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Wendy A. Lavezzi,[1] *M.D.; Barbara J. McKenna,*[2] *M.D.; and Barbara C. Wolf,*[3] *M.D.*

The Significance of Pulmonary Interstitial Emphysema in Live Birth Determination*

ABSTRACT: The utility of pulmonary interstitial emphysema (PIE) in live birth determination is not well established. Because the distinction between live birth and stillbirth may be important in criminal proceedings, we undertook this study to investigate the relationship between the histologic finding of PIE and live birth. Sixty-six cases of infant death were retrieved and compared with 21 stillborn infants. Histologic sections of the lungs were characterized as "florid PIE," "equivocal PIE," or "absent PIE." Sixteen cases of florid PIE were identified, all in live born infants. Forty-seven cases of equivocal PIE were found in 36 live born and 11 stillborn infants. In 24 cases (14 live born infants and 10 stillborns), no PIE was identified. We examined the relationship between florid PIE in infants with sudden infant death syndrome (SIDS) or "sudden unexpected death in infancy, manner undetermined" (SUDI), and also its relationship to other variables. No association was found. The presence of equivocal PIE may be an artifact of tissue processing.

Florid PIE is found only in live born infants. No correlation between the presence of florid PIE and cause of death could be determined.

KEYWORDS: forensic science, interstitial emphysema, live birth, stillbirth, asphyxia

Autopsies performed on newborn infants who have been found in a discarded fashion can be challenging to the forensic pathologist. In many of these cases, the body of the infant is disposed of by a birth mother who claims that the infant was stillborn. The pathologist is faced with the task of determining whether the infant was born alive, which may have implications in later criminal proceedings.

The criteria traditionally used for the determination of live birth at autopsy include the presence of air in the lungs or middle ear, the presence of air or food in the stomach, and the presence of inflammation in microscopic sections of the umbilical cord stump (1,2). Of these, only microscopic evidence of patchy uneven aeration of the alveolar air spaces is reliable, and has generally been used in cases involving perinatal asphyxiation (Fig. 1) (3). In contrast, the lung parenchyma of a third-trimester stillborn infant has an alveolar pattern of development without aeration of the air spaces (Fig. 2) (4).

We have previously commented on the importance of the histologic finding of pulmonary interstitial emphysema (PIE) in the determination of live birth in two infants whose bodies were discarded shortly after birth, and the use of the finding in subsequent criminal proceedings (5). PIE may not be grossly visible, and is microscopically identified as the presence of air that disrupts the tissues of the interlobular perivascular and peribronchial spaces, and often extends to and involves the visceral subpleural space. PIE is also a well-documented clinical and radiographic finding, most often resulting from mechanical ventilation of a premature infant with respiratory distress syndrome (6–12). Cases of spontaneous PIE in infants and older children have also been reported, usually related to congenital cystic lesions or severe pulmonary infection with damage to the alveolar architecture, allowing air to dissect into the interstitial space (13–15). PIE has been seen following cardiopulmonary resuscitation of infants or as a result of forceful respiratory efforts against a fixed object in the airway, such as inspissated mucus (16,17) or a foreign object (18). Prior to our recent report, PIE was not recognized as a useful criterion for live birth determination.

In criminal cases, distinction between live birth and stillbirth may be critical, as it may differentiate a homicide from unlawful disposal of a body. We undertook the current study to further elucidate the importance of PIE in fetal and infant autopsies and its role in live birth determination.

Methods

Eighty-seven cases were retrieved, including 54 cases from the autopsy files of one of us (BCW) and 33 cases from the autopsy files of the Department of Pathology and Laboratory Medicine of the Albany Medical Center. The cases included 66 infant deaths and 21 stillbirths. The live born infants ranged in age from birth to 11 months (mean 2.4 months). The causes of death in these cases included sudden infant death syndrome (28); congenital anomalies (15); sudden unexpected death in infancy, manner undetermined (9); infection (5); homicidal or accidental asphyxia (3); head injury (2), and one death each due to prematurity, drowning, hemorrhage, and hyperthermia (Table 1). The designation of "sudden unexpected death in infancy, manner undetermined" (SUDI) was reserved for cases in which no anatomic cause of death could be found, but in which police investigative reports were inconclusive regarding the circumstances of the death. Histologic sections of the lungs of these live born infants were compared with histologic sections of the lungs of 21 third trimester stillborn infants, ranging between 28 and 40 weeks gestation (mean 35 weeks). Causes of stillbirth were varied (Table 1). The number of lung sections examined ranged from 1 to 16 per case (mean 4.6). All tissue sections were fixed in 10% buffered formalin, routinely

[1] Department of Pathology and Laboratory Medicine, Albany Medical Center Hospital, Albany, NY 12208.

[2] Department of Pathology and Laboratory Medicine, Albany Medical Center Hospital, Albany, NY 12208. Present address: Department of Pathology, University of Michigan Hospitals, Ann Arbor, MI 48109.

[3] Forensic Medicine, PC, Albany, NY 12204. Present address: Palm Beach County Medical Examiner Office, West Palm Beach, FL 33406.

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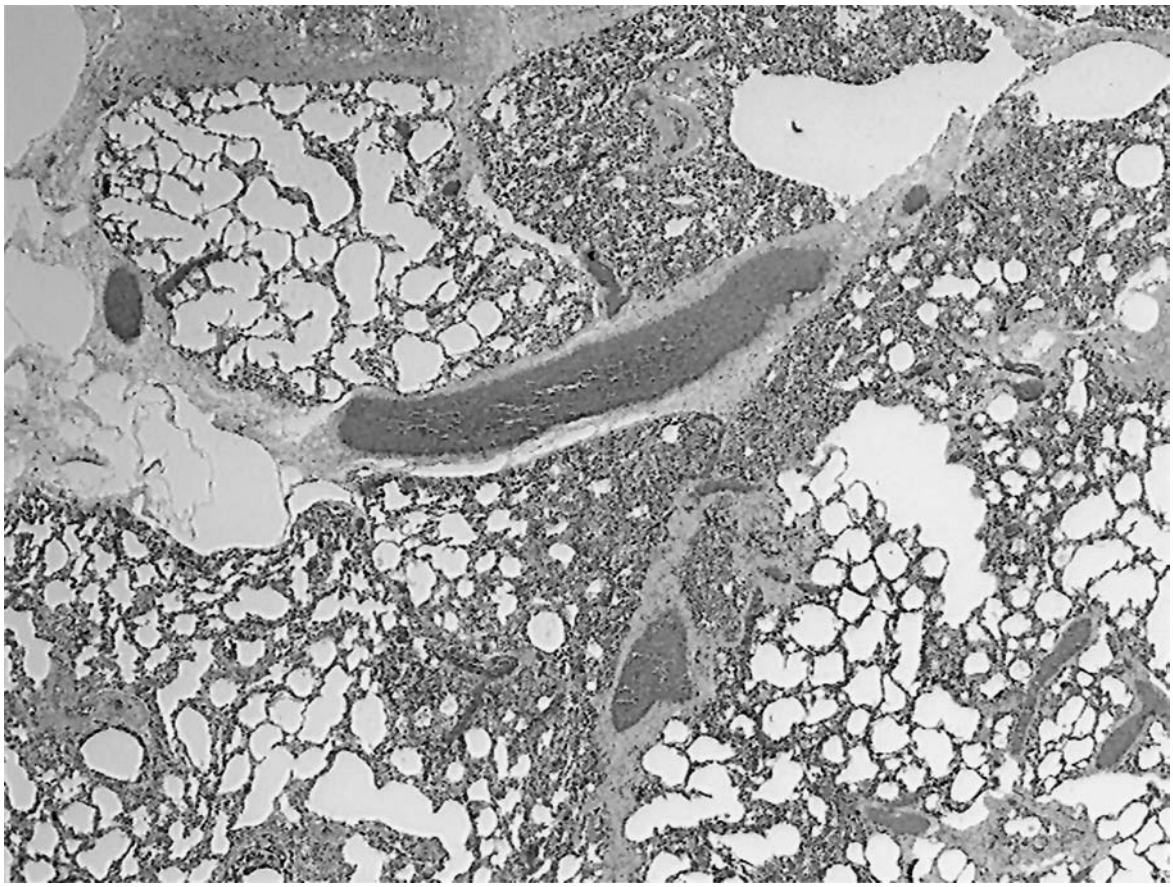

FIG. 1—*Uneven aeration of the alveoli in a live born infant, H&E, ×25.*

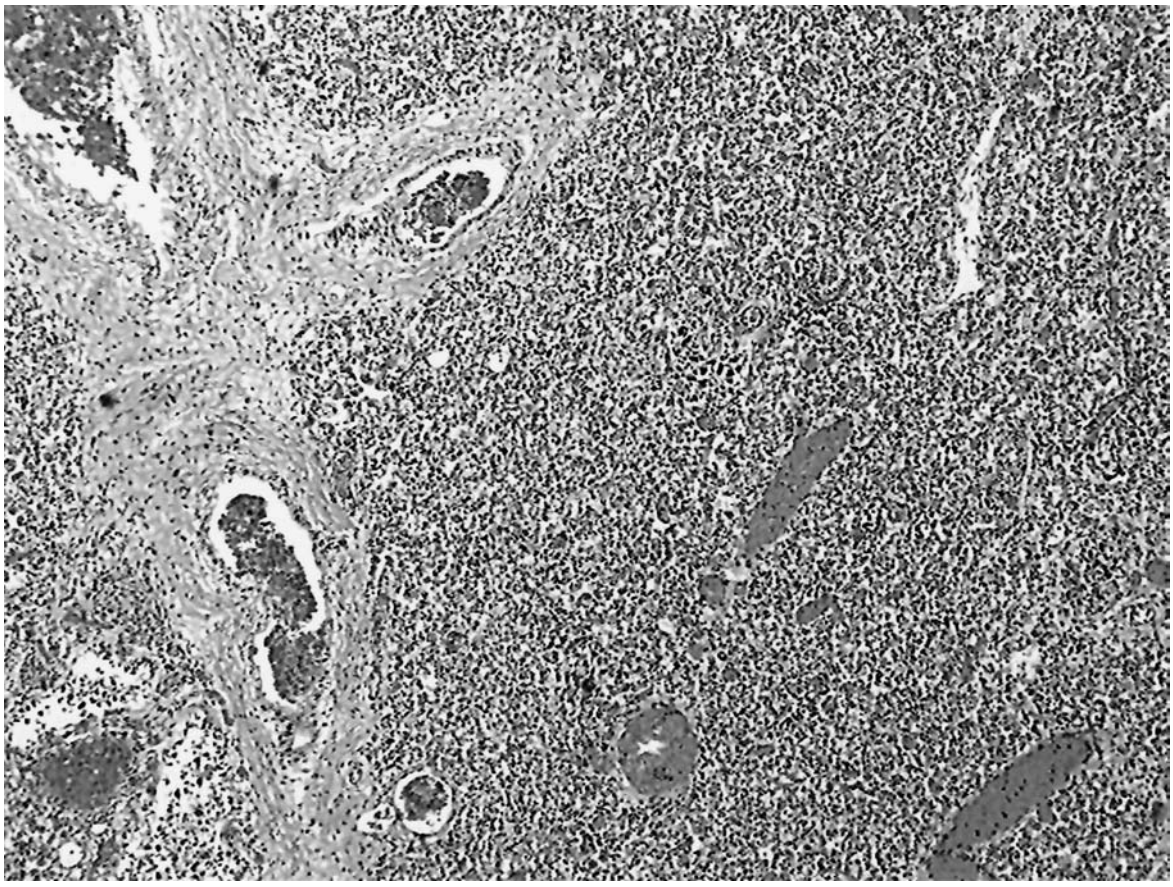

FIG. 2—*Uniformly unaerated alveoli in a stillborn infant, H&E, ×50.*

TABLE 1—*Presence or absence of PIE based on cause of death or stillbirth.*

	Florid PIE	Equivocal PIE	No PIE
Cause of Death			
SIDS	9/28 (32%)	16/28 (57%)	3/28 (11%)
congenital anomalies	2/15 (13.3%)	8/15 (53.3%)	5/15 (33.3%)
SUDI	3/9 (33.3%)	3/9 (33.3%)	3/9 (33.3%)
infection	0/5 (0%)	4/5 (80%)	1/5 (20%)
asphyxia	1/3 (33.3%)	2/3 (66.6%)	0/3 (0%)
head injury	0/2 (0%)	0/2 (0%)	2/2 (100%)
prematurity	0/1 (0%)	1/1 (100%)	0/1 (0%)
drowning	0/1 (05)	1/1 (100%)	0/1 (0%)
hemorrhage	1/1 (100%)	0/1 (0%)	0/1 (0%)
hyperthermia	0/1 (0%)	1/1 (100%)	0/1 (0%)
Cause of Stillbirth			
placental insufficiency	0/9 (0%)	5/9 (55.5%)	4/9 (45.5%)
congenital anomalies	0/3 (0%)	1/3 (33.3%)	2/3 (66.6%)
IUGR	0/2 (0%)	1/2 (50%)	1/2 (50%)
nuchal cord	0/2 (0%)	2/2 (100%)	0/2 (0%)
umbilical cord stricture	0/1 (0%)	0/1 (0%)	1/1 (100%)
preterm labor	0/1 (0%)	1/1 (100%)	0/1 (0%)
motor vehicle accident	0/1 (0%)	0/1 (0%)	1/1 (100%)
unknown	0/2 (0%)	1/2 (50%)	1/2 (50%)

processed, and stained with hematoxylin and eosin (H&E). The H&E slides were examined by two pathologists in a blinded fashion for evidence of PIE, defined as the presence of non-endothelial-lined spaces in the interstitium and subpleural zones. Based on this examination, cases were assigned to one of three categories. "Florid PIE" was defined as the presence of markedly dilated interstitial spaces often coalescing with similar subpleural dilated spaces (Figs. 3*a* and 3*b*). This finding was distinguished from the more subtle finding of focal distinct but non-distended, slit-like interstitial and subpleural spaces, which we termed "equivocal PIE" (Figs. 4*a* and 4*b*). The third category was then the absence of PIE.

The relationship between florid PIE and the practice of co-sleeping or SIDS or SUDI as a cause of death was examined in live born infants, as was any relationship to pneumonia or diffuse alveolar damage (DAD). SIDS, SUDI, co-sleeping, resuscitation, pneumonia/DAD, and decomposition were also examined for their possible relationship to equivocal PIE.

Statistics

Statistical analysis of the data was performed with the Fischer exact test, using the SISA online computer program.

Results

Sixteen cases of florid PIE were identified in both central and peripheral lung tissue sections. All of the cases in which florid PIE was present were live born infants (Table 2). The number of sections examined in cases in which florid PIE was identified ranged from 3 to 11 (mean 5). In some cases, florid PIE was present in all sections examined, and in others it was focal (e.g., in 3 of 11 sections).

An additional 47 cases of equivocal PIE were identified, including 36 live born infants and 11 stillborn infants. The number of sections examined in cases in which equivocal PIE was identified ranged from 1 to 16 (mean 4.5) and, once again, the finding was focal

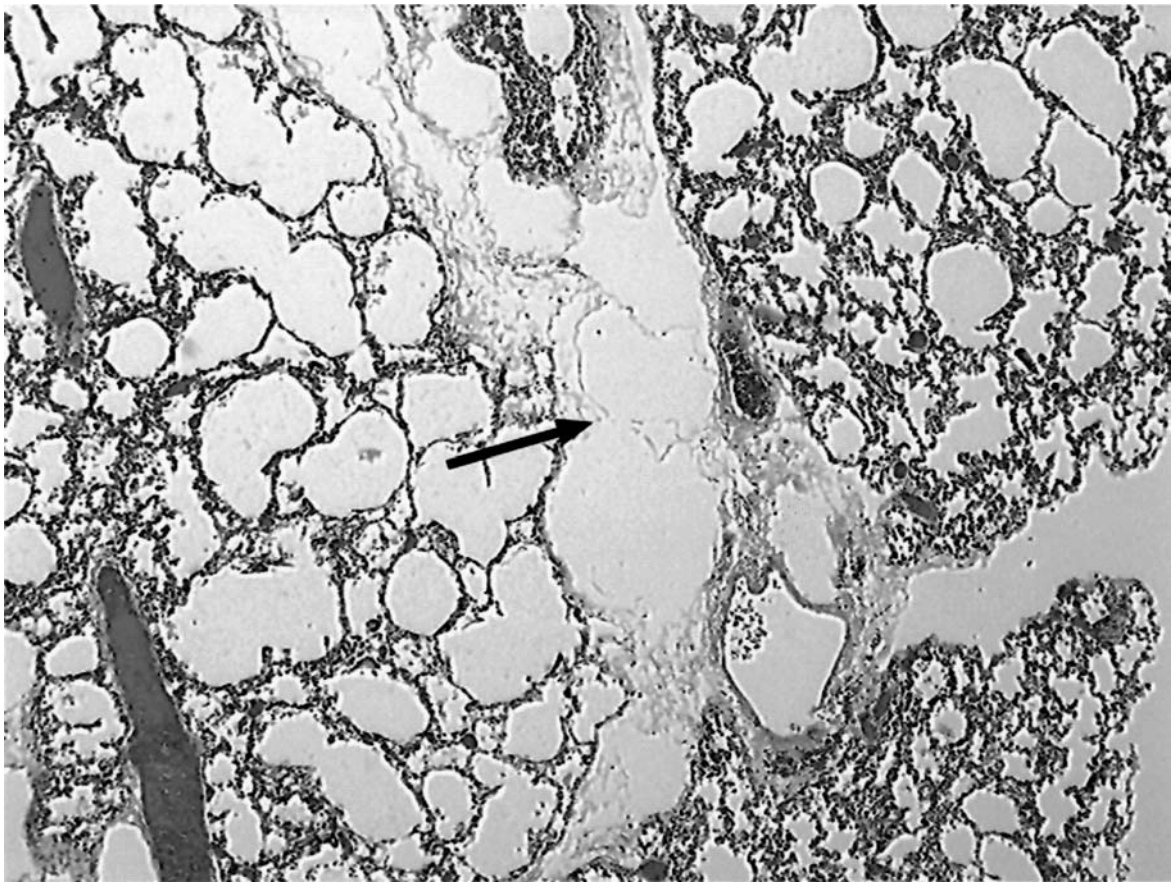

FIG. *3a—Florid PIE in a live born infant, with interstitial tissue disruption by air dissection (*arrow*), H&E, ×50.*

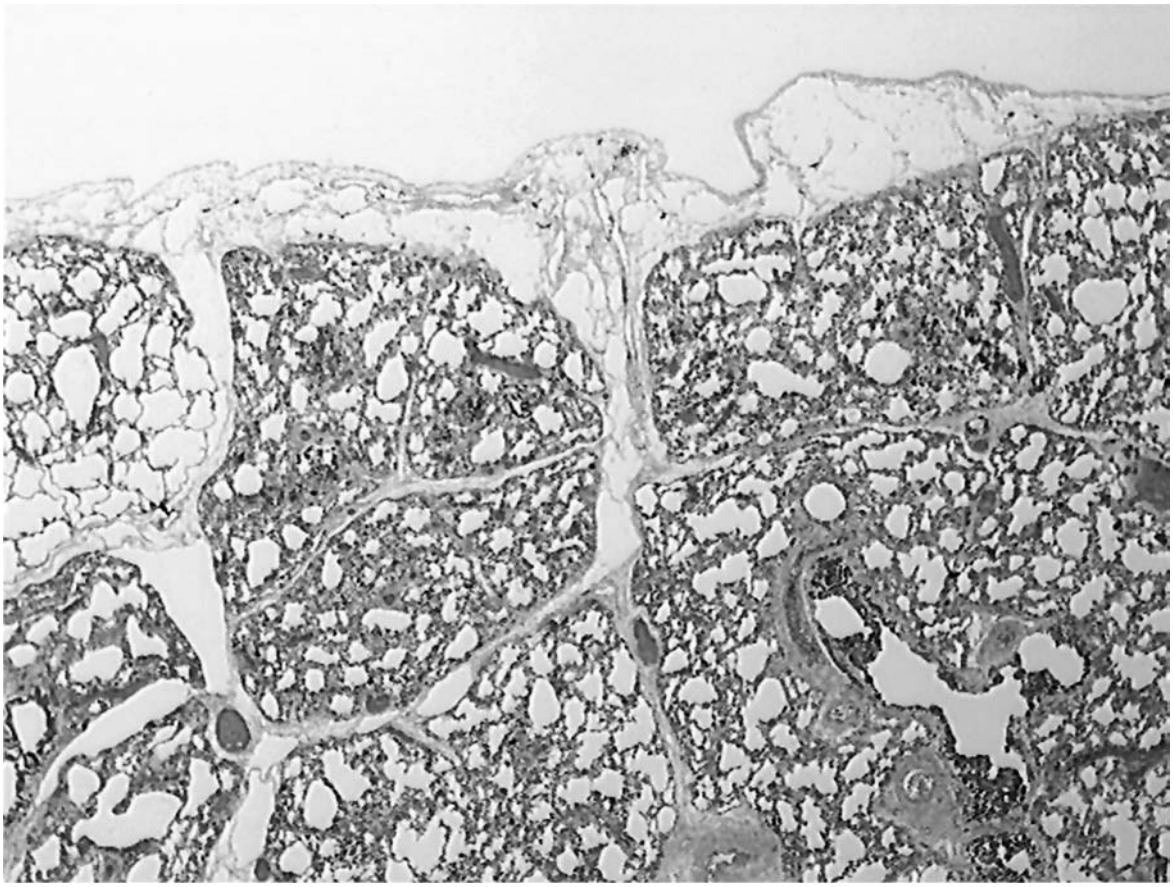

FIG. *3b—Florid PIE extending to subpleural space in a live born infant H&E, ×25.*

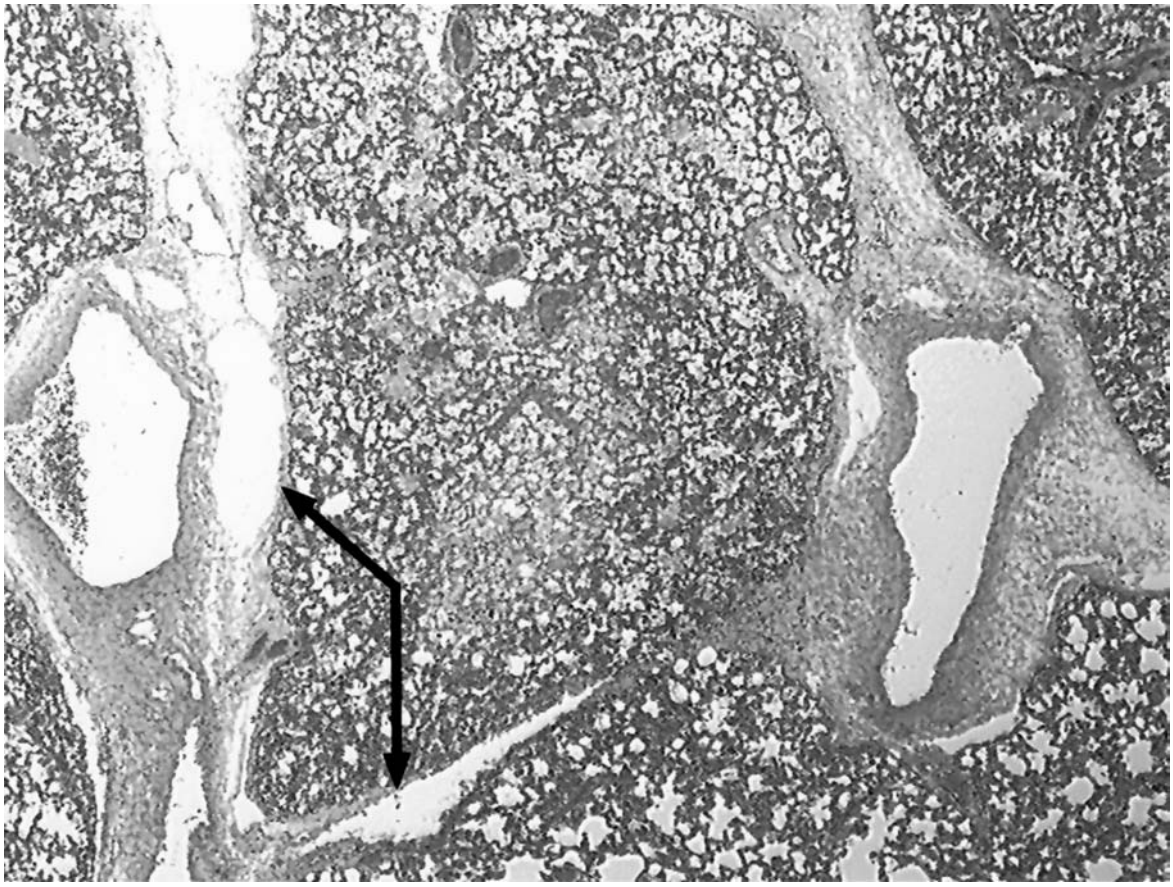

FIG. *4a—Equivocal PIE in a live born infant. Slit-like separations that may represent dilated lymphatics or artifact (*arrow*), H&E, ×25.*

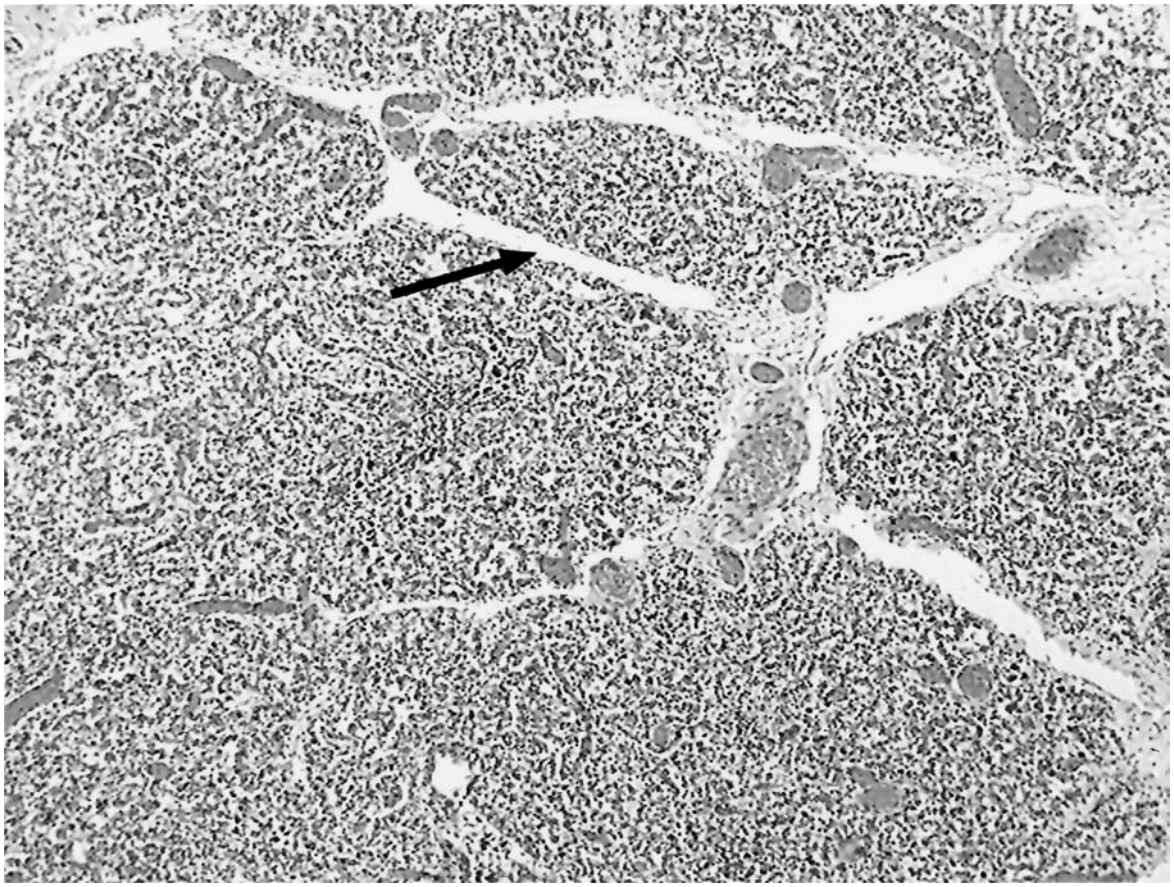

FIG. *4b—Equivocal PIE in a stillborn infant. Slit-like separations without obvious destruction of interstitial tissue (*arrow*), H&E, ×50.*

TABLE 2—*Relationship of PIE to live birth.*

	Live Birth	Stillbirth	*p*-Value
Florid PIE	16/66 (24%)	0/21 (0%)	0.007
Equivocal PIE	36/66 (54%)	11/21 (52%)	0.195
No PIE	14/66 (21%)	10/21 (48%)	0.016

in many cases. In 24 cases (14 live born infants and 10 stillborn infants), no PIE was identified (number of sections 2–10; mean 4).

All of the live born infants had full or partial aeration of the lung parenchyma, and all of the stillborn infant lungs were uniformly unaerated.

The causes of death in the 16 cases with florid PIE included sudden infant death syndrome (9), sudden unexpected death, manner undetermined (3), congenital anomalies (2), homicidal asphyxia (1), and hemorrhage (1). Causes of death in the live born infants and causes of stillbirth in cases with equivocal PIE were widely variable, similar to the cases with no PIE (Table 1).

Twelve of the 16 infants with florid PIE had experienced cardiopulmonary resuscitation and/or mechanical ventilation. In the cases of homicidal asphyxiation and hemorrhage, no resuscitation attempts were made. In the remaining two cases, information concerning resuscitation was unavailable. None of the live born infants in this study showed any gross or microscopic signs of decomposition.

Florid PIE was not independently associated with SIDS, SUDI, co-sleeping, resuscitative efforts or pneumonia/DAD (Table 3). None of the variables were significantly associated with equivocal PIE (Table 4).

TABLE 3—*Relationship in live born infants between florid PIE and potential causal variables.*

Variable	Florid PIE	*p*-Value
Resuscitation	12/58 (21%)	0.238
SIDS	9/28 (32%)	0.102
SUDI	3/9 (33%)	0.240
Co-sleeping	4/18 (22%)	0.249
Pneumonia/DAD	6/19 (32%)	0.164

TABLE 4—*Relationship in live born and stillborn infants between equivocal PIE and potential causal variables.*

Variable	Equivocal PIE	*p*-Value
Resuscitation	35/58 (60%)	0.487
SIDS	16/28 (57%)	0.716
SUDI	3/9 (33%)	0.114
Co-sleeping	12/18 (67%)	0.226
Pneumonia/DAD	10/19 (53%)	0.681
Decomposition	10/17 (59%)	0.658

Discussion

Determining live birth in an infant found in a discarded fashion can be challenging, since many of the previously reported and utilized criteria for live birth determination lack sensitivity and/or specificity. The "flotation test" for lung parenchyma, which has been used to determine the presence of air in the lung, may also indicate postmortem gas formation by bacteria, and must be correlated with the buoyancy of the other tissues in this regard. Similarly,

postmortem bacterial gas formation also limits the interpretation of air in the middle ear or stomach. The presence of food in the stomach is a very reliable indicator of live birth, but this finding is rare and its absence does not indicate that the infant was stillborn. The presence of a neutrophilic infiltrate in the umbilical cord stump (in the absence of umbilical vessel vasculitis throughout the cord) may indicate live birth, but its absence does not indicate stillbirth, since death may occur too soon after birth for the infant to mount an inflammatory response, or the cord may not have been cut while the child was alive.

Aeration of the lungs, often uneven, may be the most consistent histologic feature documenting live birth. It was entirely sensitive and specific as an indicator of live birth in the cases in this study. Its presence in all cases in this study with florid PIE supports the conclusion that florid PIE is a feature found only in live born infants.

In our previous report of two cases of discarded infants, the presence of PIE in both was considered an indicator of live birth, in combination with the histologic finding of uneven aeration of the alveolar parenchyma (5). The results of the current study, with florid PIE detected only in cases of infants born alive, support this interpretation.

We attempted to determine possible mechanisms for florid PIE in these cases by correlating its presence with several potential causal variables. Resuscitation attempts by mechanical or mouth-to-mouth ventilation are a documented cause of PIE in the literature (6–12), but no resuscitation attempts were made in two infants with florid PIE in this study, and the widespread use of resuscitative attempts in the infants in all of the categories made the relationship between ventilatory resuscitation efforts and PIE nonspecific. Severe pulmonary infections that damage lung parenchyma can also cause PIE by allowing air to escape from the disrupted alveoli and dissect into the interstitium (13–15). Although our population included some infants or stillborns with pneumonia and/or diffuse alveolar damage, the damage to the parenchyma was not severe, and no association with PIE was found. Other described causes of PIE are congenital cystic lesions of the lung and forceful respiratory efforts against a fixed object, such as inspissated mucus or a foreign body (16–18). This study did not include such cases, nor did we have any such cases with which to make a comparison.

The number of SIDS and SUDI cases with florid PIE in this study is interesting (32% and 33%, respectively). In 26 of the 37 cases of SIDS or SUDI (70%), the infants were either co-sleeping with an adult or adults, sleeping in the prone position, or both. Six of these 26 cases (23%) had florid PIE. Many epidemiologic studies have recognized an increase in the incidence of SIDS in infants sleeping in the prone position (19–22), and many additional studies have also suggested a relationship between SIDS and co-sleeping (23–31). One proposed mechanism for death in cases in which the infant was co-sleeping or lying in the prone position is accidental suffocation. Suffocation is also a plausible explanation for PIE, since the mechanism of breathing against an immovable object is a well-established cause of PIE. Determining the cause of death in cases involving SIDS, SUDI or co-sleeping relies heavily upon investigational findings in the absence of physical evidence, and accidental or intentional suffocation is difficult to determine and cannot often be excluded with certainty. When SIDS, SUDI, and co-sleeping were examined as independent variables in this study, they did not appear to be associated with the presence of florid PIE. Clearly, many more cases involving the known accidental or intentional suffocation of an infant would have to be examined in order to conclude that mechanical asphyxia could be a mechanism for florid PIE.

Equivocal PIE was found in both live born and stillborn infants, is nonspecific for the determination of live birth (Table 2), and has no significant association with any of the potential causal variables examined (Table 4). The appearance of florid PIE differs significantly from that of equivocal PIE. Florid PIE is characterized by expansion and destruction of the interstitial tissue, and in most histologic sections the areas of expansion coalesce with pockets of air in the subpleural space. Because of the obvious nature of florid PIE, the interobserver reliability for its identification in these cases was 100%. Equivocal PIE, as defined in this study, consists of slit-like separations in and around the interstitium without involvement of the subpleural space. Because of its subtle nature, the interobserver reliability of identifying equivocal PIE was 85%. Since there is no mechanism for air entry into the lungs of an infant who is known to be stillborn, it is probable that equivocal PIE is due to an artifact of tissue fixation, and in some cases may represent dilated lymphatics. The presence of decomposition did not significantly correlate with the presence of equivocal PIE, so gas formation by postmortem bacteria is also an unlikely cause. Regardless of cause, the subtle finding of equivocal PIE is not reliable as an indicator of live birth, and therefore its distinction from florid PIE is important. The term "PIE," when used in cases of live birth determination which often involve subsequent legal proceedings, should be reserved for cases with florid PIE, since this finding is specific to cases in which the infant was born alive. Although the absence of PIE significantly correlated with stillbirth in this study, it was also detected in 21% of live births, and is therefore nonspecific.

In one case in this study, florid PIE was found in only 3 of 11 sections examined, introducing the possibility that inadequate tissue sampling may have played a role in some of the other cases. The mean number of sections taken in each case also decreased slightly from cases with florid PIE (mean 5) to those with equivocal PIE (mean 4.5) to those with no PIE (mean 4), which may suggest the possibility of sampling error as a partial explanation for our findings.

It is also necessary when examining the lung tissue to distinguish the presence of PIE from the presence of dilated interstitial lymphatic spaces, since the latter may not indicate live birth. Immunohistochemical stains such as Factor VIII and CD31 have been used in other studies to make this distinction (5,32). However, because of the cellular disruption frequently seen in postmortem bronchial and endothelial structures which can compromise the interpretation of these immunohistochemical studies, morphologic evaluation of PIE with conventional H&E-stained sections may be more appropriate. If the use of PIE as a criterion for live birth determination is restricted to cases in which the PIE is florid, its distinction from dilated lymphatic spaces should be straightforward on morphologic grounds alone, since the interstitial tissue is extensively disrupted in florid PIE and would not be easily confused with well-defined intact lymphatic spaces.

In conclusion, florid PIE was a specific, but not sensitive finding in live born infants in the present study. This supports our previous observation that PIE is a reliable indicator of live birth, best interpreted in combination with the more sensitive finding of uneven or full aeration of the lung parenchyma. A direct correlation between cause of death and florid PIE could not be proven in this study.

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Additional information
Wendy A. Lavezzi, M.D.
Albany Medical Center
Department of Pathology and Laboratory Medicine
Mail Code 81
47 New Scotland Avenue
Albany, NY 12208