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## Meconium Aspiration Syndrome - Pathogenesis and Current Management

By Medha Kamat, MD; Shou-Yien Wu, MD; Tsu F. Yeh, MD

### Meconium Aspiration Syndrome - Pathogenesis and Current management

Meconium staining of the amniotic fluid (MSAF) occurs in 10-15% of live births in the United States (400,000-600,000/year). Meconium Aspiration Syndrome (MAS) is a respiratory disorder caused by inhalation of meconium into the tracheobronchial tree. MAS occurs in 0.5 % of all live births. The incidence of Meconium Aspiration Syndrome is decreasing due to the reduction of births at more than 41 weeks gestation. In a prospective study of infants born > 37 weeks age, MAS decreased from 5.8% to 1.5% during the period 1990 to 1997.<sup>1</sup> This was associated with a 33% reduction in births > 41 weeks gestation. Approximately 20,000 to 30,000 cases develop respiratory distress requiring assisted ventilation (6,700-10,000/year) and have a mortality rate of ~5% (1000-1500/year).

### Etiology of meconium passage

Meconium passage from the fetus into the amniotic fluid is a result of peristalsis, tonic contractions of the anal sphincter, and a plug of thick and viscous meconium. Intestinal peristalsis is caused by several factors one of which is higher motilin levels.<sup>2</sup> The passage of meconium may occur naturally in a term or postterm fetus with a mature gastrointestinal

tract without fetal distress. It may also be caused by spontaneous intestinal motility or bowel stimulation caused by infection or hypoxia due to relaxation of anal sphincter. Passage of meconium into the amniotic fluid may also increase the risk of infection in the fetus.<sup>3</sup> In addition, vagal stimulation produced by sporadic or repetitive cord compression may also be associated with passage of meconium in the amniotic fluid.

### Characteristics of human meconium

Human meconium is a viscous, odorless, substance with PH of 7.10-7.20. It is black or yellowish-green in color. It is composed of desquamated epithelial cells, lanugo, vernix, and intestinal secretions including bile acid and bile pigment. Water is the major liquid constituent, comprising 80% of meconium. Meconium contains blood group-specific glycoproteins and a small amount of lipid and protein that diminishes during gestation.<sup>4,5</sup> It has been shown to enhance bacterial growth. Several constituents of meconium, especially the free fatty acids have a higher minimal surface tension than surfactant and either displace it from the alveolar surface or inhibit it, resulting in diffuse atelectasis.

### Pathogenesis of MAS

It is not exactly clear as to why only some infants who pass meconium develop aspiration syndrome. Aspiration of meconium may occur during fetal gasping in utero or during initial breaths after delivery. Prolonged fetal

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hypoxia as shown in animals can stimulate fetal gasping which in turn results in inhalation of amniotic fluid in the tracheobronchial tree. Most cases of severe MAS occur as a result of chronic in utero insult as opposed to an acute peripartum event.<sup>6,7</sup>

Aspiration induces hypoxia via five major pulmonary effects: airway obstruction, surfactant dysfunction, chemical pneumonitis, bacterial infection, and pulmonary hypertension.

#### **Airway obstruction**

Complete obstruction of the airways by thick viscid meconium results in partial or complete airway obstruction. Partial obstruction causes air trapping and hyperdistention of the alveoli, commonly termed the ball-valve effect. The gas that is trapped may rupture into the pleura resulting in air leaks.

#### **Surfactant dysfunction**

Animal models of meconium aspiration have shown that meconium results in inactivation of surfactant with increased surface tension. Lung lavage fluid in infants with MAS demonstrated higher concentrations of surfactant inhibitors (total proteins, albumin, membrane derived phospholipid). Several constituents of meconium, especially the free fatty acids (eg, palmitic, stearic, oleic), have a higher minimal surface tension than surfactant and displace it from the alveolar surface, resulting in diffuse atelectasis, decreased lung volume, compliance and oxygenation.

#### **Chemical pneumonitis**

Enzymes, bile salts, and fats in meconium irritate the airways and parenchyma, causing a release of cytokines (including tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1 $\beta$ , IL-6, IL-8, IL-13) and resulting in a diffuse toxic pneumonitis that may begin within a few hours of aspiration. Finally, although meconium is sterile, its presence in the air passages can predispose the infant to pulmonary infection.

All of these pulmonary effects can produce gross ventilation-perfusion (V/Q) mismatch which can result in PPHN. Meconium and its constituents may result in direct injury of the cord vessels and amniotic membranes and may also cause vasoconstriction of the placental and cord vessels.

#### **Abnormal Pulmonary functions**

Infants with MAS typically have high airway resistance which is the most prominent feature during the first 48 hrs. Low compliance could either be due to over-inflation or partially atelectatic terminal respiratory units.

Lung volume (FRC by closed system helium dilution technique) could be low or normal. Arterial blood gases show PCO<sub>2</sub> usually in the normal range unless there is an airleak. Infants with severe MAS may show hypoxia and hypercarbia.<sup>9</sup>

#### **Persistent pulmonary hypertension in meconium aspiration syndrome**

Persistent pulmonary hypertension, or PPHN, frequently accompanies MAS with right to left shunting caused by increased pulmonary vascular resistance. A two-dimensional echocardiogram is used to evaluate pulmonary hypertension early in an infant's course. PPHN occurs in 20-40% of infants with MAS. Many infants with MAS have primary or secondary PPHN as a result of chronic in utero stress and muscle hypertrophy causing thickening of the pulmonary vessels.

This condition usually presents as persistent hypoxemia at 6-24 hours after birth. In a postnatal newborn piglet model, elevation of pulmonary arterial pressure appeared to be biphasic, early phase starting from 2-6 hours and late phase at 48 hours.<sup>8</sup> A good positive correlation was seen between tracheal aspirate TXB<sub>2</sub>, leukotriene D<sub>4</sub> and mean pulmonary arterial pressure. The use of Dexamethasone reduced tracheal aspirate TXB<sub>2</sub>, and KetoPGF<sub>1</sub> $\alpha$ . A spontaneous recovery usually occurs within 3 to 4 days if patient survives, suggesting that a functional vascu-

lar constriction is probably involved in the pathogenesis.

PPHN in infants with MAS could be due to:

1. hypertrophy or neo-muscularization of post-acinar capillaries as a result of chronic intrauterine hypoxia
2. functional pulmonary vasoconstriction as a result of hypoxia, hypercarbia or acidosis or
3. functional pulmonary vasoconstriction as a result of lung inflammation.

#### **Diagnosis**

MAS must be considered in any infant with history of MSFAF and development of respiratory distress. Infants with MAS may also present with yellow-green staining of fingernails, umbilical cord, and skin. Postmature infants may have evidence of peeling skin, long fingernails, and decreased vernix. Infants with respiratory distress present with tachypnea, intercostal retractions, grunting, and barrel-shaped chest in the presence of air trapping. Auscultation reveals rales and rhonchi. Hypoxic infants may present signs of encephalopathy.

#### **Radiologic features**

The diagnosis of MAS is confirmed by chest radiograph. The classic radiologic findings in MAS are diffuse coarse patchy infiltrates that may alternate with areas of expansion.<sup>9</sup> In infants with severe MAS, the lungs may develop an appearance of homogeneous density similar to either consolidation or atelectasis. A series of 80 cases showed that MAS with consolidation or atelectasis was most predictive of poor outcome as compared to those without atelectasis or consolidation.<sup>10</sup>

As the disease progresses, the lungs typically appear hyperinflated with flattening of the diaphragms.<sup>10</sup> Pneumothorax, pneumomediastinum or pulmonary interstitial emphysema may be present in 15-33% infants. Pleural effusions are not uncommon. Radiologic changes resolve within 7-10 days, however, in some infants they persist for several weeks.<sup>11</sup>



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## Prevention of meconium aspiration

### *Antepartum prevention*

Most cases of severe MAS are not, in fact, causally related to the aspiration, but are caused by other pathologic process occurring in utero: primary chronic asphyxia and infection. Fetal hypoxic stress may stimulate colonic activity, resulting in the passage of meconium, and also stimulate fetal gasping movements that result in meconium aspiration.

### *Prevention of intrauterine hypoxia*

The incidence of MAS has decreased over the last decade. The improvement has been attributed to the reduction rate of post-term delivery, aggressive management of fetal distress and decreased number of infants with low Apgar scores.<sup>1,13</sup> In cases where the pregnancy is complicated with meconium-stained amniotic fluid, continuous electronic fetal monitoring is indicated.<sup>14</sup> If fetal distress especially non-assuring fetal tracing is present, timely intervention should be initiated.

Fetal pulse oximetry is a new modality for ante-partum fetal surveillance. The membrane must be ruptured and the cervix be dilated at least 2-3 cm before the probe can be inserted.

### *Reduction in the rate of post-term delivery*

Post-term delivery has been shown to be associated with an increase in the number of infants passing meconium and in the rate of intrauterine hypoxia. A reduction in the rate of post-term delivery was reported to reduce nearly four times the incidence of MAS.<sup>13</sup>

The American College of Obstetricians and Gynecologists no longer describes any specific upper limit of gestational age for delivery. Many obstetricians proposed early initiation of fetal monitoring by 40 weeks and the earlier induction by 41-42 weeks.

### *Treatment of maternal infection*

Chorioamnionitis and neonatal sepsis are very commonly associated with severe MAS, as compared to those born with a history of meconium stained amniotic fluid (MSAF). Early administration of broad-spectrum antibiotic therapy in cases of maternal infection reduces both maternal and neonatal morbidity. Antibiotic prophylaxis to women with uncomplicated MSAF in the prevention of severe MAS has not been studied.

### *Intrapartum prevention of meconium aspiration*

MAS was believed to result from aspiration of meconium during intrauterine gasping or at the first breath. Interventions such as the amnioinfusion, oropharyngeal suction, and tracheal aspiration were common practices in the past two decades after reports showed these procedures decreased the incidence and severity of

MAS.<sup>15,16,17</sup> Recently, several well-organized, large scale randomized trials of these strategies have not shown a reduction in the incidence of MAS.<sup>18,19,20</sup> These interventions are now reserved in infants born with MSAF with other complications.

### *Amnioinfusion- transcervical infusion of saline*

Amnioinfusion is very effective to treat pregnancies complicated with oligohydramnios and variable decelerations. During the procedure, a sterile catheter is introduced transcervically to a depth of 30 cm, and a bolus of 800 ml of sterile saline at room temperature is infused under the force of gravity at a rate of 20 ml per minute over a period of 40 minutes. The infusion then is continued at a rate of 2 ml per minute to a maximum of 1500 ml.

Wenstrom et al. proposed amnioinfusion as a way of diluting the thickness of meconium, preventing umbilical cord compression to prevent of MAS in 1989.<sup>15</sup>

Review of previous studies shows this strategy decreases the meconium found below the cords in infants born to mothers with MSAF, but failed to show a reduction in the incidence of MAS.<sup>21,22</sup> Fraser et al. conducted an international, multicenter randomized trial involving 2000 women in labor with thick MSAF and concluded that amnioinfusion did not reduce the risk of moderate to severe MAS, and perinatal death for women in labor who had thick MSAF.<sup>18</sup>

There is insufficient evidence that amnioinfusion reduces meconium-related neonatal morbidity, therefore, it is not recommended for women with MSAF alone unless there is evidence of variable fetal heart rate decelerations.

### *Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates*

Observations in the '70s and '80s showed pharyngeal and tracheal intubation decreased the incidence and severity of MAS.<sup>16,17</sup> Until recently, suctioning of the pharynx through mouth and nose by the obstetricians after the delivery of the head, but before the delivery of the shoulder was a common practice; routine intubation and tracheal suctioning was recommended in infants with thick meconium or low Apgar scores.<sup>23</sup> Recent studies do not support universal aggressive suctioning unless infants are depressed. Since 2005, the American Heart Association, and the Neonatal Resuscitation Program recommends tracheal suctioning only if the infant is not vigorous, has absent or depressed respiration, has decreased muscle tone, or has a heart rate <100 beats/min.

A 10-Fr to 13-Fr sized suction catheter or a Delee device is connected to a negative pressure of 150 mmHg. Oropharynx of the neonate is suctioned first, followed by bilateral nasopharyngeal suctioning after the head is delivered but before the shoulder is delivered and before the infant is able to take a breath. Peng et al. showed this intervention resulted in reduction of neonatal intubation



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for MAS.<sup>24</sup> Vain et al. in a multi-center, randomized controlled trial showed that oroharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders does not prevent MAS, nor does it determine need for mechanical ventilation, mortality, or duration of ventilation, oxygen treatment and hospital stay.<sup>19</sup> In a multi-center, international collaborative trial, Wiswell et al. concluded intubation and suctioning of the apparently vigorous meconium-stained infants does not result in a decreased incidence of MAS or other respiratory disorders.<sup>20</sup>

As a result of these trials, endotracheal intubation and suctioning of meconium is no longer recommended for vigorous babies born with MSAF. However, meconium-stained, depressed infants should receive suctioning of the mouth, nose, and trachea immediately after birth and before stimulation.

### Management of MAS and persistent pulmonary hypertension

Once the infants develop MAS, the management is mainly supportive care. Maintenance of adequate oxygenation, systemic blood pressure and correction of acidosis, hypoglycemia or other metabolic disorders is the mainstay of the treatment. Infants should be cared in a neutral thermal environment and watched closely. Gentle care is preferred, and excessive handling and agitation should be avoided. Umbilical arterial catheter or radial arterial catheter should be inserted in case of moderate to severe MAS, so blood gases and blood pressure can be monitored accurately and the neonate is not disturbed.

### Antibiotics

Bacterial infection might have precipitated the passage and subsequent aspiration of meconium, thus judicious use of antibiotics is indicated. Indeed, bacterial pneumonia is indistinguishable radiographically from MAS.

### Maintain adequate systemic blood pressure and tissue perfusion

It is important to keep adequate systemic blood pressure in case of moderate to severe MAS. If infants develop PPHN, the systemic blood pressure should be kept higher than pulmonary blood pressure to overcome right-to-left shunt. In addition to maintaining intravenous fluids, volume expanders such as normal saline and albumin are needed if patients have low blood pressure. Transfusion with packed RBC is indicated to keep hematocrit greater than 40%. Vasopressors are often used. Continuous intravenous drips with dopamine (2-20 mcg/kg/min), dobutamine (2-25 mcg/kg/min) or epinephrine (0.01-0.03 mg/kg/min) are often used separately or in a combination.

### Oxygen therapy and ventilator management

Because hypoxia, acidosis, and hypercarbia increase pulmonary vascular resistance, infants should receive oxygen therapy after

birth if they show signs and symptoms of oxygen desaturation. Oxygen saturation should be maintained close to 100% or arterial PO<sub>2</sub> be maintained close to 100 mm Hg or even higher. Infants with MAS and complications of PPHN are very labile during the acute stage, and, therefore, we monitor arterial blood gases frequently and wean oxygen and ventilator support very cautiously until the acute stage is over, and baby's condition is stable.

We attempt to maintain PH around 7.35 to 7.45 in order to avoid acidosis and maintain PCO<sub>2</sub> at 35 to 40 mmHg in the first 2-3 days. As the ventilatory status is more stable, the PCO<sub>2</sub> can be kept between 40-50 mmHg.

### Sedation

Term infants may become very agitated with intubation and may not synchronize with mechanical breaths. Patients with PPHN are very sensitive to any stimulation. Analgesia and anesthesia agents are indicated. Continuous intravenous drips with morphine 100 to 150 mcg/kg loading dose over one hour followed by 10 to 20 mcg/kg/hour, or fentanyl at dose 1-5 mcg/kg/hour, or midazolam 10-60 mcg/kg/hour can be initiated. Dosage may be increased after several days of treatment because of development of tolerance. Muscle relaxant such as pancuronium 0.1 mg/kg/dose might be needed if patient's breath is not synchronized with mechanical breath.

### Ventilator management

#### Conventional ventilator

Some alveoli in MAS are atelectatic, some are over-distended, thus resulting in V/Q mismatching. Approximately 30% of infants with MAS require ventilator support<sup>(25)</sup>. These infants tend to breathe on their own to some degree. Compared with non-synchronized ventilation, infants treated with patient-triggered ventilation (synchronized intermittent mandatory ventilator SIMV, assist control ventilation ACV) required less sedation and were associated with shorter duration of mechanical ventilation. There is limited experience with the other two new modes of ventilation – pressure regulated volume control ventilation PRVCV and SIMV plus pressure support PS.

#### High frequency ventilation

High frequency ventilation (HFV) uses low pressure, and high frequency to recruit the collapsed alveoli, and delivers more homogeneous pulmonary ventilation and gas exchange. Clinical trials have shown that the HFV reduced the need for extracorporeal membrane oxygenation (ECMO) treatment and decreased air-leak in infants with PPHN. There are two types of high frequency ventilators available now in the United States: the Bunnell Life Pulse high-frequency jet ventilator (HFJV) and the SensorMedics high-frequency oscillatory ventilator (HFOV). The Infant Star was withdrawn from the market recently. HFV can be used as a primary mode of ventilator therapy or as rescue therapy when patients fail to respond to conventional ventilator. We use SIMV initially, how-



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ever, if infants require high PIP, high  $\text{FiO}_2$ , or are at a risk of developing air leak, we switch to HFOV. We allow cross-over treatment, since some babies respond differently from time to time. Clark et al. showed that among patients with severe respiratory disease, 63% who failed CMV responded to HFOV; and 23% vice versa.<sup>26</sup>

### Surfactant therapy

Meconium inactivates surfactant. Surfactant deficiency can further complicate MAS. Findlay et al. in a randomized, controlled study, concluded that surfactant replacement with 3 doses of 150 mg/kg (6ml/kg) beractant within 6 hours after birth improves oxygenation, reduces the incidence of air leaks, severity of pulmonary morbidity, requirement of ECMO treatment, and hospitalization time of term infants with MAS.<sup>27</sup> Other studies have showed similar results<sup>(28)</sup>. The acute side effects include transient oxygen desaturation and endotracheal tube obstruction occurring during bolus administration of surfactant. Surfactant can be given by bolus or slow infusion, although the dose is not defined. In our practice, we give 100 mg/kg of beractant through intra-tracheal indwelling catheter through the side hole of endotracheal tube to infants with severe MAS.

### Inhaled nitric oxide

Nitric oxide is a potent vasodilator. Inhaled NO (iNO) can be delivered to the alveoli and reach the vascular bed through a ventilator, resulting in selective pulmonary vasodilatation. Once in the bloodstream, NO is metabolized by hemoglobin, thus has limited systemic effects. In general, iNO is initiated when the oxygen index (OI) exceeds 25 and the starting dose is at 20 ppm. Although brief exposures to higher doses (40 to 80 ppm) appear to be safe, sustained treatment with 80 ppm iNO increases the risk of methemoglobinemia. The lowest effective initial dose for iNO in term newborns who have PPHN has not been determined, but sustained improvement in oxygenation has been demonstrated for doses lower than 10 ppm.<sup>29,30</sup> Methemoglobin and nitrogen dioxide concentration should be monitored q 4 to 12 hours. Serial echocardiograms are useful in monitoring the pressure gradients and myocardial functions of these infants. Patients usually are maintained on low dose of iNO (5-20 ppm) for 2-6 days, and then gradually weaned to avoid rebound hypoxemia.

The OI is calculated as:  $\text{OI} = (\text{mean airway pressure}) \times \text{FiO}_2 \times 100 / \text{post-ductal PaO}_2$ .

Initiating iNO treatment early at OI greater than 15 did not change the incidence of ECMO requirement or death, length of hospital stay, duration of mechanical ventilation or incidence of chronic lung disease.<sup>31</sup>

Combination of HFOV and iNO therapy is often more successful than treatment with HFOV or iNO alone in patients with PPHN especially those patients with RDS or MAS as underlying disease.<sup>32</sup>

### Steroid

Infants with severe MAS may also suffer from intrauterine hypoxia and have adrenal insufficiency. Physiological replacement with hydrocortisone may be helpful. However, a double blind trial using hydrocortisone did not show beneficial effect.<sup>33</sup> The anti-inflammatory effect of dexamethasone may decrease the risk of developing PPHN in animal models with MAS.<sup>8</sup>

### Phosphodiesterase (PDES) Inhibitor- Sildenafil, Milrinone

Sildenafil inhibits cGMP specific PDES type 5, increases cGMP concentration and may result in pulmonary vasodilatation or enhance the activity of nitric oxide. Because PDE-5 is primarily distributed within the arterial wall smooth muscle of the lungs and penis, sildenafil acts selectively in both these areas without inducing vasodilatation in other areas of the body. Sildenafil is only available in enteral form in the market. Revatio manufactured by Pfizer was approved by the FDA for the treatment of pulmonary hypertension in adults. Limited data are available in neonates. Baquero et al. reported oral sildenafil improved OI in infants with severe PPHN.<sup>34</sup> The dose is 0.3 to 1 mg/kg/dose via orogastric tube every 6 to 12 hours. The potential side effects include worsening of oxygenation, systemic hypotension and bleeding tendency.

Milrinone is a specific PDE<sub>3</sub> inhibitor which increases cAMP concentration, and decreases pulmonary vascular resistance.

### Extracorporeal membrane oxygenation (ECMO)

The use of adjunctive therapies dramatically decreased the need for ECMO therapy in the last decade,<sup>35</sup> but some infants with MAS and PPHN still developed persistent respiratory failure despite the optimal medical treatments.<sup>26</sup> ECMO provides cardiopulmonary support while allowing the underlying pulmonary or cardiac dysfunction to resolve without the risk of further injury from barotrauma or hyperoxia. The ECMO treatment results in 94% survival rate in these high risk infants who had predictive mortality rate of 80% without ECMO therapy.

The selection criteria include:

1. Gestation age of at least 34 weeks.
2. Birthweight of at least 2000g.
3. Lack of major coagulopathy or active bleeding.
4. No major intracranial bleeding.
5. Mechanical ventilation of less than 10-14 days duration and reversible lung disease.
6. Failure of optimal medical management and infants who have a high predicted mortality rate.

Oxygen index (OI) and alveolar-arterial difference in oxygen tension (A-aDO<sub>2</sub>) are commonly used to predict the likelihood of mortality. The OI of 40 or greater and/or A-aDO<sub>2</sub> greater than 600 mm Hg are predictive of 80% risk of mortality.

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### Potential therapy for PPHN

A number of vasodilators are now under investigation such as: calcium channel blockers- (nifedipine, diltiazem, verapamil), prostacycline (PGI<sub>2</sub>) analogues (epoprostenol, treprostinil, iloprost) and endothelin receptor antagonist (ETRA) (bosentan, sitaxentan and ambrisentan).

### Outcome of meconium aspiration syndrome

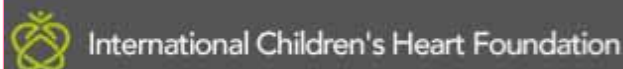
The mortality of MAS-related illness declined over the decades: 4.2% during 1973-1987 in USA to 2.5% during 1995-2002 in Australia and New Zealand.<sup>1,13</sup> The perinatal deaths are related to perinatal depression, airway obstruction and development of PPHN.

Pulmonary sequelae are common in infants with severe MAS. Nearly 50% of the infants had episodes of reactive airway diseases during the first six months of age. Mild airway obstruction or exercise-induced asthma was more common in these children at six to eight years.<sup>36,37</sup>

Long-term neurological outcomes of infants with MAS depend upon the underlying disorders. The neurologic outcomes are related to the presence or absence of intrauterine asphyxia, hypoxic-ischemic encephalopathy and PPHN. Infants who required ECMO treatment had more complications than those who did not.

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## Medical News, Products and Information

### Repeat C-Section Before 39 Weeks Raises Risk of Neonatal Illness

Newswise — Women choosing repeat cesarean deliveries and having them at term, but before completing 39 weeks gestation, are up to two times more likely to have a baby with serious complications including respiratory distress resulting in mechanical ventilation and NICU admission.

UAB researchers, led by Alan T.N. Tita, MD, PhD, Assistant Professor in the UAB Department of Obstetrics and Gynecology Division of Maternal-Fetal Medicine, and colleagues reported in a study published January 8, 2009 in the *New England Journal of Medicine* that women who choose to have their babies delivered via repeat cesarean at 37 or 38 weeks without a medical or obstetric indication, risk serious complications for their child.

"The Caesarean rate in the United States has risen dramatically, from 20.7% in 1996 to 31.1% in 2006. A major reason is the decline in attempted vaginal births after cesarean. Because elective cesareans can be scheduled to accommodate patient and physician convenience, there is a risk that they may be performed earlier than is appropriate," Tita said. "We knew from previous small studies that infants born before 39 weeks' gestation are at increased risk for respiratory distress. Because nearly 40% of the Caesarean performed in the United States each year are repeat procedures, we undertook this large study to describe the timing of elective repeat cesareans and assess its relationship with the risk of various adverse neonatal outcomes."

Tita and colleagues studied 13,258 women who had elective repeat cesarean sections at the 19 centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network from 1999 through 2002. They were selected from the Cesarean Section

Registry of the network. The registry contains detailed, prospectively collected information on nearly 50,000 women with a prior cesarean who underwent either repeat cesarean delivery or a trial of labor at the 19 centers over the 4-year period. The 13,258 women studied were those who underwent an elective Caesarean of a viable infant at 37 weeks gestation or later in the absence of labor or other obstetric or medical indications for early cesarean delivery (prior to 39 weeks).

The researchers looked at whether an infant who was delivered at 37 weeks later died or was diagnosed with a number of conditions, including respiratory distress syndrome and/or transient tachypnea of the newborn, newborn sepsis, seizures, necrotizing enterocolitis, hypoxic ischemic encephalopathy, required ventilator support within 24 hours of birth, had umbilical cord arterial pH (a measure of oxygenation) below 7.0, an Apgar score at five minutes of three or below, was admitted to a neonatal intensive care unit or required prolonged hospitalization.

Of the 13,258 women who had elective repeat cesarean sections, as many as 35.8 percent were delivered before 39 weeks. Babies born at 37 weeks, were two times more likely to suffer with conditions common to babies born too soon, and at 38 weeks, they were one and a half times more likely.

Tita said these findings, along with other studies, underscore the importance of not delivering a baby before 39 weeks for the sake of convenience.

"Unfortunately, these early deliveries are associated with a preventable increase in neonatal morbidity and NICU admissions, which carry a high personal and economic cost. These findings support recommendations to delay elective delivery until 39 weeks gestation and should be helpful in counseling women on the necessity of waiting to deliver."

### Masimo Launches First Non-adhesive Pulse Oximetry Sensor Designed For Extremely Low Birth Weight Babies

Masimo (Nasdaq: MASI), the inventor of Pulse CO-Oximetry and Measure-Through Motion and Low Perfusion pulse oximetry, announced a new SofTouch<sup>TM</sup> disposable pulse oximetry sensor developed specifically for the fragile skin and size of extremely low birth weight (ELBW) infants (<500 grams-1,000 grams) in conjunction with the *Neonatology 2008 Conference* in Miami, Florida. The new LNCS<sup>®</sup> SofTouch NeoPt-500 sensor is exclusively designed to fit ELBW babies and features special soft foam and non-adhesive attachments to prevent injury to even the most sensitive skin of premature infants.

Barbara Haley, CRTT, NICU Clinical Coordinator, Respiratory Care Services at California Pacific Medical Center in San Francisco, CA, stated, "We love the LNCS SofTouch NeoPt-500 for the improvement in care it facilitates. It is smaller than other neonatal sensors -- making it a near-perfect fit even for our smallest preemies -- and it is much softer on the skin to maintain skin integrity. We've also found that the NeoPt-500 makes nurses more efficient because the wrap is so much easier to apply and secure."

LNCS SofTouch NeoPt-500 is the first non-adhesive pulse oximetry sensor made specifically for the needs of newborns weighing down to 500 grams or less. At just 20 mm in size, the NeoPt-500 has dimensions that are smaller than typical neonatal sensors. This means that the distance between the emitter and detector on the NeoPt-500 is much smaller -- enabling the sensor to fit better and more securely on the tiniest hand or foot.

Mitchell Goldstein, MD, Associate Professor, Pediatrics at Loma Linda University Children's Hospital in Loma Linda, CA, stated, "The new LNCS(R) SofTouch NeoPt-500 sensor solves the problems associated with typical pulse oximetry sensors in ELBW



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infants. ELBW neonates are much more susceptible to skin burn injury and full thickness ulcer formations caused by improper sensor design and placement. Skin injury compromises the body's most basic protection mechanism and, in this most vulnerable population, the problems and risks associated with sensors not designed or intended for ELBW newborns have much greater consequences. Masimo is a unique company that not only understands this, but designs and develops clinically-relevant solutions to overcome these challenges."

Masimo SofTouch sensors are designed for single-patient use whenever skin sensitivity is a concern. SofTouch sensors incorporate a hook and loop wrap -- allowing the sensor to be quickly and securely applied on wet and slippery sites, and easily repositioned if necessary. Newborn skin is further protected by soft foam material that surrounds the sensor attachment for maximum comfort, and the NeoPt-500 contains no adhesive materials exposed to skin contact areas. This prevents epidermal stripping and skin trauma typically caused by applying and repositioning an adhesive sensor.

Joe E. Kiani, Founder and CEO of Masimo, stated, "The new LNCS SofTouch NeoPt-500 sensor underscores our core philosophy of 'doing what is best for patient care.' We believe that every patient deserves appropriate monitoring solutions. That's why Masimo provides over 100 different sensors, each uniquely designed to deliver the performance and measurement clinicians want -- including 15 different sensor options to address the challenging needs and specific requirements of neonatal patients."

For additional information about Masimo and its products - [www.masimo.com](http://www.masimo.com).

### World Breakthrough in Treating Premature Babies

A six-year study led by Dr. Maria Makrides from the Women's and Children's Health Research Institute and Professor Bob Gibson from the University of Adelaide has demonstrated that high doses of fatty acids administered to pre-term infants via their mother's breast milk or infant formula can help their mental development.

The findings were published in January 2009 in the *Journal of the American Medical Association* (JAMA).

Researchers found that a major lipid in the brain, the omega-3 fatty acid known as Docosahexaenoic acid (DHA), is not developed sufficiently in babies born before 33



weeks' gestation, leading to possible impaired mental development.

To counter this, increased doses of DHA (1000 mg per day) were administered to lactating mothers with pre-term infants, in the form of tuna oil capsules. If required, infants were given supplementary formula with matching DHA levels.

Of 657 premature babies tested in a trial involving five Australian hospitals, about 50% fewer infants on high-DHA diets had significantly delayed mental development compared with low DHA diets.

Premature girls in particular, who were exposed to DHA-rich diets, showed much better mental development than girls fed the low DHA diet.

Professor Gibson said his team was at a loss to explain why premature male babies, who are more susceptible to cognitive problems, did not respond to the same extent, with no obvious differences in mental development between the control group and those administered high doses of DHA.

"Boys may have a faster metabolic rate than girls and need higher doses of DHA to make a difference," he said. "We need to do a lot more work in this area to find out why."

Infants weighing less than 1250 gm (about a third of a full-term baby's weight) who were fed a high-DHA diet also scored better on the mental development scale, with a 40% reduction in the incidence of mild mental delay.

The project was primarily funded by the National Health and Medical Research Council, with the University of Adelaide and Women's and Children's Health Research Institute (WCHRI) now in the process of formalizing a joint venture agreement in the area of food, nutrition and health.

Dr. Makrides is the Deputy Director of the WCHRI, and Professor of Nutrition at the University of Adelaide. Professor Gibson is a Professor of Functional Food Science in the School of Agriculture, Food and Wine.

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