N/A | N/A | 64 | 58 | 90 |
| Yinon et al. (2010) ([12] & unpublished data) | 132 | 62 | 34 (19–42) | 47.5 | 65.2 | 38 | 62 |
| Walsh et al. (2011) [43] | 15 | 60 | N/A | N/A | 53 | 33 | 83 |
| Pellegrinelli et al. (2012) [39] | 27 | 74 | 31 (27–35) | 78 | 52 | 47 | 85 |
| Miyoshi et al. (2013) [44] | 15 | 73 | NA | N/A | 60 | 46 | 100 |
| **Total** | **335** | **59–100%** | **32.7** | **46–89%** | **48–68%** | **33–66%** | **60–100%** |

*Long-term outcomes following PAS*

Long-term outcome of children who underwent PAS *in utero* is sparse. A recent series evaluated neurodevelopmental and respiratory outcomes among 48 hydropic fetuses that underwent PAS for pleural effusions; of these 48 fetuses, 41 were live born and 31 survived the neonatal period [53]. Fifteen percent of surviving infants were discharged on home oxygen and 35% required readmission in their first 2 years of life for respiratory complications, most commonly related to infections. Neurodevelopmental impairment was seen in 15% of children at long-term follow-up [53].

## Pleurodesis

Sclerotherapy is most commonly used for the treatment of venous and lymphatic disorders in adults and macrocystic lymphangiomas in children [54]; however, fetal applications are limited and have been reported in acardiac twins [55], multifetal reduction [55], placental chorioangiomas [56], and cystic hygromas [57,58]. More recently, OK-432, a sclerosant derived from a low-virulence Su-strain of type 3 Group A *Streptococcus pyogenes* of human origin treated with penicillin G, has been successfully used in fetal pleurodesis with primary pleural effusions [59]. OK-432 can be directly injected into the pleural space after aspiration of pleural fluid, inducing adherence of the visceral and parietal pleura [59] and has been successfully employed in the treatment of massive unilateral effusions [59–61], hydropic pleural effusions [62,63], and can be used as early as 16–21 weeks of gestation, when shunting can be technically challenging [64].

In a review of 45 fetuses undergoing OK-432 administration for primary bilateral pleural effusions, 27 of which were hydropic at presentation, the one-year survival was 36% (16/45) overall, with decreaseed survival in hydropic (15%) *vs.* nonhydropic (67%) fetuses [65]. When outcomes were compared for primary fetal pleural effusions treated with OK-432 and PAS in a review of the literature, although published experience with OK-432 was significantly smaller, survival trends were similar for hydropic (55% (113/206) vs. 30% (12/40)) and nonhydropic fetuses (85% (61/72) vs. 82% (28/34)) undergoing PAS and pleurodesis, respectively [66]. The authors reported neurodevelopmental follow-up for 13 infants treated with OK-432 for fetal pleural effusions, and outcomes were normal for 10/11 survivors [66]. Within this cohort, one fetus was noted to have a cerebral lesion 3 weeks following OK-432 administration, likely representing a frontal horn cyst. Neurodevelopmental testing was normal, and whether this lesion was an incidental finding or related to OK-432 administration is difficult to ascertain. One maternal death has been reported following OK-432 administration, secondary to an amniotic fluid embolism occurring 8 weeks following treatment; again, the relationship between the two events remains uncertain [60]. Renal insufficiency has also been described in a neonate treated with OK-432 prenatally; however, this may have been related to right hydronephrosis diagnosed antenatally rather than OK-432 administration [62]. Although safety and long-term outcome data are lacking for OK-432, further investigation is warranted, as its use may be particularly relevant at very early gestations. Moreover, pleurodesis is less invasive and technically simpler than PAS and may obviate the need for neonatal treatment, making it a particularly attractive therapeutic option.

## Approach to prenatal management of primary pleural effusions

In small-to-moderate unilateral effusions without hydrops or mediastinal shift, conservative management is appropriate. However, as many effusions will progress, ultrasound monitoring every 1–2 weeks is warranted. PAS should be considered in hydropic fetuses where the pleural effusion is suspected to be the primary underlying cause [3,67]; we also advocate treating large isolated pleural effusions in the absence of hydrops, which are occupying more than half of the thoracic cavity with mediastinal shift or which are rapidly increasing in size or associated with polyhydramnios [12]. After shunt insertion, ultrasound surveillance should be weekly to ensure that the shunt(s) has not blocked or dislodged and to monitor for fluid reaccumulation.

As the major complications with shunt insertion are PPROM and preterm delivery, which is of less clinical concern after 34 weeks when compared to the potential challenges of resuscitation and ventilation of a hydropic neonate, we suggest that shunting should be considered even at late gestational ages

to allow fluid re-equilibration between different fetal compartments and potentially improve neonatal ventilation. Peripartum thoracocentesis just before delivery or intrapartum may also be considered to facilitate neonatal resuscitation if effusions are large [34,68,69]. Furthermore, since PAS allows ongoing drainage patients may await spontaneous onset of labor, rather than necessitating labor induction [12].

As mode of delivery does not impact neonatal outcome [4,12], cesarean section should only be performed for standard obstetrical indications. Delivery is recommended in a tertiary care center, with adequate neonatal and pediatric support to resuscitate a potentially severely compromised neonate, specifically with the ability to urgently insert chest tubes, provide ventilator support including high-frequency ventilation, manage PPHN, and fluid and nutrition abnormalities [6]. At birth, shunts should be immediately clamped to avoid a pneumothorax.

## Thoracocentesis and thoracoamniotic shunting: technical aspects

Thoracocentesis can be performed using a 20- or 22-gauge needle under ultrasound guidance, similar to an amniocentesis. In practice, we rarely perform thoracocentesis and instead usually proceed directly to PAS for suspected primary pleural effusions.

Several different shunts are currently available for antenatal use (Fig. 2). The characteristics of the shunt, including size and flexibility of the material used, may play a role in promoting catheter migration [45,67,70], with smaller shunts possibly being at higher risk of dislodgment and obstruction despite being theoretically less traumatic [70]. The most commonly used shunt is a *"Rodeck"* silicone double pigtail catheter (Rocket Medical plc., Washington, Tyne & Wear, UK; Inner diameter [ID] 1.5 mm and outer diameter [OD] 2.1 mm). The*"Harrison"* shunt (Cook Medical, Bloomington, USA; ID 0.97 mm and OD 1.67 mm) is also available, which is smaller and more flexible than the Rocket shunt. Additional shunt/catheters include a 4F-angiographic single pigtail catheter (Cordis, Johnson & Johnson, The Netherlands) and a double basket polyethylene catheter (Hakko Co., Nagano, Japan; ID 0.9 mm, OD 1.47 mm), which is inserted through a sharp trocar (Hakko Co., Nagano, Japan; ID 1.66 and OD 2.14 mm), this is the thinnest available catheter and is short with a straight conformation. A nitinol wire mesh shunt (Somatex® Medical Technologies, Berlin: 18G, OD 2.6 mm) is available in Europe. There is

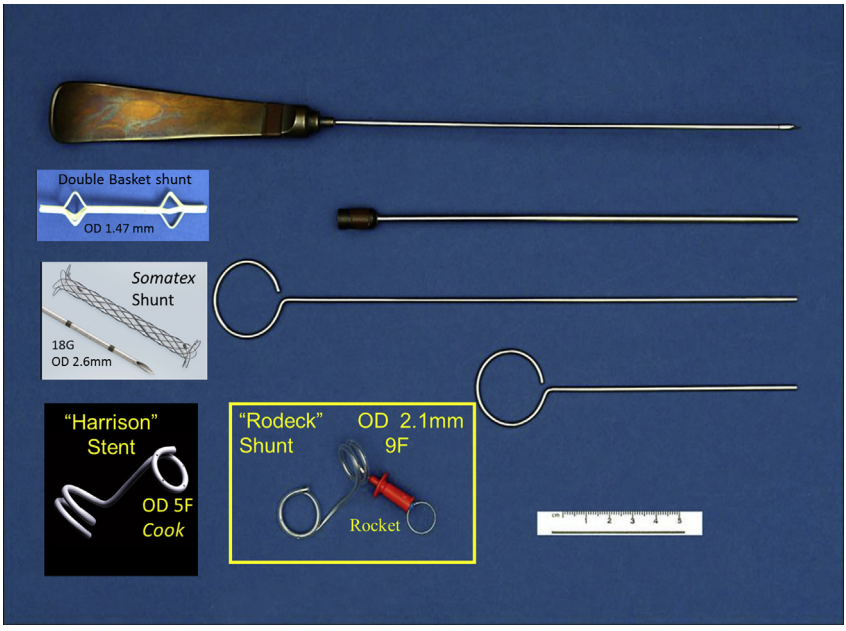


**Fig. 2.** Instruments for pleuro-amniotic shunting *in utero.*

no preferred shunt type for PAS antenatally and shunt dislodgment has been described with all [12,45,46]; choice depends on individual preference and experience.

We have previously described the technique for PAS in detail [6] and have summarized our approach below using the Rocket device. Shunting can be performed under local anesthesia with intravenous sedation using remifentanil and midazolam; fetal paralytic agents are not typically required. We administer prophylactic antibiotics, typically a first-generation cephalosporin, at the start of the procedure as well as betamethasone for fetal lung maturity if between 24 and 34 weeks of gestation or at viability if shunted <24 weeks. We do not routinely administer tocolytics, however, either rectal indomethacin or oral nifedipine may be used.

A 9F (OD 3 mm) trocar and cannula (Rocket Medical plc. Washington, Tyne & Wear, UK, or Karl Storz GmbH, Tüttlingen) (Fig. 2) is introduced transabdominally under ultrasound guidance into the amniotic cavity while avoiding the placenta and maternal vessels. The trocar should be introduced into a pocket of amniotic fluid, sufficiently distant from the fetus to facilitate deposition of the external end of the shunt into the amniotic cavity. Occasionally, amnioinfusion may be necessary to optimize fetal position or provide a window of access into the uterine cavity. Once within the amniotic cavity, the trocar is inserted perpendicularly through the fetal chest wall into the effusion as close as possible to the mid-axillary line at the base of the scapula, whilst avoiding the nipple. The sharp trocar tip is advanced well into the effusion, the trocar is removed, and a double pigtail silastic catheter is inserted through the cannula. A pusher rod advances the distal half of the catheter into the fetal pleural effusion. The cannula is then gently withdrawn from the thorax, and finally, the pusher deposits the remaining catheter into the amniotic cavity. Prematurely advancing the pusher rod can result in dislodgment of the entire shunt into the pleural space. With bilateral effusions, we try to insert both shunts at a single sitting to avoid multiple uterine entries. The fetus can usually easily be rotated to facilitate access to both pleural cavities, using the blunt end of the shunt cannula. Amnioreduction may be performed at the end of procedure in the presence of polyhydramnios.

## Summary

Fetal pleural effusions can be associated with significant perinatal morbidity and mortality. Detailed ultrasound assessment and genetic testing can exclude associated abnormalities in the majority of

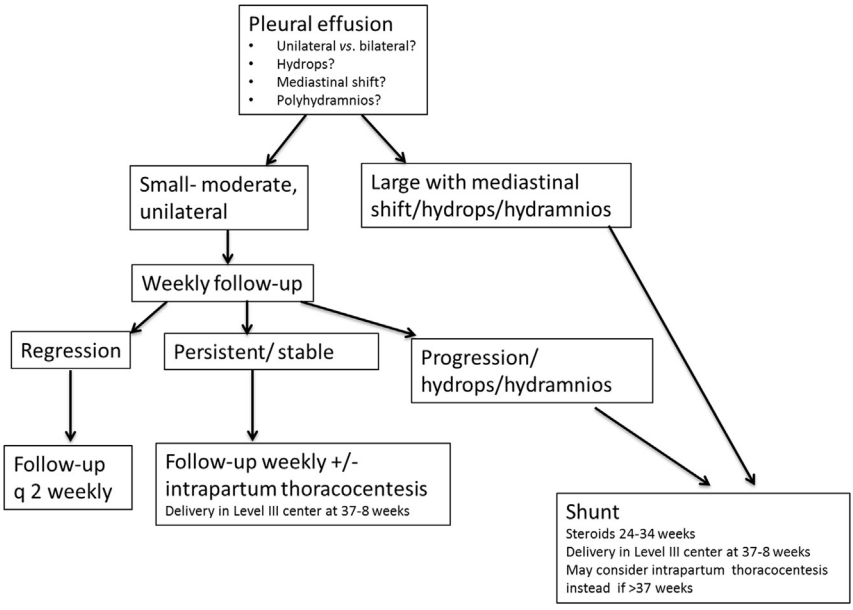


**Fig. 3.** Proposed algorithm for the management of fetal pleural effusions.

cases. For isolated primary effusions, *in utero* decompression has demonstrated significant improvement in perinatal survival, particularly in hydropic fetuses. Affected pregnancies should be referred to a regional fetal medicine center with expertise in prenatal diagnosis and fetal intervention, and delivery should also occur at centers with neonatal expertise. The approach to prenatal management of pleural effusions is summarized in Fig. 3. In a small proportion of infants, additional diagnoses, including specific genetic syndromes, may only be recognized postnatally, and hence, a detailed examination is warranted after birth by a pediatrician and/or geneticist. Because of the paucity of long-term data in children with antenatally diagnosed and treated pleural effusions, large multicenter collaborations evaluating neurodevelopmental and respiratory outcomes are needed.

## Conflicts of interest

The authors have no conflicts of interest.

**Practice points**

- Fetal pleural effusions, although uncommon, are an important cause of perinatal morbidity and mortality
- Secondary etiologies should be excluded with a detailed evaluation for causes of immune and nonimmune hydrops, structural malformations, genetic abnormalities, congenital infections, and fetal anemia.
- In fetuses with primary pleural effusions, fetal chest shunting may be lifesaving particularly in the presence of significant mediastinal shift and hydrops, and in ~50% of cases, hydrops will resolve.
- Delivery should occur in a tertiary care center with expertise for advanced neonatal support

**Research agenda**

- Sonographic predictors of pulmonary hypoplasia in fetuses with primary pleural effusions should be further evaluated.
- Long-term neurodevelopmental and respiratory outcomes in fetuses treated in *utero* are lacking and should be further studied.

## References

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