

## Current topic

# Pulmonary vascular air embolism in the newborn

S K LEE AND A K TANSWELL

*The Lawson Research Institute, St Joseph's Health Centre and the Department of Paediatrics, University of Western Ontario, London, Canada*

Pulmonary vascular air embolism is a rare, and almost invariably fatal, complication of positive pressure ventilation of newborn infants. There have only been 50 cases described in the world literature to date.<sup>1-16</sup> The rarity of the condition and the clustering of some cases, which may be related to specific local factors, do not allow a meaningful calculation of incidence.

### Characteristics of reported cases

Adequate numbers of cases have been reported to develop a profile of those infants susceptible to pulmonary vascular air embolism. The reported characteristics of these infants, and three additional unreported cases of our own, are summarised in table 1. Affected infants are usually premature with a mean gestational age of 30 weeks, and a mean

birth weight of 1328 g. The average postnatal age at onset was the third day of life. This, with a male:female ratio of 2.1 (33:16) in those cases where sex was documented, reflects the 91% incidence of the respiratory distress syndrome of the newborn in this population. The remaining 9% of cases were term infants with various diagnoses including meconium aspiration, viral pneumonia, amniotic fluid aspiration, and congenital alveolar dysplasia.

As would be expected all infants had severe pulmonary insufficiency, as evidenced by average peak inspiratory/expiratory ventilator pressures (PIP/PEP) of 41/7 cm H<sub>2</sub>O with a peak fractional inspiratory oxygen of 0.9. Among all the cases reported there is no correlation between PIP/PEP and gestational age, or with time of occurrence. The time of occurrence of pulmonary vascular air embolism does, however, correlate with gestational age ( $n=41$ ; linear regression equation:  $y=9.6x-228.98$ ;  $r=0.464$ ;  $p<0.01$ ) for the total populations in which this was reported. The most significant correlations were observed when only data for premature infants of <37 weeks' gestation ( $n=37$ ;  $r=0.593$ ;  $p<0.001$ ), or <2500 g birth weight ( $n=45$ ;  $r=0.552$ ;  $p<0.001$ ) were included in the regression analyses. The four reported infants with birth weights of >2449 g had a mean (SD) time of occurrence of 113 (92) hours, while the four reported infants with a gestational age of >36 weeks' gestation had a mean time of occurrence of 69 (38) hours.

### Clinical signs

Diagnosis is usually made from a radiograph ordered for suspected air leak, but there are associated phenomena reported for these infants (table 2) which may suggest the diagnosis. There was an overall incidence of air leak syndromes, other than pulmonary vascular air embolism, of 94%. The presenting signs of pulmonary vascular air embolism were usually sudden and dramatic. The

Table 1 *Characteristics of the population of infants reported to have developed pulmonary vascular air embolism. (No=the number of reported cases for which each characteristic was documented)*

	No of cases	Mean (SD)	Range
Gestational age (weeks)	47	29.7 (4.2)	24-40
Birth weight (g)	53	1328 (590)	670-3110
Age at occurrence (hours)	47	63 (91)	3-456
Fractional inspiratory oxygen	27	0.9 (0.1)	0.5-1.0
Peak inspiratory ventilator pressure (cm H <sub>2</sub> O)	45	40 (17)	20-90
Peak expiratory ventilator pressure (cm H <sub>2</sub> O)	38	7 (6)	0-40

Unreported cases (SK Lee and AK Tanswell): case 1, boy of 25 weeks' gestation weighing 850 g; peak inspiratory/peak expiratory ventilator pressure (PIP/PEP) was 36/5 cm H<sub>2</sub>O; he had pulmonary interstitial emphysema and arrhythmia. Case 2, girl of 27 weeks' gestation weighing 880 g; PIP/PEP was 34/4 cm H<sub>2</sub>O; she had pulmonary interstitial emphysema, pneumothorax, and arrhythmia. Case 3, boy of 24 weeks' gestation weighing 640 g; PIP/PEP was 18/4 cm H<sub>2</sub>O; he had pulmonary interstitial emphysema and arrhythmia.

Table 2 Associated phenomena in infants who develop pulmonary vascular air embolism. The % values shown are the totals derived from the collected literature in which clinical events were reported

Phenomenon	%
Air leak syndrome	94
Interstitial emphysema	63
Pneumothorax	36
Pneumomediastinum	24
Pneumopericardium	14
Arrhythmia/abnormal electrocardiogram	49
Catheter air	40
Circulatory collapse	35
Cutaneous signs	11

most common signs included sudden collapse with either pallor or cyanosis, hypotension, bizarre electrocardiogram irregularities varying from tachycardia to bradycardia, with the latter being more common. A millwheel murmur was heard in several cases and the heart sounds were also noted to be distant and diminished. Blanching and migrating areas of cutaneous pallor were noted in several cases and, in one of our own cases we noted bright pink vessels against a generally cyanosed cutaneous background. This we attributed to direct oxygenation of erythrocytes adjacent to free air in the vascular system, while the tissues continued to be poorly perfused and oxygenated. The most distinctive sign of pulmonary vascular air embolism, observed in half of the reported cases, is the finding of free air when blood is withdrawn from the umbilical arterial catheter. Columns of air, or a frothy mixture of blood and air, were often obtained. Another related phenomenon, observed in two reported patients<sup>16</sup> and in one of our infants, was an inappropriate high arterial oxygen concentration recorded from intra-aortic oxygen electrodes in direct contact with gas bubbles. This was also observed using a transcutaneous oxygen monitor in one case.<sup>16</sup> A radiograph is diagnostic, and free air may be seen in both the arterial and venous systems, as well as in the heart (figure). In 75% of reported cases the radiographs were taken antemortem. Postmortem radiographs need to be interpreted with caution as intravascular air may appear as early as 25 minutes after death.<sup>3</sup>

The typical case of pulmonary vascular air embolism will be of very low birth weight and have respiratory distress syndrome, requiring very high ventilation pressures, with an existing air leak. The embolism will usually occur in the first week of life and, in most cases, there will be unusual phenomena which should alert the physician to the possibility of

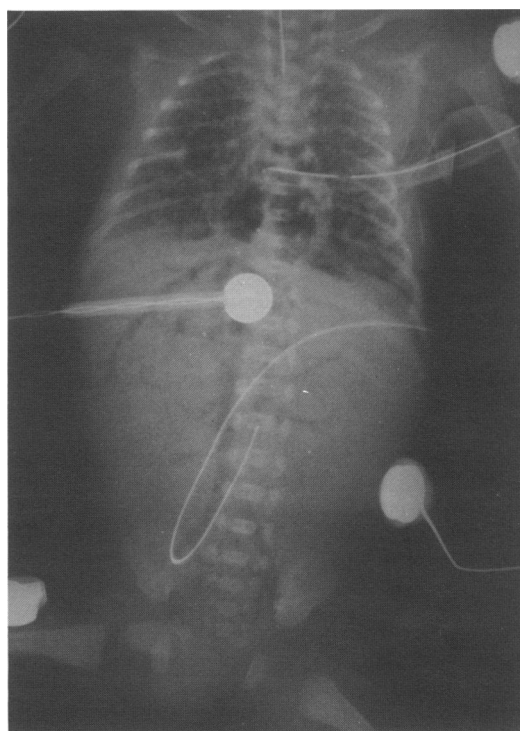


Figure Anteroposterior chest and abdominal radiograph of a case of pulmonary vascular air embolism, showing pulmonary interstitial emphysema with a left thoracotomy tube, intracardiac air, and air in the major vessels of the neck, chest, and abdomen.

this rare occurrence. A bizarre pattern on electrocardiography, the presence of catheter air, a millwheel murmur, migrating pallor in small vessels, and acute massive fluctuations of continuously monitored oxygen tension are all suggestive, and justify immediate aspiration through an umbilical arterial catheter if present.

### Mortality

Only four of the 53 infants in this review survived the immediate event. One infant died from a recurrence 16 days after the first episode,<sup>9</sup> while another died from pneumonia 13 days after surviving pulmonary vascular air embolism.<sup>15</sup> Of the two long term survivors, the case described by Kogutt<sup>6</sup> had asymptomatic pulmonary vascular air embolism shown by a routine radiograph. The other is one of our own cases who, despite a myocardial infarction as a result of the pulmonary vascular air embolism,

survived until 7 months of age when he died from respiratory failure due to viral pneumonia superimposed on chronic bronchopulmonary dysplasia.

### Pathogenesis

Gregory and Tooley postulated that air embolism occurred as a consequence of air being injected into pulmonary veins by mechanical ventilation.<sup>1</sup> A potential portal of entry into the pulmonary interstitium had been previously shown by Macklin and Macklin using gelatin varmine particle techniques to show microscopic alveolar rupture in pulmonary interstitial emphysema.<sup>17</sup> Further extension of free air into the capillary bed was shown by Lenaghan *et al* with the demonstration of air embolism in mechanically ventilated dogs with pulmonary interstitial emphysema.<sup>18</sup> He observed fistularisation distal to the terminal bronchiole which occurred at lower pressures in shocked lungs, and was not ameliorated by the use of prophylactic chest tubes. Bowen *et al* were finally able to demonstrate a direct communication between the airway, the interstitium, and small vascular channels with barium studies at autopsy of a human infant who died from pulmonary vascular air embolism. There are a number of reasons why gas is found in both the arterial and venous systems, including retrograde flow into the right heart through an incompetent pulmonary valve,<sup>18</sup> and passive retrograde flow of gas bubbles because of their buoyancy.<sup>8</sup>

While there seems to be a relationship between pressure applied and the type of air leak observed in dogs, with successively higher pressures required for pneumothorax/pneumomediastinum, pneumoperitoneum, and air embolism,<sup>19</sup> we were unable to identify any specific threshold levels for pulmonary vascular air embolism from the analysis of the data provided by the reports in the literature. Air leak syndromes, however, did precede pulmonary vascular air embolism in 94% of the reported cases, and its development would therefore seem to require a greater pressure than the other air leak syndromes. The observed correlation of the timing of pulmonary vascular air embolism with gestational age or birth weight, but no relationship with inflation pressure, suggests that barotrauma is inflicted earlier in the more immature lung, and that the development of pulmonary vascular air embolism is determined as much by the physical characteristics of the lung being inflated as by the characteristics of the inflation. The mature infants with pulmonary vascular air embolism had a time of onset somewhat earlier than would be predicted from the regression line developed for premature infants. It is possible that these infants had an inherent predisposition to

air leak due to abnormal tissue elastance, though this is only speculation in the absence of appropriate histological evaluation.

Trauma to the lung may have a more significant part to play in the development of pulmonary vascular air embolism than has been generally appreciated. In two of our three cases there was evidence of trauma related to the introduction of chest tubes. Lung perforation occurs in 25–30% of infants with respiratory distress syndrome who have chest tubes inserted for drainage of pneumothoraces.<sup>20</sup> Laceration of lung tissue is reported to favour reversal of the intra-bronchial pressure—pulmonary venous pressure gradient thereby increasing the risk of pulmonary vascular air embolism.<sup>21</sup>

Cardiac arrhythmia is a common presenting sign of pulmonary vascular air embolism, which may be due both to the effects of air embolism on the heart and on the brain. Studies in cats suggest that arrhythmias produced by cerebral air embolism can be abolished by sympathectomy.<sup>22</sup>

The prognosis for pulmonary vascular air embolism remains poor, and the neurologic outcome for survivors is unclear. Injection of air into the carotid artery of adult gerbils rapidly results in multifocal brain lesions.<sup>23</sup> Studies in dogs suggest that outcome may be better if the embolised gas is oxygen rather than air,<sup>24</sup> as might be expected from its better solubility. Many of the human infants that develop this complication of ventilatory treatment will already be receiving 100% oxygen, but when this is not the case a change to 100% oxygen might have some protective effect.

### Prevention and treatment

Our analysis does not allow us to establish clear guidelines for prevention. Avoidance of high airway pressures would be advantageous, though these are rarely applied if there is an alternative. High frequency ventilation may eventually offer such an alternative, while the use of surfactant applied down the airways may reduce the need for extremely high ventilation pressures. In those infants who have pneumothorax it may be possible to reduce the incidence of pulmonary vascular air embolism by using soft rubber catheters, instead of stiff plastic chest tubes, for drainage as these may be less traumatic to the surface of the lung.

Where pulmonary vascular air embolism has occurred, early withdrawal of air from the umbilical artery catheter may be of benefit, especially if the air leak is small and self sealing, or the air has been introduced through an intravascular line. In this situation it may be worthwhile attempting to minimise neurological damage by using 100% oxygen

and placing the infant in the Trendelenberg and left posterior-anterior position.<sup>4</sup>

The incidence of pulmonary vascular air embolism is likely to increase with the improved survival of very low birthweight infants, and the incidence may already be higher than we appreciate, because of a lack of recognition of the acute event, and the rapid loss of signs after death.<sup>11</sup> The prognosis for the condition remains poor, but may improve with greater recognition allowing earlier aggressive management.

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Correspondence to Dr A K Tanswell, The Lawson Research Institute, St Joseph's Health Centre, 268 Grosvenor Street, London, Ontario, Canada N6A 4V2.