Meconium Aspiration

6

Catherine M. Owens

CONTENTS

6.1 Introduction

Aristotle originally coined the term 'meconium'. He used the Greek word meconium-arion to mean 'opium like' (Wiswell and Bent 1993), as he believed that meconium precipitated fetal sleep. It is probable that he recognised the association between the presence of the meconium in the amniotic fluid and subsequent fetal death or neonatal depression. Depending on the population studied, the frequency of meconium-stained amniotic fluid (MSAF) at delivery varies between approximately 8% and 19% of all term deliveries (Gregory et al. 1974; Wiswell et al. 1990; Suresh and Sarkar 1994; Falciglia et al. 1992; Nathan et al. 1994; Yoder 1994; Peng et al. 1996). Other factors, such as maternal ethnicity, result in a higher prevalence of meconium aspiration syndrome (MAS): the prevalence of MSAF in black is 1.5-fold that in white women (Alexander et al. 1994), and the likelihood of MSAF increases with advancing gestational age in all ethnic groups.

Regardless of the aetiology of meconium passage, its presence is causally associated with adverse fetal and neonatal outcomes, including death, acute respiratory complications and long-term pulmonary and neurological abnormalities. Depending upon the population studied and the criteria used for making the diagnosis of MAS, approximately 2–33% of infants born through MSAF will develop MAS. Approximately a third of infants with MAS will then require mechanical ventilation (Wiswell et al. 1990; Fleischer et al. 1992). The complication of persistent pulmonary hypertension of the newborn (PPHN) exists in approximately one third of these infants (Fleischer et al. 1992). Sadly, the mortality associated with MAS is high, ranging from 4% to 19% (Wiswell et al. 1990; Coltart et al. 1989), and in a large majority of these patients mortality is due to complicating PPHN.

Subsequent neurological complications, such as early-onset neonatal seizures due to hypoxia, have also been reported in these infants born with thick MSAF (Lien et al. 1995). Indeed, the increased likelihood of hypotonia in infants born through moderate to thick, as opposed to thin, amniotic fluid, whether meconium-stained or clear, is quite different. An article by Berkus et al. (1994) showed a seven-fold risk of neonatal seizures, and a five-fold risk of floppy (hypotonic) infants born through moderate to thick, compared with thin, MSAF. Also of relevance is the presence of the long-term pulmonary sequelae of MAS.

C. M. Owens, MD
Radiology Department, Great Ormond Street Hospital for Sick Children NHS Trust, London, WC1N 3JH, UK

A study by Yuksal et al. (1993) showed abnormal obstructive pulmonary function tests, with increased functional residual capacity (FRC) and airway hyper-reactivity in infants at 6 months of age with a history of MAS. Those infants who required greater respiratory support in the neonatal period were significantly more symptomatic and required bronchodilator therapy more frequently. Late childhood sequelae include persistent airway hyper-reactivity and abnormal pulmonary function data later in childhood (MacFarlane and Heaf 1988; Swaminathan et al. 1989).

6.2 Pathophysiology of Meconium Passage

Meconium is a green, viscous substance composed mainly of water (between 70% and 80%). Other components include mucus, gastrointestinal secretions, bile acids, bile, pancreatic juice, serous debris and swallowed amniotic fluid, lanugo, vernix caseosa and blood (Wiswell and Bent 1993; Holtzman et al. 1989). The presence of meconium in the fetal gastrointestinal tract can be seen as early as at 10–16 weeks of gestation, and indeed at birth between 60 g and 200 g of meconium can be present in the intestinal tract of the term infant. It is uncommon for the fetus to pass meconium in utero, as there is no strong peristalsis, and this combined with the presence of a tonically contracted anal sphincter and the relative seal of a terminal cap of thick meconium, further decreases the likelihood of meconium passage. The passage of meconium is probably a physiological maturational event in many term and post-term infants, with meconium passage being rare before 37 weeks of gestation (Matthews and Warshaw 1979), but it may occur in over a third of cases of postmature pregnancy lasting longer than 42 weeks (Usher et al. 1988; Miller and Read 1981). This may relate to higher levels of the hormone motilin, which is known to be responsible for GI motility in adults (and shown to be higher in term and post-term than preterm infants) (Lucas et al. 1980). This further supports the hypothesis that maturation of the GI tract has a large role in the passage of meconium.

Also of great importance is the observation that the passage of meconium in utero is associated with ante- or intrapartum fetal acidaemia (Nathan et al. 1994; Miller and Read 1981). A study by Alexander et al. (1994) shows that in the presence of fetal distress the odds of MSAF are twice as common as in its absence. The hypothesis that fetal hypoxia causes an increase in intestinal peristalsis, with anal sphincter relaxation resulting in meconium passage, is widely accepted. As a result of distress, fetal gasping results in meconium aspiration.

It is also thought that oligohydramnios may result in compression of the fetal head and the fetal umbilical cord, which may precipitate a vagal response and meconium passage.

6.3 Pathophysiology of Meconium Aspiration Syndrome

The definition of MAS is: respiratory distress in an infant born through MSAF where symptoms cannot be otherwise explained (Cleary et al. 1992)

Many neonatal clinicians find the wide variety of chest X-ray findings amongst infants with MAS diverse enough to make specific radiographic features unnecessary as part of their diagnostic pathway, reflecting the extraordinarily complex pathophysiology of MAS. A prospective reason linking the passage of meconium and respiratory symptoms can either be secondary to aspiration of meconium in utero or at birth, or follow alterations in the pulmonary vascular system which occur as a result of asphyxia, or indeed the presence of meconium itself (Fig. 6.1) (Fuloria and Wiswell 1999). It is believed by various investigators that the presence of thick, as against moderately viscous or thin, meconium increases the likelihood of MAS (Suresh and Sarkar 1994; Ting and Brady 1975; Narang et al. 1993). A paper by Wiswell and Bent (1993) describes a large, multicentre trial, which demonstrated a direct relationship between meconium thickness and degree of severity of subsequent respiratory disease within the neonate. It appears that the degree of symptomatology is directly related to the viscosity of meconium, and large amounts of thick meconium can potentially completely obstruct large airways. However, it is more common for the substance to migrate distally to the peripheral airways, where it causes either complete or partial obstructions (see Fig. 6.2). Complete obstruction leads to atelectasis and ventilation–perfusion (V/Q) mismatch. Par-

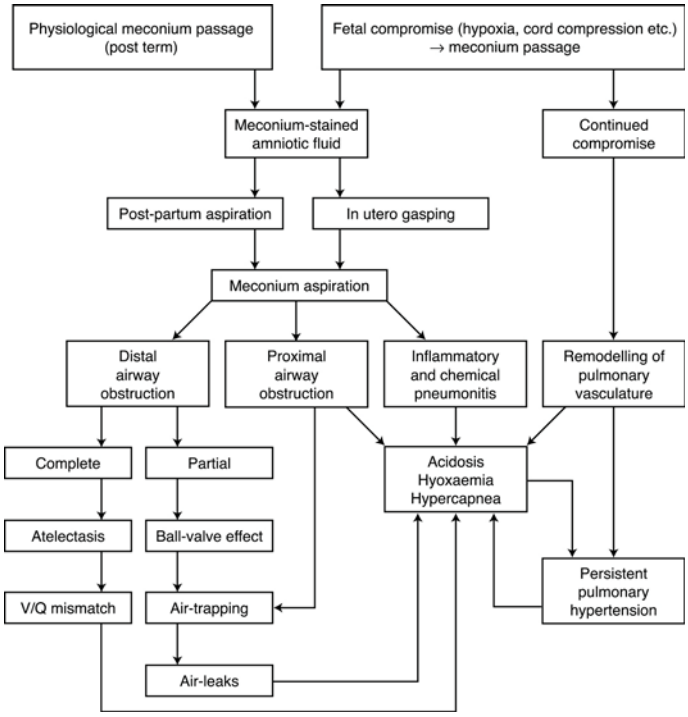


Fig. 6.1. Diagram to show the pathophysiological effects of meconium passage and meconium aspiration

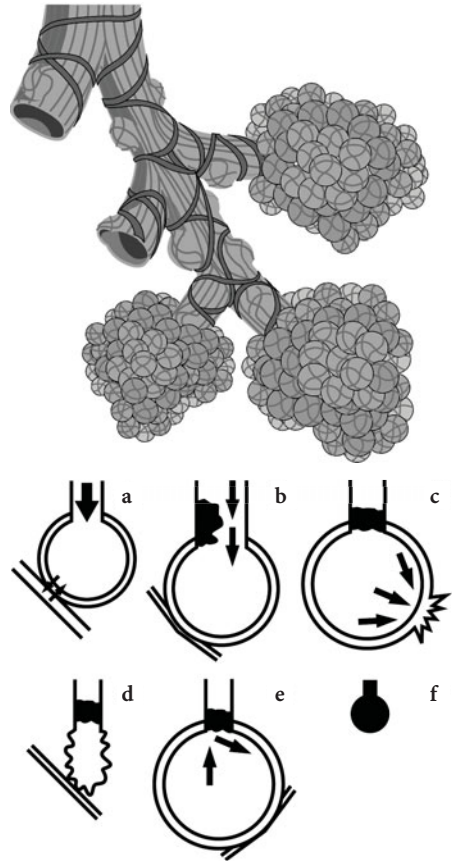


Fig. 6.2a–f. Diagrammatic representation of the dynamic effects of meconium aspiration on lung function. **a** Normal alveolar function with normal gaseous exchange across the alveolar membrane. **b** Complete obstruction of the alveolar unit with subsequent atelectasis and consequent intrapulmonary shunting. **c**, **d**. The 'ball-valve effect' with either (**c**) partial or (**d**) complete occlusion of the airway, and hence impossibility of air escape from the alveolar unit. **e** Overdistension and rupture of the alveolar unit with consequent air leak. **f** Atelectasis as a result of inadequate surfactant coating of the lungs due to meconium plugging

tial obstruction results in a "ball-valve" effect: gas flows into the airways on inspiration, but due to the smaller diameter on exhalation gas becomes trapped distally, and these obstructive properties result in the chest X-ray and histological findings classically seen in MAS, i.e., areas of atelectasis and consolidation adjacent to a distended hyper-expanded region (Stocker 1992; Tyler et al. 1978; Wiswell et al. 1992).

After several hours, the intense, inflammatory response to the presence of the toxic antigen (meconium) results in margination of polymorphonuclear leucocytes diffusely throughout the lungs (Stocker 1992; Tyler et al. 1978; Wiswell et al. 1992). The presence of these cells releases chemical mediators which adversely affect the tissues, and more specifically the presence of bile salts contained within meconium causes specific cytotoxicity in type II pneumocytes. This further contributes to the picture of the "chemical" pneumonitis (Oelberg et al. 1990). All of the aforementioned mechanisms lead to hypoxia, acidosis and hypercapnoea. These factors then in turn produce pulmonary vasoconstriction, resulting in persistent pulmonary hypertension of the newborn (PPHN). Approximately two thirds of cases of PPHN are associated with MAS (Abu-Osa 1991).

Many infants respond to fetal hypoxia by remodelling pulmonary vasculature, resulting in thick muscularisation of the pulmonary vessels which aberrantly extends more distally than is appropriate along the intra-acinal vessels (Goetzman 1992;

Murphy et al. 1984). Although there is some dispute regarding PPHN concomitant with MAS, the vicious cycle of shunting, hypoxaemia and acidosis may lead to further pulmonary hypertension, which may be either difficult or impossible to treat successfully.

Correlation of radiological appearances with outcome was studied by Yeh et al. (1979), who noted that the presence of consolidation or atelectasis on the chest radiograph appeared to be more predictive of poor clinical outcome. However, Valencia and his colleagues (Stocker 1992) were unable to predict the severity of the illness in infants with meconium aspiration accurately from the admission chest radiograph alone.

Using rabbit models of MAS, Tyler et al. (1978) showed an early onset of airway obstruction (as defined by alveolar collapse) correlated with ventilation–perfusion mismatch and an increase in functional residual capacity (FRC). In a similar model it has also been shown that chemical dysfunction in lungs is most prevalent during the early phase of MAS, with diminished dynamic and specific lung compliance, but unchanged static lung compliance suggestive of partial random obstruction of large airways (Tran et al. 1980; Wiswell et al. 1998). Unfortunately this study is of limited duration, only considering the effects of meconium on the neonate within the first 2 hours of life; any effects occurring more than 2 hours after meconium aspiration were not, then, evaluated. Similar findings were observed by Yeh et al. (1982; Oelberg et al. 1990), who evaluated pulmonary function tests in the first 3 days of life in neonates with mild MAS which did not result in the need for mechanical ventilation. It was demonstrated that dynamic and specific lung compliance were lower and airway resistance higher in these infants than in controls. It is important to note that poor correlation between the chest radiograph and clinical status may ensue, and children with substantial chest X-ray abnormalities and only minimal respiratory symptoms are observed as well as mild radiographic changes in severely ill neonates, a picture that is noted particularly in association with PPHN (Cleary et al. 1992).

6.4 Inflammation

The presence of meconium in the airways induces an inflammatory response (see Fig. 6.3). A retrospective review of autopsied cases with histological evidence of meconium exposure showed that 60% of all cases with pulmonary inflammation were noted to be secondary to meconium aspiration.

Within an hour of exposure to meconium there is a profound pulmonary inflammatory response. Abundant neutrophils and macrophages are found in the alveoli, large airways and lung parenchyma.

Using rabbit models, in the latter stages of MAS there is characteristic microvascular endothelial damage with development of intrapulmonary shunts, alveolar collapse and cellular necrosis consistent with chemical pneumonitis (Tyler et al. 1978).

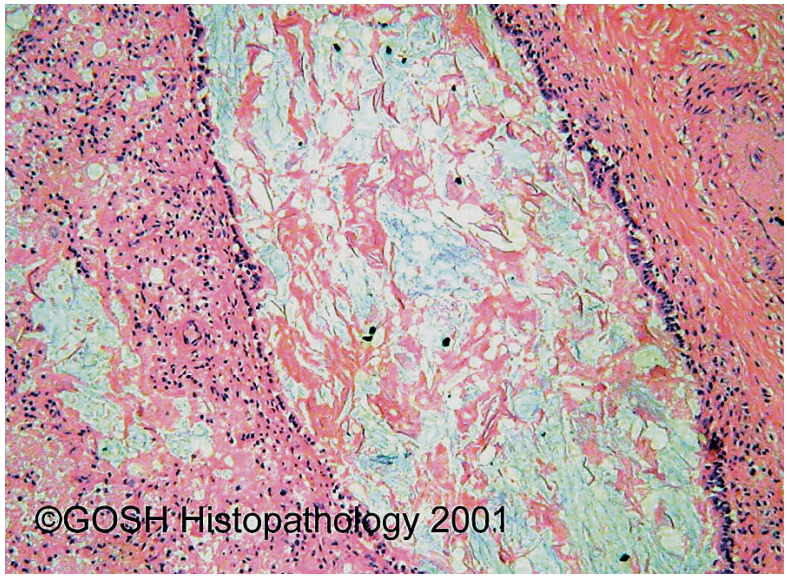


Fig. 6.3. Lung specimen from post mortem of child who died with meconium aspiration syndrome (MAS), demonstrating plugging of the airway with keratin and proteinaceous debris. (Haematoxylin-eosin)

Meconium has also been shown in vitro to inhibit the action of pulmonary surfactant function (Moses et al. 1991; Clark et al. 1987; Sun et al. 1993). In isolated rat alveolar cells, at low concentrations of meconium Higgins et al. (1996) demonstrated absence of toxicity to type II pneumocytes. However at higher concentrations of meconium (greater than 1%) he demonstrated dose-dependent cytotoxicity that was inhibited in the presence of heat-treated meconium, suggesting that a protein moiety may be partly responsible for this action (Sun et al. 1993). A cytotoxic effect of meconium has also been inferred by other investigators, who have demonstrated decreased production of surfactant protein B (SP-B) in the presence of high concentrations of meconium (Antunes et al. 1997).

As many as a third of infants with MAS develop PPHN (Fleischer et al. 1992), and approximately two thirds of infants with PPHN had associated meconium aspiration. The development of PPHN maybe a result of acidosis, hypoxia, or hypercapnoea associated with aspiration of meconium, or due to acute or chronic hypoxia in utero. The neonatal pulmonary vasculature is known to exhibit a greater vasoconstrictive response than do adult pulmonary arteries (Akopov et al. 1998). Additionally, the vessels possess a unique capability to undergo rapid changes in architecture, particularly thickening of the media and adventitia, distal extension of smooth muscle (Murphy et al. 1981) and increased tortuosity and muscularisation of the alveolar septal arterioles (Thureen et al. 1997).

6.5 Signs and Symptoms

Clinically, the infant with meconium aspiration syndrome can be quite depressed at birth, demonstrating pallor, cyanosis, apnoea, grunting and intercostal muscle retraction. As a consequence of air trapping and alveolar over-distension the chest can adopt a barrel configuration, and clinically rales and rhonchi are auscultated on physical examination.

Depending on the severity of meconium aspiration, both respiratory and metabolic acidosis may develop due to hypoxaemia and hypercarbia. The hypoxaemia and hypercarbia are secondary to ventilation–perfusion (V/Q) mismatch. Acidosis from any origin increases the risk of or potentiates PPHN.

Aspiration of meconium produces a chest radiographic picture characterised by (Tsu et al. 1979):
- Diffuse patchy nodular infiltrates, focal or general, asymmetric or symmetric
- Hyperinflation
- Air leaks
- Pleural effusion
- Cardiomegaly

Infiltrates. Complete airway occlusion results in atelectasis. This can be bilateral, diffuse, patchy or more nodular.

The lining of the alveolar sacs are more susceptible to injury and predispose to cellular necrosis which causes fluid accumulation in the airway, resulting in alveolar oedema. Cellular damage to capillary walls also results in inflammation leading to pulmonary oedema and pleural effusion secondary to leakage from capillary vascular beds (see Fig. 6.4)

Hyperinflation and Air Leaks. Partial occlusion of the airway and air sacs by meconium debris causes air trapping. (Fig. 6.5) Partial occlusion results in hyperinflation of the lungs shown by hypertransradiency of the lungs with depression of the hemidiaphragm. Overdistension of airway and terminal saccules may lead to alveolar rupture with free air dissecting into the interstitial lymphatics (Fig. 6.6a), pleural spaces (Fig. 6.6b, c) and mediastinum (Fig. 6.6d).

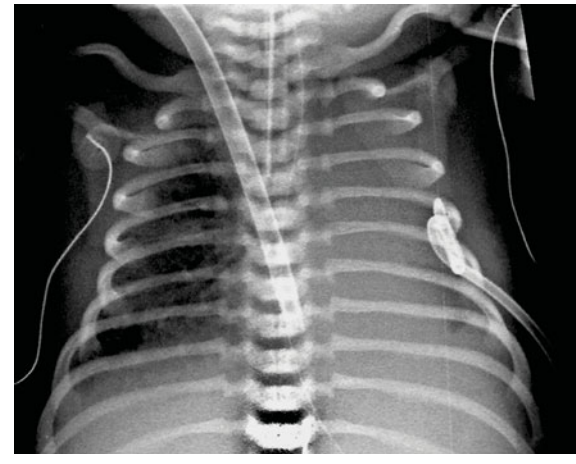


Fig. 6.4. Frontal radiograph of a child on veno-venous (VV) extracorporeal membrane oxygenation (ECMO) with coarse consolidation throughout the lungs and some overaeration of the anterior segment of the right lower lobe. There is a left basal intercostal drain draining a left pleural effusion, and a small right lamellar pleural effusion is also present

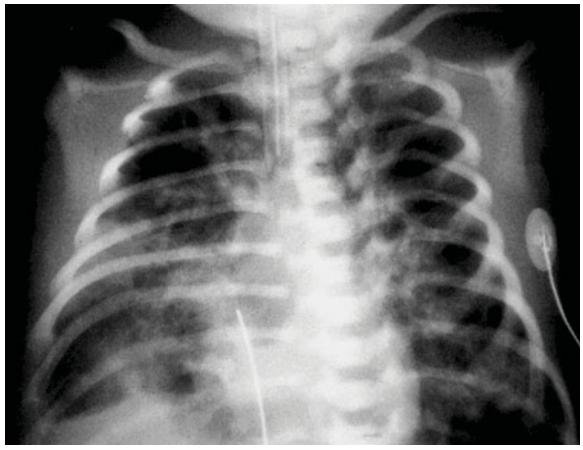
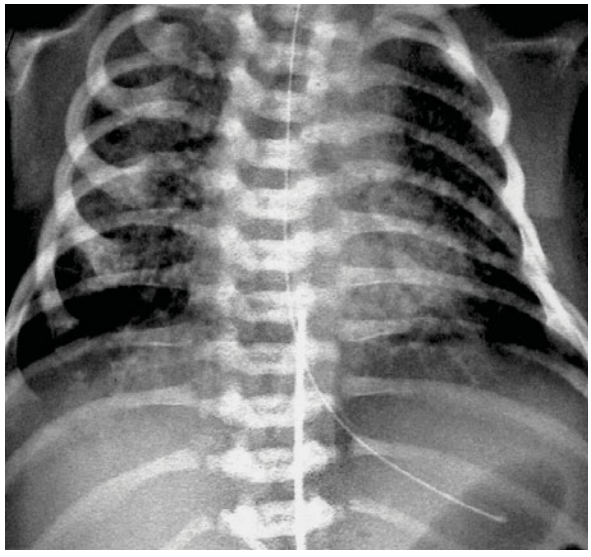
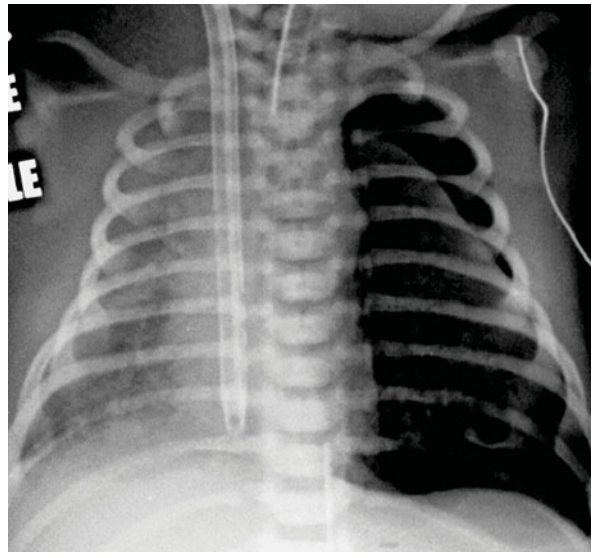


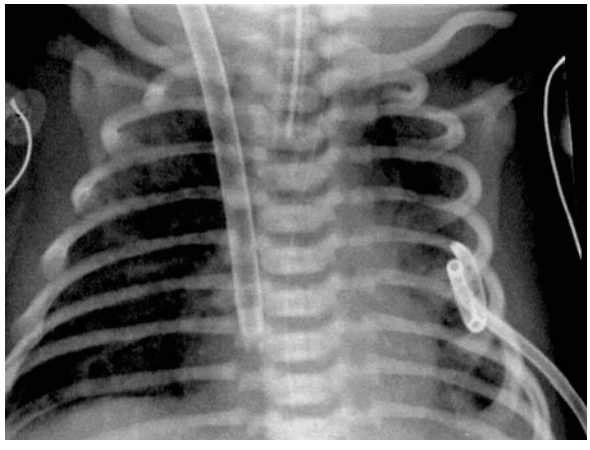
Fig. 6.5. Frontal chest radiograph showing areas of air trapping alternating with areas of atelectasis – classic features of neonatal MAS



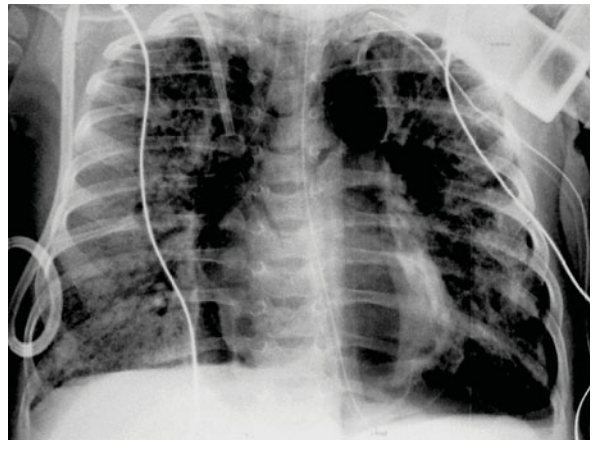
a



b



c



d

Fig. 6.6. a Frontal chest X-ray of child with MAS and early left upper lobe pulmonary interstitial emphysema (PIE). **b** Frontal radiograph of a child receiving VV ECMO with left-sided PIE and a large left pneumothorax causing mediastinal shift to the right. **c** Following suction on the intercostal drain the left pneumothorax has been almost completely drained, leaving a tiny anterior pneumothorax. **d** Child with MAS treated with conventional ventilation, showing extensive barotrauma-related complications with a large loculated pneumomediastinum and a left basal pneumothorax

Pleural Effusions. These are the result of inflammatory processes causing cellular necrosis and atelectasis which prevent the airway and air sacs from clearing pulmonary fluid effectively (Fig. 6.4).

Cardiomegaly. Cardiomegaly may occur as a result of direct intrauterine asphyxia associated with meconium aspiration and PPHN or the delayed effects of persistent pulmonary hypertension of the newborn.

In an interesting radiological study, Tsu et al. (1979) recorded the radiographic features present in the radiographs of 80 children with clinical and X-ray features of aspiration syndrome. The radiographic features present in the chest radiographs were divided into five separate categories, including consolidation or atelectasis, infiltration, hyperinflation, air leak and cardiomegaly. The incidence of respiratory failure was assessed in each category. The study showed that infants with consolidation or atelectasis had a higher incidence of respiratory failure and an increased mortality compared with those who did not have findings of consolidation or atelectasis (P 0.001) . Similarly, infants who had air leaks had a higher incidence of respiratory failure than those who did not show air leaks. The presence of air leak in infants with consolidation or atelectasis did not seem to be a significant contributing factor in causing either respiratory failure (10/17) or death (5/17), when their findings were compared with those of infants with consolidation or atelectasis but without air leak (13/27 and 18/27, respectively). Interestingly, infants who had consolidation or atelectasis as the sole radiographic feature also had a significantly higher (P<0.05) incidence of respiratory failure and death than those infants who had no consolidation. The authors suggest that consolidation or atelectasis appears to be the most significant determinant of respiratory failure and mortality.

This study leads to the conclusion that aspiration of meconium may produce two different radiographic patterns with different prognostic implications, i.e., one with consolidation or atelectasis, which has a poorer prognosis, and one without consolidation or atelectasis, which has a good outcome (due to aspiration of thin meconium or amniotic fluid). It appears that the initial chest X-ray with consolidation or atelectasis may be produced by aspiration of thick or sticky meconium in these infants and more severe clinical course and poorer outcome can be expected. On the other hand radiographic features of infiltration may be produced by aspiration of thin dilute meconium leading to a more benign course (similar to that of wet lung syndrome/TTN or amniotic fluid aspiration).

The authors also state that prevention is better than cure, i.e. reducing the potential of developing consolidation or atelectasis by deep oropharyngeal suctioning before delivery of the shoulder or prompt endotracheal suction of thick meconium is mandatory in cases of MASF.

6.6 Management of the Infant with Meconium Aspiration Syndrome

6.6.1 Conventional Mechanical Ventilation

One third of infants with MAS will require mechanical ventilation (Wiswell et al. 1990). The best method of ventilation management is controversial. Air leaks are a common complication of MAS (Fig 6.6a–d), especially amongst infants requiring positive pressure ventilation, and it has been shown by investigators (Yeh et al. 1982) that air trapping and increased functional residual capacity (FRC) may be exacerbated in patients on positive end expiratory pressure (PEEP) or CPAP (continuous positive airway ventilation), which are paradoxically believed to improve oxygenation in babies with MAS. The best strategy for ventilator settings once a child requires intermittent mandatory ventilation is controversial. There are advocates of using low inspiratory pressures and short inspiratory times with rapid ventilator rates to maintain arterial blood gases within normal limits, but there are no published data to substantiate their opinion that this arrangement is superior to the more commonly used ventilator settings. Additionally, one of the commoner treatments of infants with PPHN is hyperventilation (Fox and Duara 1983), with a principal goal of achieving respiratory alkalosis in an attempt to achieve vasodilatation within the pulmonary vascular bed. As two thirds of neonates with PPHN have associated MAC, hyperventilation is a common approach to the management of MAS. To date, however, there have been no prospective randomised trials comparing various mechanical ventilation strategies in the management of MAS.

6.6.2 High-frequency Ventilation

High-frequency ventilation (HFV) is a global description with several techniques, which provide effective gaseous exchange at low tidal volumes. Potential benefits of HFV may include less barotrauma, increased mobilisation of airway secretions, better attainment of respiratory alkalosis and fewer adverse histopathological changes.

6.6.3 Surfactant Therapy

Pulmonary immaturity due to surfactant deficiency is widely accepted as a primary cause of respiratory distress syndrome (RDS) in premature neonates. By contrast, however, the term infant who is more likely to suffer from MAS has a mature respiratory system with a normal alveolar surfactant pool. The surfactant deficiency seen in MAS is not the result of an insufficient quantity of surfactant, but is probably caused by inhibited surfactant function or alterations in surfactant composition. There is, however, limited information on the specific adverse effects of meconium on surfactant. In high concentrations, meconium has a direct cytotoxic effect on type II pneumocytes.

To date there has only be one randomised control trial specifically assessing the use of exogenous surfactant therapy for MAS (Findlay et al. 1996). In this study 20 affected infants were treated with 1.5+ standard dose of bovine lung surfactant administered as an infusion over 20 minutes. Significant improvements in oxygenation occurred 6–12 hours later, typically following additional surfactant doses. Six (30%) of the infants still required oxygen therapy at discharge. The authors therefore suggested further clinical trials before the widespread use of this therapy for MAS. Cleary and Wiswell (1998) conclude that surfactant therapy for MAS in humans still needs rigorous investigation.

6.6.4 Inhaled Nitric Oxide

Substantial effort has been invested in the assessment of the use of inhaled nitric oxide (INO) as a pulmonary vascular relaxing agent in the treatment of pulmonary artery hypertension.

In neonatal piglet models of MAS, Holopainen et al. (1999) found that prophylactic INO resulted in better oxygenation but did not affect the development of pulmonary hypertension. Further studies comparing the use of INO with conventional ventilation in patients diagnosed with MAS showed that INO led to better oxygenation and a lesser need for extracorporeal membrane oxygenation (ECMO) than was observed in control infants. There was no difference between the two groups in mortality, duration of mechanical ventilation or length of hospitalisation, however (The Neonatal Inhaled Nitric Oxide Study Group 1997). Roberts et al. (1997). It seems that although INO leads to better oxygenation in infants with MAS, this is not followed by any significant difference in the primary outcome (death or the need for ECMO).

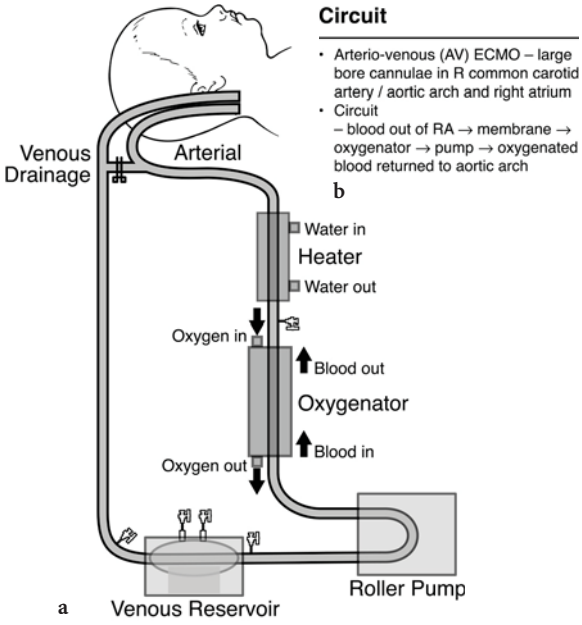
6.6.5 Extracorporeal Membrane Oxygenation

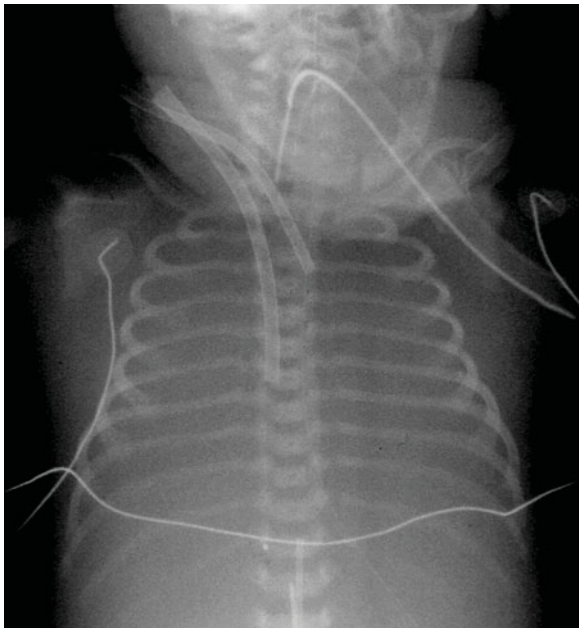
The use of ECMO in the treatment of MAS was first described by Bartlett et al. (1977), who used ECMO to treat eight moribund neonates with MAS. Three of the infants survived, as compared with 90% mortality in conventionally treated groups. The use of veno-arterial (VA) ECMO became increasingly popular throughout the United States during the 1980s, with consistently encouraging results in neonates with severe MAS (Lillehei et al. 1989). Criteria for the institution of ECMO support were also refined over this time, and an oxygenation index greater than 40 was suggested as the referral criterion. The oxygenation index is calculated as follows.

$$\text{Oxygenation index} = \text{Paw} + \text{FIO}_2/P_a\text{O}_2$$

where P_{aw} is the mean airway pressure, FIO_2 is the inspired oxygen fraction + 100 and P_aO_2 is the arterial oxygen tension in millimetres of mercury (mmHg). The recent publication of the UK Collaborative ECMO Trial Group (1996) has resulted in ECMO becoming a relatively well-accepted method of support for neonates with MAS in the UK. The results of the trial suggest that for every four infants receiving ECMO for MAS there was one extra survivor. Furthermore, although infants with MAS tend to be relatively less well than other term neonates with respiratory failure when treated conventionally, the converse is true when ECMO support is used. The survival figures for neonates with MAS who receive ECMO are

extremely encouraging, and UK ECMO centres currently quote survival figures of around 90% for neonates in whom the primary indication is pulmonary hypertension without associated severe lung injury.





c

Fig. 6.7. a Diagram and **b** summary of AV ECMO circuit **c** Chest X-ray of a child on AV ECMO. The (venous) catheter to the *right* lies in the right atrium and the more medially placed (arterial) catheter (midline) is within the right common carotid artery. An ET tube is noted, and a umbilical venous line is present with its tip at the level of the distal right atrium. The lungs are almost entirely collapsed

6.6.5.1 ECMO Technique

There are two methods of ECMO, both of which can be used to support neonates with MAS. Most ECMO centres initially used VA support, in which the right common carotid artery and internal jugular veins were cannulated, thus providing cardiac and respiratory support (Fig. 6.7a–c). More recently, however, veno-venous (VV) ECMO has emerged as the method of choice for neonates with hypoxic respiratory failure without significant haemodynamic instability (Delius et al. 1993) (Fig. 6.8).

In VV ECMO a double-lumen venous catheter is inserted into the right internal jugular vein with its tip in the right atrium. One lumen carries venous blood from the patient to the oxygenator, and the arterial lumen returns oxygenated blood to the heart (Andrews et al. 1983; Klein et al. 1985; Peek et al. 1996) - (Figs. 6.7, 6.9). Most patients with MAS now receive VV ECMO.

Potential advantages of VV ECMO over VA ECMO are the reduced risk of intracranial haemorrhage and the theoretical advantage of preserving the intact carotid circulation. Cannulation of the arteries, as well as predisposing to arterial intracranial bleeds during ECMO (Fig. 6.10), are believed to cause haemodynamic disruption of flow after decannulation, either as a result of ligation of the vessel or because of the presence of a substrate causing turbulence or aneurysm formation if the vessel is repaired (Desai et al. 1999; Jacobs et al. 1997).

6.6.5.2 Duration of ECMO Support

ECMO support is usually required for between 100 and 120 hours (Desai et al. 1999) in MAS, the shortest

Arterio-venous (A-V) ECMO	Veno-venous (V-V) ECMO
Venous catheter • RA • tip = radiodense dot beyond apparent end of catheter • SVC or IVC placement → venous obstruction	• blood diverted from and returned to RA • one double lumen large bore catheter in RA • circuit provides no additional cardiac support ie. used for 'respiratory' neonates with good cardiac function • may be converted to V-A ECMO
Arterial catheter • aortic arch / origin R common carotid artery • directed down descending aorta (up overloads heart) • 'coiled' structure • small radiolucent portion beyond apparent tip	

Fig. 6.8. Table detailing AV and VV ECMO techniques

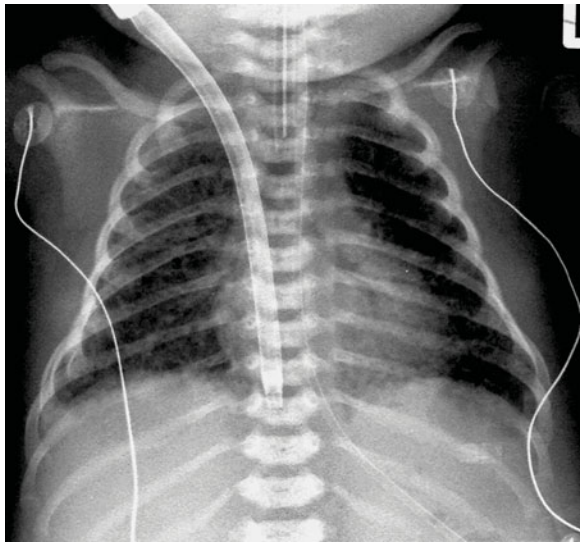


Fig. 6.9. Chest X-ray of a child with MAS treated with VV ECMO. The large VV ECMO catheter is noted with its tip in the right atrium. MAS has caused asymmetrical coarse reticulonodular change in the lungs

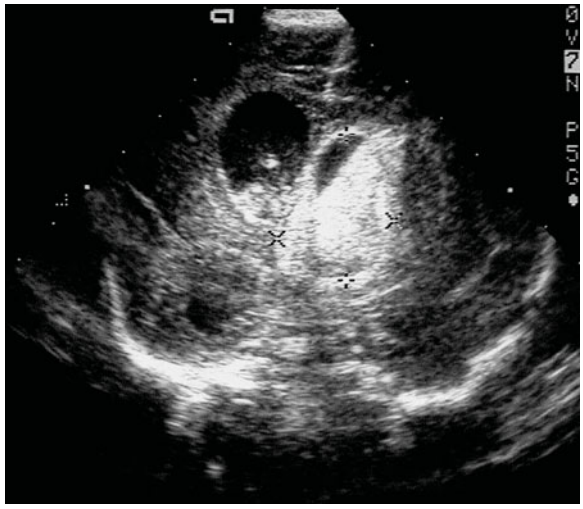


Fig. 6.10. Cranial ultrasound showing bilateral ventricular dilatation with large left intraventricular haemorrhage (IVH) in a child on ECMO

duration for any neonatal diagnosis (Fig. 6.11). This duration will inevitably be significantly increased if pressure/volume ventilation has led to air leaks before cannulation. Whilst undergoing ECMO, the infant receives resting ventilation with slow background ventilation at a moderate level of PEEP to maintain lung expansion (rate 10 per minute, pressures 20/10). Serial radiographs will show a complete

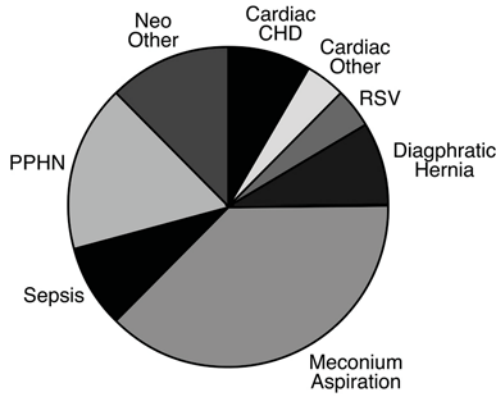


Fig. 6.11. Pie chart showing relative breakdown of indications for neonatal (*Neo*) ECMO (*CHD* chronic heart disease, *PPHN* persisting pulmonary hypertension of the newborn, *RSV* respiratory syncytial virus)

white-out during the first 2 or 3 days (Fig. 6.12a), with subsequent appearance of air bronchograms and resolution of the change as the lungs recover (Fig. 6.12b). Lung compliance can be estimated both manually and mechanically whilst the patient is on ECMO. Unless precipitous decannulation is required for other reasons, e.g. a large intracranial bleed, the infant is weaned from support when only minimal ventilatory support is needed to provide adequate lung expansion, oxygenation and gas exchange. At this stage there is usually radiological evidence of significant lung recovery.

In terms of long-term morbidity, survivors of ECMO do not appear to have a higher rate of disability or neurological damage than do conventionally treated severely hypoxic neonates with MAS, despite the greater proportion surviving.

6.7 Long-term Pulmonary Sequelae of MAS

MacFarlane and Heaf (1988) found a high prevalence of asthmatic symptoms (39%) and abnormal bronchial hyper-reactivity to exercise (33%) amongst survivors of neonatal MAS. This was much higher than the estimated prevalence of 10–12% in this age group in the general population. These children were not atopic or from atopic families and had not suffered other respiratory insults known to be associated with bronchial hyper-reactivity in later childhood. These findings of abnormal bronchial reactivity to

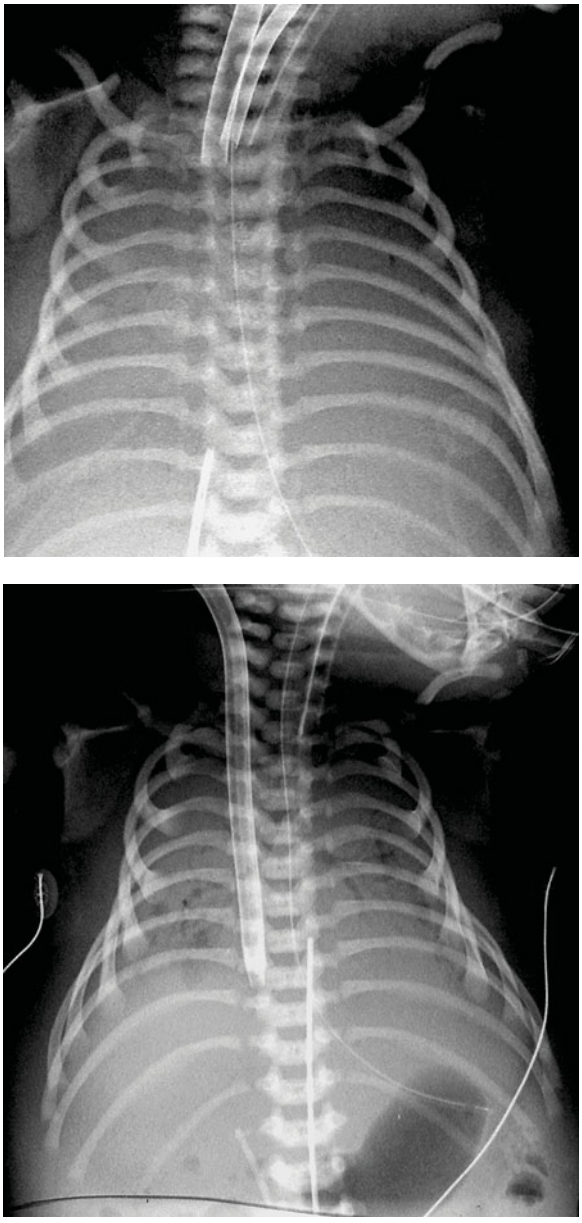


Fig. 6.12. a Chest X-ray showing complete 'white-outs' of both lungs due to low pressure maintenance ventilation (at 10 respirations per minute) for child on AV ECMO. **b** Chest X-ray of child on VV ECMO, with bilateral atelectasis and bibasal air bronchograms

exercise and mild expiratory air flow limitation make neonatal MAS another factor in the wide range of insults in the developing respiratory tract that can cause abnormalities of pulmonary function in later life. Aspiration of other foreign material (such as hydrocarbons or fresh water) is also associated with later abnormalities in pulmonary function, especially abnormal bronchial reactivity, long after symptoms have resolved. It seems likely, therefore, that the developing respiratory tract is vulnerable to damage by many insults, and the nonspecific response is abnormal bronchial hyper-reactivity and limitation of airflow (Mok and Simpson 1984)

6.8 Conclusion

Meconium aspiration syndrome is a common neonatal problem with significant morbidity and mortality. It frequently leads to respiratory failure and even death. One third of the infants affected require ventilatory support, and a significant portion will die. MAS is the primary cause of lung disease in infants requiring ECMO oxygenation, and this despite significant advances in management. Initially emphasis should be placed on prevention and all MSAF-complicated pregnancies should be carefully monitored: in each case the obstetrician should perform thorough oropharyngeal suctioning as soon as the infant's head is in the perineum, when the paediatrician should perform thorough pharyngeal suctioning.

Endotracheal intubation and endotracheal suction should be restricted to those depressed infants who require positive pressure ventilation. Although there are no prospective randomised control trials assessing the effects of various mechanisms of mechanical ventilator strategies in the management of MAS, the use of surfactant and of inhaled NO appears to have significantly reduced the need for ECMO in the management of MAS.

Radiology has a crucial role in the management of these complex patients, and it is important to be acquainted with all forms of clinical management and their potential radiological complications.

References

Abu-Osa YK (1991) Treatment of persistent pulmonary hypertension of the newborn: update. Arch Dis Child 66:74–77

Akopov SE, Zhang L, Pearce WJ (1998) Maturation alters the contractile role of calcium in ovine basilar arteries. Pediatr Res 44:154–60

Alexander GR, Hulsey TC, Robillard P-Y et al (1994) Determinants of meconium-stained amniotic fluid in tern pregnancies. J Perinatol 14:259–263
Andrews AF, Klein MD, Tomasian JM, Roloff DW, Bartlett RH (1983) Venovenous extracorporeal membrane oxygenation in neonates with respiratory failure. J Pediatr Surg 18:339–346
Antunes MJ, Friedman M, Greenspan JS et al (1997) Meconium decreases surfactant protein B levels in rat fetal lung explants. Pediatr Res 41:137 (abstract)
Bartlett RH, Gazzinga AZ, Huxtable RF et al (1977) Extracorporeal circulation (ECMO) in neonatal respiratory failure. J Thorac Cardiovasc Surg 74:826–833
Berkus MD, Langer O, Samueloff A et al (1994) Meconium-stained amniotic fluid: increased risk for adverse neonatal outcomes. Obstet Gynecol 84:115
Clark DA, Nieman GF, Thompson JE et al (1987) Surfactant displacement by meconium free fatty acids: an alternative explanation for atelectasis in meconium aspiration syndrome. J Pediatr 110:765–170
Cleary GM, Wiswell TE (1999) Meconium-stained amniotic fluid and the meconium aspiration syndrome. An update (review). Pediatr Clin North Am 45:511–529
Collaborative ECMO trial group (1996) UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. Lancet 341:75–82
Coltart TM, Byrne DL, Bates SA (1989) Meconium aspiration syndrome: a 6 year retrospective study. Br J Obstet Gynaecol 96:411–414
Delius R, Anderson H, Schumacher R et al (1993) Venovenous compares favourably with venoarterial access for extracorporeal membrane oxygenation in neonatal respiratory failure. J Thorac Cardiovasc Surg 106:329–338
Desai SA, Stanley C, Gringlas M et al (1999) Five year follow-up of neonates with reconstructed right common carotid arteries after extracorporeal membrane oxygenation. J Pediatr 134:428–433
Falciglia HS, Henderschott C, Potter P et al (1992) Does DeLee suction at the perineum prevent meconium aspiration syndrome? Am J Obstet Gynecol 167:1243–1249
Findlay RD, Taeusch HW, Walther FJ (1996) Surfactant replacement therapy for meconium aspiration syndrome. Pediatrics 97:48
Fleischer A, Anyaegbunam A, Guidette D et al (1992) A persistent clinical problem: profile of the term infant with significant respiratory complications. Obstet Gynecol 79:185–190
Fox WW, Duara S, (1983) Persistent pulmonary hypertension in the neonate. J Pediatr 103:505–514
Fuloria M, Wiswell TE (1999) Resuscitation of the meconium-stained infant and prevention of meconium aspiration syndrome. J Perinatol 19:234–241
Goetzman BW (1992) Meconium aspiration. Am J Dis Child 146:1282
Gregory GA, Gooding CA, Phibbs RH et al (1974) Meconium aspiration in infants: a prospective study. J Pediatr 85:848–852
Higgins ST, Wu A-M, Sen N et al (1996) Meconium increases surfactant secretion in isolated rat alveolar type II cell. Pediatr Res 39:443–447
Holopainen R, Aho H, Laine J, Halkola L, Kaapa P (1999) Nitric oxide inhalation inhibits pulmonary apoptosis but not inflammatory injury in porcine meconium aspiration. Acta Paediatr 88:1147–1455
Holtzman RB, Banzhaf WC, Silver RK et al (1989) Perinatal management of meconium staining of the amniotic fluid. Clin Perinatol 16:825–838
Jacobs JP, Goldman AP, Cullen S et al (1997) Carotid artery pseudonaeurysm as a complication of ECMO. Ann Vasc Surg 11:630–633
Klein MD Andrews AF Wesley JR et al (1985) Venovenous perfusion in ECMO for newborn respiratory insufficiency. Ann Surg 210:520–526
Lien HM, Towers CV, Quilligan EJ et al (1995) Term early-onset neonatal seizures: obstetric characteristics, etiologic classifications, and perinatal care. Obstet Gynecol 85:163–169
Lillehei CW, O'Rourke PP, Vacanti JP, Crone RK (1989) Role of extracorporeal membrane oxygenation in selected pediatric respiratory problems. J Thorac Cardiovasc Surg 98:968–970
Lucas A, Adrian TE, Christofides N et al (1980) Plasma motilin, gastrin, and enteroglucagon and feeding in the human newborn. Arch Dis Child 55:673–677
Macfarlane PI, Heaf DP (1988) Pulmonary function in children after neonatal meconium aspiration syndrome. Arch Dis Child 63:368–372
Matthews TG, Warshaw JB (1979) Relevance of the gestational age distribution of meconium passage in utero. Pediatrics 64:30–31
MillerFC, Read JA (1981) Intrapartum assessment of the postdate fetus. Am J Obstet Gynecol 141:516–520
Moses D, Holm BA, Spitale P et al (1991) Inhibition of pulmonary surfactant function by meconium. Am J Obstet Gynecol 164:477–481
Mok JYQ Simpson H (1984) Outcome of acute bronchitis, bronchiolitis and pneumonia in infancy. Arch Dis Child 59:306–309
Murphy JD, Rabinovitch M, Goldstein JD et al (1981) The structural basis of persistent pulmonary hypertension of the newborn. J Pediatr 98:962–967
Murphy JD, Vawter GF, Reid LM (1984) Pulmonary vascular disease in fatal meconium aspiration. J Pediatr 104:758
Narang A, Nair PMC, Bhakoo O et al (1993) Management of meconium stained amniotic fluid: a team approach. Indian Pediatr 30:9–13
Nathan L, Leveno KJ, Carmody TJ et al (1994) Meconium: a 1990s perspective on an old obstetric hazard. Obstet Gynecol 83:329–332
Oelberg DG, Downey SA, Flynn MM (1990) Bile salt-induced intracellular Ca+ + accumulation in type II pneumocytes. Lung 168:297
Peek GJ, Firmin RK, Moore HM, Sosnowski AW (1996) Cannulation for neonates for venovenous extracorporeal life support. Ann Thorac Surg 61:1851–1852
Peng TCC, Gutcher GR, Van Dorsten JP (1996) A selective aggressive approach to the neonate exposed to meconium-stained amniotic fluid. Am J Obstet Gynecol 175:296–303
Roberts JD, Fineman JR, Morin FC et al (1997) Inhaled nitric oxide and persistent pulmonary hypertension of the newborn. N Engl J Med 336:605
Stocker JT (1992) The respiratory tract. In: Stocker JT, Dehner LP (eds) Pediatric pathology. Lippincott, Philadelphia, p 505
Sun B, Curstedt T, Robertson B (1993) Surfactant inhibition in experimental meconium aspiration. Acta Paediatr 82:182–189

Suresh GK, Sarkar S (1994) Delivery room management of infants born through thin meconium stained liquor. Indian Pediatr 31:1177–1181

Swaminathan S, Quinn J, Stabile MW et al (1989) Long-term pulmonary sequelae of meconium aspiration syndrome. J Pediatr 114:356–361

The Neonatal Inhaled Nitric Oxide Study Group (1997) Inhaled nitric oxide in full-term and nearly full term infants with hypoxic respiratory failure. N Engl J Med 336:597

Thureen PJ, Halliday HL, Hoffenberg A et al (1997) Fatal meconium aspiration in spite of appropriate perinatal airway management: pulmonary and placental evidence of prenatal disease. Am J Obstet Gynecol 176:967–975

Ting P, Brady JP (1975) Tracheal suction in meconium aspiration. Am J Obstet Gynecol 122:767–771

Tran N, Lowe C, Sivieri EM et al (1980) Sequential effects of acute meconium aspiration on pulmonary function. Pediatr Res 14:34–38

Tsu F, Yeh MD, Harris V et al (1979) Roentgenographic findings in infants with MAS. JAMA 242:60–62

Tyler DC, Murphy J, Cheney FW (1978) Mechanical and chemical damage to lung tissue caused by meconium aspiration. Pediatrics 62:454–459

Usher RH, Boyd ME, McLean FH et al (1988) Assessment of fetal risk in postdate pregnancies. Am J Obstet Gynecol 158:259–264

Wiswell TE, Bent RC (1993) Meconium staining and the meconium aspiration syndrome. Pediatr Clin North Am 40:955–981

Wiswell TE, Tuggle JM, Turner BS (1990) Meconium aspiration syndrome: have we made a difference? Pediatrics 85:715–721

Wiswell TE, Foster NH, Slayter MV et al (1992) Management of piglet model of he meconium aspiration syndrome with high frequency or conventional ventilation. Am J Dis Child 146:1287

Wiswell TE, Meconium in the Delivery Room Trial Group (1998) Delivery room management of the apparently vigorous meconium-stained neonate: results of the multicentre collaborative trial. Pediatr Res 43:23 (abstract)

Yeh TF, Harris V, Srinivasan G et al (1979) Roentgenographic findings in infants with meconium aspiration syndrome. JAMA 242:60–63

Yeh TF, Lilien LD, Barathi A et al (1982) Lung volume, dynamic lung compliance, and blood gases during the first 3 days of postnatal life in infants with meconium aspiration syndrome. Crit Care Med 10:588–592

Yoder BA (1994) Meconium-stained amniotic fluid and respiratory complications: impact of selective tracheal suction. Obstet Gynecol 83:77–84

Yuksel B, Greenough A, Gamsu HR (1993) Neonatal meconium aspiration syndrome and respiratory morbidity during infancy. Pediatr Pulmonol 16:358–361