Yorkshire and Humber Neonatal ODN (South) Clinical Guideline

Title: Management of Meconium Aspiration

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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire and Humber Neonatal ODN (south). The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Best practice recommendations represent widely used evidence-based practice and high quality standards that all Neonatal Units across the Network should implement.

Subsequent suggested recommendations may be put into practice in local units.

However, alternative appropriate local guidelines may also exist.

A. Summary page - Quick reference guide

Delivery room management

- Appropriately trained staff should attend deliveries with meconium when indicated.
- Units should have local guidelines for the attendance of medical staff at deliveries with meconium.
- NLS guidance for the management of meconium at delivery should be followed
- Oropharyngeal suction on the perineum is not recommended (A)
- Actions to restrict respiratory effort after delivery are not recommended (D)
- Local units should ensure staff are competent in the management of infants delivered through meconium.
- Local units should ensure appropriate equipment is available to aspirate the trachea.
- Infants should be assessed and admission to NICU considered if there is a need for respiratory support, ongoing respiratory distress, evidence of encephalopathy or other clinical factors requiring NICU care.

Postnatal ward care

- Units should have a local guideline for postnatal observations in infants born through meconium. If any concerns arise the infant should be reviewed by the neonatal team. (D)

Management of meconium aspiration syndrome on the neonatal unit

All patients:

- Maintain a thermoneutral environment
- Maintain oxygen saturations 95-98%
- Support blood pressure with inotropes as required
- Commence first line antibiotics
- Consider the need for therapeutic hypothermia

Patients not mechanically ventilated:

- Nurse infants with mild respiratory distress in humidified oxygen, if required
- Avoid nasal CPAP
- Treat symptomatic pneumothoraces in non-ventilated patients

Ventilated patients:

- Treat all pneumothoraces
- Give sedation and have a low threshold for giving muscle relaxant
- Give surfactant 200mg/kg/dose
- Aim to use longer expiratory times
- Avoid high PEEP
- Arterial blood pressure and blood gas monitoring
- Consider use of transcutaneous monitoring to provide continuous CO2/O2 trends
- If there are increasing ventilatory needs/oxygen requirements/PPHN/resistant hypotension, early discussion with the tertiary centre should be sought with the possibility of transfer for further support of the infant.
- Consider potential need for ECMO at this time and/or when transport team commences inhaled nitric oxide.

B. Full guideline

1. Background

The prevalence of meconium at 38 weeks gestation is approximately 10%[1]. Meconium aspiration syndrome occurs in a small proportion of these infants. However, the mortality associated with MAS and pulmonary hypertension can be as high as 20%[2]. These infants can pose significant respiratory problems with a high incidence of pulmonary air leaks, hypotension and pulmonary hypertension.

2. Aim

To provide evidence-based recommendations to improve the management of infants delivered through meconium across the Yorkshire and Humber Neonatal ODN (south).

3. Areas outside remit

Antenatal obstetric management of meconium staining of the liquor was felt to be outside of the remit of this guideline.

4. Core guideline

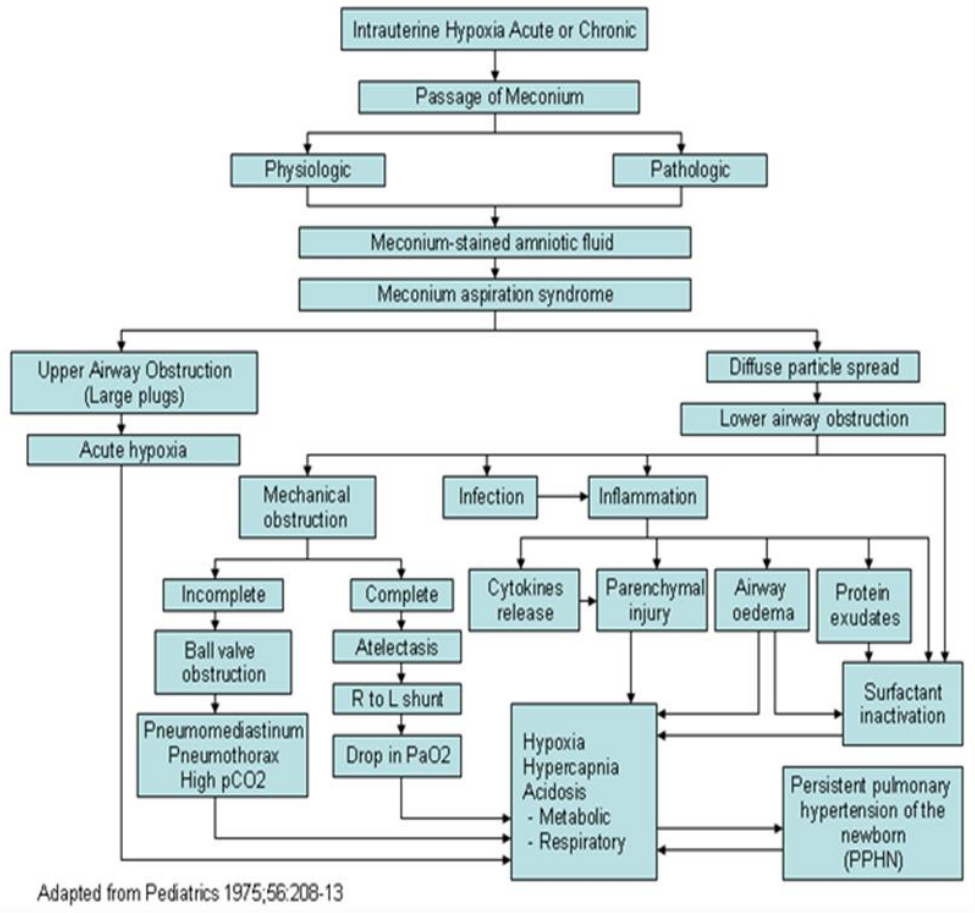
4.1 Introduction

Meconium is formed from 12-16 weeks gestation.

The frequency of meconium staining of the amniotic fluid increases with increasing gestational age:

- Prevalence of true meconium staining is <5% in pre-term infants and infection such as Listeria should be considered in this group.
- Prevalence increases to 10%+ after 38 weeks and 30% at 42 weeks gestation [1].
- Aspiration (meconium seen below the vocal cords) occurs in 20-30% of infants delivered through meconium.
- 1-9% of these infants develop meconium aspiration syndrome (MAS) [2].
- Mortality associated with MAS and pulmonary hypertension can be as high as 20%[2]. MAS is also associated with neonatal seizures and chronic seizure disorders [3].

Pathophysiology of Meconium Aspiration Syndrome



Passage of meconium in utero is typically thought to indicate fetal stress. Predisposing factors include breech presentation and gastroschisis. In some infants it may be a physiological maturational event. Fetal stress may be due to chronic or acute hypoxia, acidaemia or infection. Inhalation of meconium can occur antenatally, with fetal gasping stimulated by hypoxia, or during the intra-partum or postpartum stages. Meconium is also thought to affect the umbilical vessels causing vasoconstriction and fetal hypoperfusion.

Inhalation of meconium compounds the underlying pathology in a number of ways. Aspirated meconium causes mechanical obstruction resulting in air trapping and an increased risk of air leak (pneumothorax, pneumomediastinum). It also causes a chemical pneumonitis and inactivates surfactant. Although meconium is sterile these processes predispose to infection. This can result in pulmonary vasoconstriction and pulmonary hypertension, which can be a significant complication.

4.2 Delivery room management

A Neonatal Practitioner (ST1-3/ANNP) should attend the delivery when meconium staining of the liquor is present as guided by local guidelines. If there is thick meconium and the Neonatal Practitioner is not skilled at intubation senior help should be summoned as soon as possible. NLS guidance for the management of meconium at delivery should be followed including the use of pulse oximetry to monitor heart rate and oxygen saturations[4] .

There is no evidence to support:

- routine suction of the infant's nose/mouth on the perineum[5,6].

- compression of the neonatal thorax to minimise respiratory effort during transfer to the resuscitaire.

Normal thermal management of the infant should take place. Dry and wrap the baby whilst making an assessment.

Vigorous infants do not require any special measures[7]. If the baby is floppy, unresponsive and covered in thick meconium it is reasonable to inspect the upper airway under direct vision and the oropharynx cleared of material which might cause obstruction. However, in a bradycardic baby the emphasis MUST be to inflate the lungs within the first minute after birth and this should not be delayed[4]. There is no evidence to support routine tracheal suctioning in this situation unless there is evidence to suggest that the trachea is blocked[5].

If appropriate expertise is available, tracheal intubation and suction may be useful. However, if attempted intubation is prolonged or unsuccessful, start mask ventilation, particularly if there is persistent bradycardia[4].

Following resuscitation:
If the baby was born in poor condition with meconium in the lower airway, and is now pink in air, review clinically after 15 minutes. If there are any concerns, admit to the neonatal unit. If not, admit to the postnatal ward for regular observations (see section 4.3).

Infants requiring continued respiratory support, having evidence of encephalopathy or respiratory distress in the delivery room following resuscitation should be admitted to the Neonatal Unit.

Recommendations

- Appropriately trained staff should attend deliveries with meconium when indicated.
- Units should have local guidelines for the attendance of medical staff at deliveries with meconium.
- NLS guidance for the management of meconium at delivery should be followed.
- Oropharyngeal suction on the perineum is not recommended (B).
- Actions to restrict respiratory effort after delivery are not recommended (D).
- Local units should ensure staff are competent in the management of infants delivered through meconium.
- Local units should ensure appropriate equipment is available to aspirate the trachea.
- Infants should be assessed and admission to NICU considered if there is a need for respiratory support, ongoing respiratory distress, evidence of encephalopathy or other clinical factors requiring NICU care.

4.3 Postnatal ward care

Infants born through meconium, not requiring admission to the neonatal unit, should receive observations. The NICE guideline recommends when there has been significant meconium staining and the baby is healthy perform observations at 1 and 2 hours of age and then 2-hourly until 12 hours of age[8]. The guidance is less clear for ‘light’ meconium staining. A recent study from the Netherlands suggests that babies with and Apgar score >8 at 5 minutes can be safely discharged home. All babies with MAS in this study presented by 15 minutes of age[9]. Midwives should be asked to observe the baby closely for temperature, colour and responsiveness,

respiratory rate and effort, and muscle tone. They should contact the neonatal team if any signs of concern arise.

Recommendations

- Units should have a local guideline for postnatal observations in infants delivered through meconium. If any concerns the infant should be reviewed by the neonatal team (D).

4.4 Further management of meconium aspiration syndrome

For infants admitted to the NICU the following general measures should be undertaken. Also, consider the need for:

- Therapeutic hypothermia (see Y&H Guideline).
- Arterial (either peripheral or umbilical) and central venous access and obtain early as these infants require close and accurate monitoring of blood pressure as well as assessment of oxygenation and acid-base balance with arterial blood gases.
- Inotropic support to treat hypotension.
- Early discussion with the tertiary centre and/or transfer. In infants with increasing ventilatory and oxygen requirements or evidence of PPHN not responding to the general measures below early discussion with the tertiary centre consultant should be initiated for implementation of further strategies such as inhaled nitric oxide or HFOV.

4.4.1 General Measures

- **Maintain a thermoneutral environment**

Infants with severe MAS have often been hypoxic for a prolonged period of time.

  - Nurse in a thermoneutral environment of 36.0-37.0 ºC to minimise secondary reperfusion injury to the neonatal brain.
  - Consider the need for therapeutic hypothermia if the infant meets the criteria (see Guideline Y&H Therapeutic Hypothermia).

- **Undertake appropriate investigations**
  - **CXR** - will often demonstrate a spectrum of disease from widespread patchy infiltration, +/- small pleural effusions, to diffuse homogenous opacification. With severe disease a picture similar to CLD can be seen as the disease progresses.
  - Blood tests are indicated to rule out infection and should include an FBC, CRP and blood culture.

If clinical evaluation show mild distress and laboratory tests are negative, no further testing is required unless respiratory distress persists.

  - Infants with severe respiratory distress should be immediately assessed with dual pulse oximetry. A difference of ≥ 5% - 10% between the pre-ductal and post-ductal saturations suggests a right→left shunt from the pulmonary artery to the descending aorta. This indicates the presence of PPHN.
  - An ECHO may be useful in severe cases of MAS to rule put congenital cyanotic heart disease and to assess pulmonary vascular resistance.
  - Cranial ultrasound – performed if neurological damage is suspected (hypotonia, seizures) which may show hypoxaemic brain injury, hypodensity, cerebral oedema or ICH

- CFAM if abnormal neurology, hypotonia or seizures – may show seizure activity, decreased amplitude (diffuse oedema or diffuse injury)

- **Provide respiratory support - See section below.**

- **Avoid hypotension**
  - Consider intra-arterial monitoring early
  - Use inotropes to maintain the systemic blood pressure and reduce right to left shunting. See guideline for management of Neonatal Hypotension.
    - Other strategies for improving pulmonary hypertension include; maintaining adequate oxygenation - oxygen is a potent pulmonary vasodilator, minimal handling, sedation and paralysis to reduce the incidence of acute pulmonary hypertensive crises.

- **Start antibiotics**

Although meconium is a sterile substance the mechanical obstruction in the distal airways predisposes to infection.
  - Use routine antibiotics in these infants unless otherwise indicated.

- **Minimal handling**

  This helps to minimise pain and reduce pulmonary hypertensive crises.

- **Maintain nutrition**
  - Consider parenteral nutrition in infants requiring prolonged ventilatory support.

Recommendations

All patients:

- Maintain a thermoneutral environment.
- Maintain oxygen saturations 95-98%.
- Support blood pressure with inotropes as required.
- Commence first line antibiotics.
- Consider the need for therapeutic hypothermia.

4.4.2 Respiratory

A spectrum of respiratory disease is seen in meconium aspiration syndrome. Infants should be managed with adequate respiratory support dependent upon clinical condition indicated by:

a) Effort of breathing.
b) Oxygen requirement – aim to keep oxygen saturations 95-98%.
c) Blood gas indices.

<u>Mild respiratory distress</u>

- Behave as a variant of transient tachypnoea of the newborn.
- Symptoms and signs persisting for 24 to 48 hours.
- Typically have normal/near normal blood gas indices.
- Manage with humidified oxygen, if required.
- Non-tension pneumothoraces may not always need treatment. However, infant must be closely observed.

Pneumothorax

- If there is clinical suspicion of a pneumothorax transillumination and/or a chest x-ray should be performed immediately. In an infant with MAS who is not collapsed it is advisable to obtain a chest x-ray.

Moderate-severe respiratory distress

- Due to mechanical obstruction of the distal airways with meconium. The ball-valve effect results in increased airway resistance, pulmonary over-expansion and a significantly increased incidence of pneumothorax and other air leaks.
- Thorax may look hyperinflated with a barrel appearance and increased anterior-posterior diameter.
- Chest x-ray with hyperexpanded lung fields, along with widespread patchy infiltrations and in 20-30% of cases small pleural effusions may be seen.
- In infants with spontaneous breathing and good respiratory effort, CPAP can be cautiously considered if FiO2 >0.4 to maintain saturations within normal limits[16].
- CPAP should be avoided in presence of air leaks and air trapping on CXR. Complications include abdominal distension, air trapping because of underlying ball-valve mechanism or excessive flow, and distending pressure.

Ventilation

- Aim to optimise oxygenation whilst minimising air-trapping.
- Use of conventional modes is recommended aiming to use longer expiratory times to allow gas removal from the lungs.
- High positive end expiratory pressures should be used with caution.
- Low threshold for commencing sedation and muscle relaxation as have a role in the management of persistent pulmonary hypertension and reducing the incidence of air trapping and pneumothorax.
- Regular CXR may be required for patients requiring mechanical ventilation.
  Arterial blood gases should be frequently reviewed and the use of transcutaneous PaCO2 and PaO2 monitoring, in addition to routine saturation monitoring, is encouraged. Good oxygenation, PaO2 > 10 KPa, should be achieved whilst the paCO2 and pH should be maintained in the normal range, 4-6 KPa and >7.3 respectively, to avoid exacerbation of pulmonary hypertension.

- Pneumothoraces require treatment with chest drain insertion.
- Calculate the Oxygenation Index to help guide management (see section 4.5 below for more details):

$$\text{OI} = \frac{\text{MAP (cm of water)} \times \text{FiO2 (\%)}}{\text{Post-ductal PaO2 (mmHg)}} \qquad (1\ \text{KPa} = 7.5\ \text{mm Hg})$$

Surfactant

Meconium in the airways causes inactivation of surfactant. This is an ongoing process and results in alveolar collapse and hence V/Q mismatch. In a Cochrane Review, it was concluded that surfactant administration in MAS may reduce the severity of respiratory illness and decrease the number of infants with progressive respiratory failure requiring support with ECMO. There is no evidence that surfactant therapy reduces mortality[10].

- Give surfactant 200mg/kg to all infants requiring intubation for MAS.
- A second (and subsequent doses) should be given dependent upon clinical status rather than a defined time period. Subsequent doses may also be indicated, and further administration should be discussed with the consultant.

Other strategies

Consider:

Surfactant lavage – Animal studies suggest a benefit from surfactant lavage. This has also been demonstrated in a small human study (66 randomised infants) where two 15ml/kg aliquots of dilute surfactant were instilled and recovered from the lung. There were minimal side effects seen and although the duration of respiratory support was not altered fewer infants undergoing lavage died or required ECMO[11]. Lavage transiently reduced oxygen saturation without substantial heart rate or blood pressure alterations. Mean airway pressure was more rapidly weaned in the lavage group.

- Study protocol – Surfactant diluted with 0.9% saline to give a final concentration of 5mg/ml.
- Two aliquots of 15ml/kg administered, with a recovery period between administrations to allow oxygen saturations to reach > 80%. Lavage fluid was instilled via a catheter placed 0.5cm beyond ETT tip over 20 seconds. This was followed by three positive pressure inflations (PIP as high as 30cmH2O) and then as much fluid as possible removed using suction at-150mmHg pressure[11] .
- Lung lavage may be beneficial, but further clinical trials are needed to determine long-term outcomes[12,13].

Not Indicated:

- **Bronchial lavage with saline** has been shown to be dangerous and should not be performed[14.]
- **Physiotherapy** - not indicated in the treatment of meconium aspiration syndrome. It may be used in the management of further complications after the first few days.
- **Steroids** - There is insufficient evidence to support the use of corticosteroids in the management of MAS[15].
- Although **amnioinfusion** may be helpful in reducing cord compression in oligohydramnios. Antepartum management (amnioinfusion): therefore, is a beneficial effect in reducing the presence of meconium below the cord and lowering caesarean section rate. However, routine prophylactic amnioinfusion has not been shown to be beneficial in reducing MAS , therefore amnioinfusion is not recommended (A)

Recommendations

Patients not mechanically ventilated:

- Nurse infants with mild respiratory distress in humidified oxygen, if required.
- Avoid nasal CPAP.

- Treat symptomatic pneumothoraces in non-ventilated patients.

Ventilated patients:

- Treat all pneumothoraces.
- Give sedation and have a low threshold for giving muscle relaxant.
- Give surfactant 200mg/kg/dose.
- Aim to use longer expiratory times.
- Avoid high PEEP.
- Arterial blood pressure and blood gas monitoring.
- Consider use of transcutaneous monitoring to provide continuous CO2/O2 trends.

4.4.3 Discussion with and/or transfer to tertiary centre

Infants with MAS requiring mechanical ventilation can have complex and challenging needs with significant PPHN and ventilatory support. They may benefit from management strategies available at the tertiary centre e.g. HFOV and iNO. Therefore, early discussion with the tertiary centre should be facilitated in particular if the peak inspiratory pressure is ≥ 26 cmH20, if there is progressive respiratory deterioration or high oxygen requirements or unresponsive hypotension. These discussions may or may not result in the transfer of the infant. Please refer to the Network Indications for Transfer and Seeking Advice from Tertiary Centre Guideline.

Consider infants with:

i. Progressively worsening or persistently poor blood gases (pH <7.22) on 3 consecutive blood gases over a six hour period despite appropriate interventions.
ii. increasing oxygen requirements or persistently high oxygen requirements >60% for 6 hours, despite appropriate interventions.
iii. increasing pressure requirements or persistently high (≥26 cmH20) pressure requirements for 6 hours.

The need for ECMO should also be considered at this time and it is appropriate to liaise with the tertiary centre and local ECMO centre if:

- Oxygenation Index ≥ 25
- Continued deterioration.
- No immediate response to inhaled nitric oxide when commenced by the transport service.

Recommendations

- If there are increasing ventilatory needs/oxygen requirements/PPHN/resistant hypotension early discussion with the tertiary centre should be sought with the possibility of transfer for further support of the infant.

4.5 Further respiratory management – tertiary centre

HFOV

High frequency oscillation may be used when conventional ventilation is failing. However, it may further exacerbate gas trapping. High frequency oscillation may however be an appropriate ventilation strategy later in the course of the disease as lung disease becomes homogenous.

- Commence MAP 2 cmH20 above that on conventional ventilation. Infants require early and repeated chest x-rays.

Nitric Oxide

Echocardiographic evaluation is recommended before initiating nitric oxide therapy to rule out cardiac disease and to assess pulmonary artery pressure and ventricular function.
The use of nitric oxide with an initial concentration of 20ppm[16] in the management of meconium aspiration syndrome is recommended. The oxygenation index (OI) is a measure of the severity of hypoxic ischaemic failure. If the OI is greater than 25 and conventional ventilatory support, blood pressure and perfusion have been optimized inhaled nitric oxide therapy may be beneficial.

Oxygenation Index (OI)

$$OI = \frac{\text{MAP (cm of water)} \times \text{FiO2 (\%)}}{\text{Post-ductal PaO2 (mmHg)}}$$

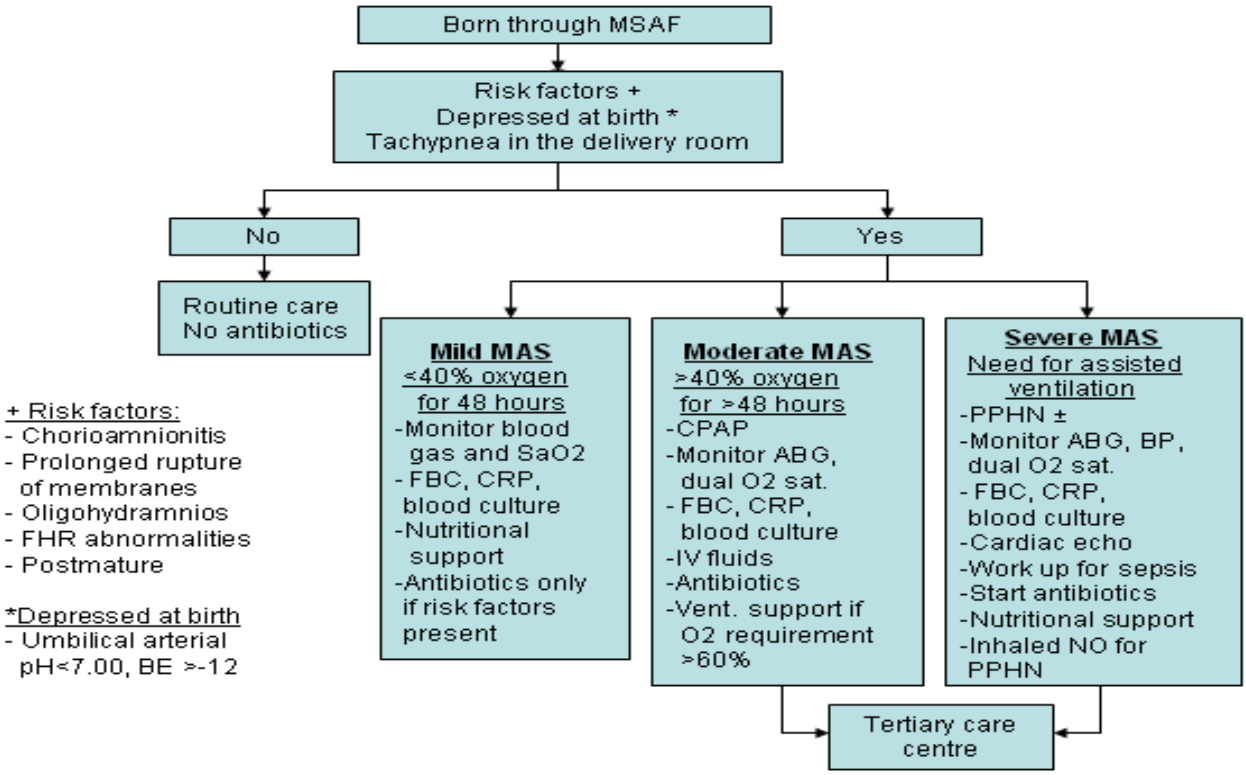
(1 KPa = 7.5 mm Hg.)

Extra-corporeal Membranous Oxygenation (ECMO)

ECMO has been shown to be effective in mature infants with severe but potentially reversible respiratory failure. Its use in this category of infants, such as those with MAS, results in significantly improved survival without increased risk of severe disability amongst survivors[14].

Referral for ECMO should be discussed with the Consultant on-call when the Oxygenation Index is ≥ 25, if there is continuing deterioration with low PaO2, or lack of response to HFOV and/or inhaled nitric oxide.
Between 95% and 98% of babies with severe meconium aspiration syndrome who require ECMO survive.

Possible clinical presentations and management of infants born in Meconium stained amniotic fluid(MSAF)



5. Audit criteria

- Local guideline for attendance of medical practitioner at meconium delivery.
- Appropriate equipment is available in the delivery room for management of meconium.
- Staff have appropriate training to manage infants delivered through meconium in the delivery room.
- Appropriate dosage of surfactant given to all infants with MAS requiring mechanical ventilation.

6. References

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C. Appendices

1. Evidence grading

Appendix 1. Grades of recommendation

Grade	
A	Requires at least one meta-analysis, systematic review or RCT rated as 1++, and directly applicable to the target population, and demonstrating overall consistency of results
B	Requires a body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	Requires a body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+