Clinical features and diagnosis of meconium aspiration syndrome

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INTRODUCTION — Meconium aspiration syndrome (MAS) is defined as respiratory distress in newborn infants born through meconium-stained amniotic fluid (MSAF) whose symptoms cannot be otherwise explained [1]. MAS can present with varying degrees of severity from mild respiratory distress to life-threatening respiratory failure.

The clinical features and diagnosis of MAS will be discussed here. The management and complications of MAS are discussed elsewhere. (See "Prevention and management of meconium aspiration syndrome".)

EPIDEMIOLOGY — In the United States, a retrospective multicenter study of 162,075 term infants born between 1997 and 2007 reported 1.8 percent of infants had an admission diagnosis of MAS [2].

MAS occurs in about 2 to 10 percent of infants born through meconium-stained amniotic fluid (MSAF). This was illustrated in a study from a single tertiary center of 20,047 live births between 1994 and 1998 that reported MSAF occurring in 9.2 percent and MAS in 0.1 percent of all live births [3].

This 10-fold difference in the incidence of MAS may be due to differences between the two studies in the rigor that MAS was diagnosed and measures used to prevent MAS. (See "Prevention and management of meconium aspiration syndrome", section on 'Prevention'.)

The incidence of MSAF varies with gestational age with a nadir at about 31 weeks. This was best illustrated by a large English multicenter study of about 500,000 singleton births that reported rates of MSAF in preterm, term, and postterm infants of 5.1, 16.5, and 27.1 percent, respectively [4]. However, in the subgroup of premature infants, rates were higher for those born ≤30 weeks compared with those with a gestational age between 31 and 36 weeks. After 31 weeks, the incidence of MSAF increases with gestational age. After excluding preterm infants, the rates of MSAF were higher in black (22.6 percent) and South Asian infants (16.8 percent) compared with those who were white (15.7 percent). Logistic regression analysis showed independent predictors for MSAF included advanced gestation, black or South Asian ethnicity, and vaginal breech delivery.

The risk of MAS and MSAF is greatest in postmature and small for gestational age infants [5]. Changes in obstetric care, especially a reduction in postmature births, appear to be associated with a decrease in the incidence of MAS. This was illustrated in the following studies:

- In a prospective study of 1365 infants ≥37 weeks gestational age born through MSAF at a single center from 1990 to 1998, MAS decreased nearly fourfold (from 5.8 to 1.5 percent in 1990 to 1992 and 1997 to 1998, respectively) [6]. This was associated with a significant reduction in births ≥41 weeks gestation (from 42 to 28 percent), as well as increased use of amnioinfusion, diagnosis of nonreassuring fetal heart rate patterns, and cesarean delivery.

- A significant decrease in the incidence of severe MAS (requiring intubation and mechanical ventilation) was also noted over an eight-year period in Australia and New Zealand from 1995 to 2002 [7]. The lowest incidence was 0.35 per 1000 live births in 2002. The lower incidence was attributed to improving

obstetrical management with fewer deliveries beyond 41 weeks gestation and fewer infants with five-minute Apgar scores of less than 7 (calculator 1). These two changes accounted for approximately 62 percent of the reduction in severe MAS cases.

PATHOPHYSIOLOGY — The pathophysiology of MAS involves intrauterine passage of meconium, aspiration, and pulmonary disease, which results in hypoxemia and acidosis (algorithm 1). Persistent pulmonary hypertension of the newborn (PPHN) frequently accompanies severe MAS and contributes to hypoxemia [8]. (See "Persistent pulmonary hypertension of the newborn".)

Birth depression occurs in 20 to 33 percent of infants born through meconium-stained amniotic fluid (MSAF) [9-11] and likely is caused by pathologic intrauterine processes, primarily chronic asphyxia and infection. This intrauterine stress leads to the passage and aspiration of meconium by the fetus.

Composition of meconium — Meconium is a thick, black-green, odorless material first demonstrable in the fetal intestine during the third month of gestation. Meconium results from the accumulation of debris, including desquamated cells from the intestine and skin, gastrointestinal mucin, lanugo hair, fatty material from the vernix caseosa, amniotic fluid, and intestinal secretions. It contains blood group-specific glycoproteins and a small amount of lipid and protein that decreases during gestation [12,13]. The black-green color results from bile pigments.

Meconium is sterile. However, when aspirated into the lung, it may stimulate the release of cytokines and other vasoactive substances that lead to cardiovascular and inflammatory responses in the fetus and newborn [14,15]. In patients with MAS, pulmonary function improves with the fall of proinflammatory cytokines over the first 96 hours of life [16]. There are also animal data that implicate pancreatic phospholipase A2 as a potential source of the lung injury [17].

Meconium passage — Passage of meconium occurs early in the first trimester of pregnancy [18]. Fetal defecation slows after 16 weeks gestation and becomes infrequent by 20 weeks, concurrent with innervation of the anal sphincter [19]. From approximately 20 to 34 weeks, fetal passage of meconium remains infrequent [20]. Almost all fetuses and newborn infants who pass meconium are at term or postterm gestation.

Meconium passage may be caused by increased peristalsis and relaxation of the anal sphincter due to increased vagal outflow associated with umbilical cord compression or increased sympathetic inflow during hypoxia [21-24]. In one study, fetuses that passed meconium prior to birth had higher motilin levels in cord blood compared to those who did not [24]. The higher levels of motilin, a regulatory intestinal peptide, were thought to be related to increased parasympathetic tone due to fetal hypoxia. (See "Overview of the development of the gastrointestinal tract", section on 'Hormonal regulation'.)

Aspiration — Meconium in amniotic fluid can be aspirated during fetal gasping or in the initial breaths after delivery. Normally, fetal breathing activity results in movement of lung fluid out of the trachea [25]. However, as shown in animals, prolonged hypoxia stimulates fetal breathing and gasping that can lead to inhalation of amniotic fluid [25-29]. Pathologic evidence suggests that this process also occurs in humans. Meconium has been found in the lungs of infants who were stillborn [30] or who died soon after birth without a history of aspiration at delivery [31,32].

Meconium that remains in the hypopharynx or trachea after delivery can be aspirated during the initial breaths. This is more likely to occur in a depressed infant.

Pulmonary disease — Aspirated meconium can interfere with normal breathing by several mechanisms. These include airway obstruction, chemical irritation and inflammation, infection, and surfactant inactivation. However, it is likely that most cases of severe MAS are primarily caused by intrauterine pathologic processes, primarily asphyxia and infection, rather than the aspiration of meconium by itself [33].

   Airway obstruction — Airway obstruction can be complete or partial. Complete obstruction leads to distal atelectasis. Partial airway obstruction occurs when particulate meconium partly occludes the airway. Because

the airway diameter is larger in inspiration, gas can enter around the partial obstruction. However, as the airway narrows during exhalation, the meconium plug occludes the airway completely, trapping the gas distally. This process is known as a ball valve effect and can lead to overdistention of the lung and alveolar rupture, with resulting pneumothorax or other air leak complications [34,35]. (See "Pulmonary air leak in the newborn".)

Chemical irritation and inflammation — Components of meconium cause inflammation of the lung that is apparent 24 to 48 hours after inhalation. Direct injury and inflammation result in an exudative and inflammatory pneumonitis with epithelial disruption, proteinaceous exudation with alveolar collapse, and cellular necrosis [35-39]. In animal studies, pancreatic phospholipase A2 appears to directly contribute to lung injury [17].

Infection — MSAF is a risk factor for bacterial infection of the amniotic cavity and should alert the clinician to the potential for increased neonatal morbidity [40-42] Although meconium is sterile, the mucopolysaccharide component provides an excellent growth medium for microorganisms, especially *Escherichia coli* [43]. Meconium also may inhibit phagocytosis by polymorphonuclear cells and their oxidative burst [44]. (See "Neonatal pneumonia".)

Surfactant — Several studies have shown the deleterious effects of meconium on surfactant metabolism.

- Increased inactivation – Animal models of meconium aspiration demonstrate inactivation of surfactant with increased surface tension, and decreased lung volume, compliance, and oxygenation [45-49]. In human infants, concentrations of surfactant inhibitors (eg, total protein, albumin, membrane-derived phospholipid) were higher in lung lavage fluid in those with MAS than in controls [36]. However, surfactant phospholipid and surfactant protein A levels were not different. In addition, several meconium components (eg, free fatty acids) have a higher minimal surface area and may displace surfactant from the alveolar surface.

- Decreased synthesis – In a small study, there was a trend toward lower surfactant synthesis in neonates with MAS or persistent pulmonary hypertension (PPHN) who required extracorporeal membrane oxygenation, compared to control infants who required ventilatory support for nonpulmonary indications [50]. Lower tracheal aspirate concentrations of phosphatidylcholine (PC), a component of surfactant, and lower incorporation of radiolabeled carbon in PC were seen in infants with MAS or PPHN compared to controls.

Hypoxemia — Hypoxemia results from several causes, including decreased alveolar ventilation related to lung injury, and ventilation-perfusion imbalance with continued perfusion of poorly ventilated lung units. PPHN frequently accompanies MAS, with right-to-left shunting caused by increased pulmonary vascular resistance, and resultant hypoxemia. (See "Persistent pulmonary hypertension of the newborn".)

CLINICAL FEATURES — In addition to the pulmonary manifestations of MAS, the following features are seen:

- A history of meconium-stained amniotic fluid (MSAF) or evidence of meconium staining on physical examination of the infant. The vernix, umbilical cord, and nails may be meconium-stained, depending upon how long the infant has been exposed in utero [51]. In general, nails will become stained after six hours and vernix after 12 to 14 hours of exposure.

- Birth depression occurs in 20 to 33 percent of infants born through MSAF [9-11,52]. These infants have neurologic and/or respiratory depression at birth typically due to hypoxia or shock [52]. (See "Etiology, clinical manifestations, evaluation, and management of neonatal shock".)

- Affected infants are frequently small for gestational age or postmature [5]. Characteristic findings of postmaturity include peeling skin, long fingernails, and decreased vernix. (See "Infants with fetal (intrauterine) growth restriction" and "Postterm infant".)

Pulmonary findings — Infants with MAS typically have respiratory distress with marked tachypnea and cyanosis. Reduced pulmonary compliance and use of accessory muscles of respiration are evidenced by intercostal and subxiphoid retractions and abdominal (paradoxical) breathing, often with grunting and nasal flaring.

Infants who develop MAS exhibit signs of respiratory distress immediately after birth. In a study of 394 term infants with MSAF, MAS developed in 18 patients with Apgar scores <8 (19 percent) and in one patient with an Apgar score ≥9 (0.3 percent) [53]. All 19 patients had signs of respiratory distress within 15 minutes of birth, which required ventilatory support in 16 of the infants. These results demonstrate that full-term infants with MSAF without any sign of respiratory distress or depression immediately after birth are unlikely to develop MAS.

Affected infants typically have a barrel-shaped chest with an increased anterior-posterior diameter caused by overinflation. Auscultation reveals rales and rhonchi. These signs usually are seen immediately after birth. However, some patients are asymptomatic at birth and develop worsening signs of pulmonary decompensation as the meconium moves from the large airways into the lower tracheobronchial tree.

In patients with severe MAS, pneumothorax and pneumomediastinum are common findings. Patient with severe disease are at risk for respiratory failure, which is often associated with persistent pulmonary hypertension (PPHN). Infants with pulmonary hypertension and right-to-left shunting may have a gradient in oxygenation between pre- and postductal arterial blood samples. In addition, echocardiography may demonstrate right-to-left shunting. (See "Pulmonary air leak in the newborn", section on 'Risk factors' and "Persistent pulmonary hypertension of the newborn", section on 'Maladaptation'.)

DIAGNOSIS — The diagnosis of MAS is made by the following clinically based findings:

- There is evidence of meconium-stained amniotic fluid (MSAF) on infant. (See 'Clinical features' above.)

- Respiratory distress at birth or shortly after birth. (See 'Pulmonary findings' above.)

- Characteristic radiographic features. The initial chest film may show streaky, linear densities similar in appearance to transient tachypnea of the newborn. As the disease progresses, the lungs typically appear hyperinflated with flattening of the diaphragms [54-56]. Diffuse patchy densities may alternate with areas of expansion. In infants with severe disease who require high concentrations of supplemental oxygen and mechanical ventilation, the lungs may develop an appearance of homogeneous density similar to respiratory distress syndrome. Radiographic changes resolve over the course of 7 to 10 days but sometimes persist for several weeks. Air leak occurs in 10 to 30 percent of infants with MAS [10,57]. (See "Transient tachypnea of the newborn" and "Pulmonary air leak in the newborn", section on 'Risk factors'.)

- If the infant requires intubation because of depression, the diagnosis is made by the presence of meconium in the trachea. (See "Prevention and management of meconium aspiration syndrome", section on 'Neonatal care'.)

Although arterial blood gas measurements typically demonstrate hypoxemia and hypercarbia, these findings are nonspecific and are not used to diagnosis MAS. However, arterial blood gas measurements and pulse oximetry are used to assess the respiratory status of the infant. (See 'Evaluation' below.)

DIFFERENTIAL DIAGNOSIS — The differential diagnosis of MAS includes other causes of neonatal respiratory distress, which occur in 4 to 9 percent of infants born through meconium-stained amniotic fluid (MSAF) [52]. They include:

- Transient tachypnea of the newborn (60 percent)
- Delayed transition from fetal circulation (18 percent)
- Sepsis or pneumonia (11 percent)

- Persistent pulmonary hypertension of the newborn (3 percent)
- Miscellaneous conditions, including pulmonary edema, pneumothorax, hypovolemia, blood aspiration (8 percent)

MAS is distinguished from these based on the history, clinical course, and radiographic findings as follows:

- Transient tachypnea of the newborn (TTN) is a frequent cause of respiratory distress in late preterm infants (34 to 37 weeks gestation), whereas MAS is most frequently seen in postmature infants (>41 weeks gestation). In addition, patients with TTN improve quickly in contrast to those with MAS. (See "Transient tachypnea of the newborn".)

- Infants with delayed transition from fetal circulation improve quickly in comparison to those with MAS. (See "Physiologic transition from intrauterine to extrauterine life".)

- Respiratory distress syndrome (RDS) generally occurs in preterm infants, whereas MAS usually occurs in postmature infants. (See "Pathophysiology, clinical manifestations, and diagnosis of respiratory distress syndrome in the newborn", section on 'Clinical manifestations'.)

- Pneumonia may be difficult to differentiate from MAS. As a result, infants with presumed MAS are treated with antibiotics while awaiting the results of cultures. (See "Neonatal pneumonia" and "Prevention and management of meconium aspiration syndrome" and "Prevention and management of meconium aspiration syndrome", section on 'Antibiotics'.)

- Congenital cyanotic heart disease is differentiated from MAS by physical examination, chest radiography, and echocardiography. (See "Diagnosis and initial management of cyanotic heart disease in the newborn".)

- Isolated air leaks such as pneumothorax is differentiated from MAS by history (absence of meconium-stained amniotic fluid) and chest radiography. (See "Pulmonary air leak in the newborn", section on 'Risk factors'.)

EVALUATION — The evaluation for suspected MAS includes the following:

- Chest radiograph is used in confirming the diagnosis of MAS. (See 'Diagnosis' above.)

- Arterial blood gas is used to assess the respiratory status of the affected neonate. It is used to determine whether mechanical ventilation is indicated in patients with severe respiratory distress. Pulse oximetry is used to continue to monitor the infant's oxygenation. (See "Mechanical ventilation in neonates", section on 'Indications for ventilation' and "Oxygen monitoring and therapy in the newborn", section on 'Pulse oximetry'.)

- Echocardiography may be indicated in patients with severe respiratory distress to exclude the diagnosis of structural heart disease, and to identify patients with persistent pulmonary hypertension (PPHN). In PPHN, echocardiography demonstrates normal structural anatomy with evidence of pulmonary hypertension (eg, flattened or displaced ventricular septum) and right-to-left shunting. (See "Persistent pulmonary hypertension of the newborn", section on 'Diagnosis'.)

- Because it is difficult to differentiate MAS from pneumonia, blood cultures and, if possible, tracheal aspirate cultures are obtained. Empiric antibiotic therapy is started while awaiting culture results. (See "Management and outcome of sepsis in term and late preterm infants", section on 'Initial empiric therapy'.)

SUMMARY AND RECOMMENDATIONS — Meconium aspiration syndrome (MAS) is defined as respiratory distress in an infant born through meconium-stained amniotic fluid (MSAF) whose symptoms cannot be otherwise explained. MAS can present with varying degrees of severity from mild respiratory distress to life-threatening with respiratory failure.

- With changes in obstetric care, the incidence of MAS has declined to about 0.1 to 1.8 percent of live births in developed countries. Risk factors for MAS include postmaturity and small for gestational age. (See 'Epidemiology' above.)

- The pathophysiology of MAS involves intrauterine passage of meconium, aspiration, and pulmonary disease resulting in hypoxemia, acidosis, and potentially pulmonary hypertension (algorithm 1). Pulmonary disease is a result of aspirated meconium interfering with normal lung function due to airway obstruction, chemical irritation and inflammation, and deleterious effects on surfactant metabolism (ie, inactivation and reduced production). (See 'Pathophysiology' above.)

- Infants with MAS typically have a history of MSAF or evidence of meconium staining on physical examination. They are frequently small for gestational age or postmature. Many infants with MAS also have neurologic or respiratory depression due to perinatal hypoxia. (See 'Clinical features' above.)

- Patients present with respiratory distress with marked tachypnea, cyanosis, intercostal and subxiphoid retractions, abdominal breathing, grunting, and nasal flaring. The chest appears barrel-shaped (increased anterior-posterior diameter) due to overinflation. In patients with severe MAS, complications include air leaks (eg, pneumothorax) and persistent pulmonary hypertension (PPHN). (See 'Pulmonary disease' above and "Pulmonary air leak in the newborn" and "Persistent pulmonary hypertension of the newborn".)

- The diagnosis of MAS is based on the clinical findings of MSAF or meconium-stained infant, respiratory distress, and characteristic radiographic features. The radiologic findings are initially streaky, linear densities, followed by hyperinflation, and alternating diffuse patchy densities with areas of expansion. In patients who require intubation, the diagnosis is established by the presence of meconium in the trachea. (See 'Diagnosis' above.)

- MAS is differentiated from other causes of neonatal respiratory distress (eg, transient tachypnea of the newborn, neonatal pneumonia, and congenital cyanotic heart disease) based upon the history, physical examination, clinical course, and radiographic findings. (See 'Differential diagnosis' above.)

- The evaluation of suspected MAS includes chest radiography, arterial blood gas and pulse oximetry, blood cultures, and if possible, tracheal aspirate cultures. In patients with more severe disease, an echocardiography may be indicated to exclude structural heart disease and/or PPHN. (See 'Evaluation' above.)

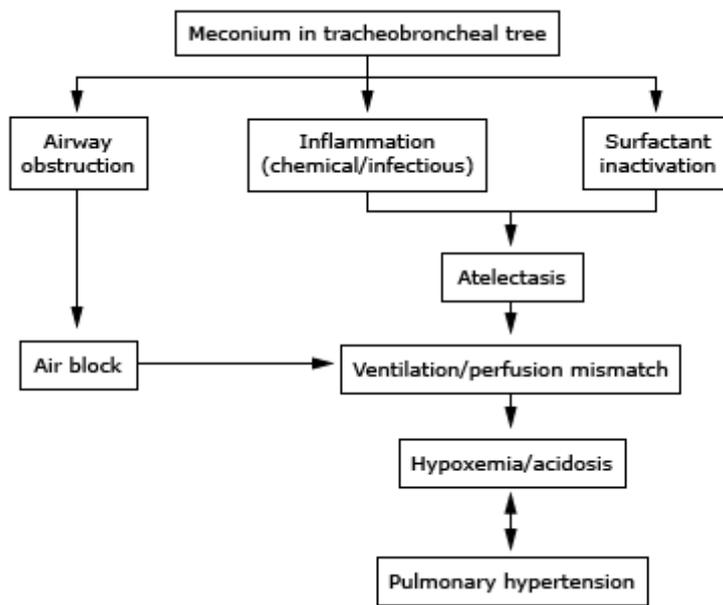Use of UpToDate is subject to the Subscription and License Agreement.

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GRAPHICS

Pathophysiology of meconium aspiration syndrome

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