The Epidemiology of Meconium Aspiration Syndrome: Incidence, Risk Factors, Therapies, and Outcome

Peter A. Dargaville, MBBS FRACP, MDa,b, Beverley Copnell, RN, RSCN, BAppSc, PhDa,c, for the Australian and New Zealand Neonatal Network

aDepartment of Pediatrics, Royal Hobart Hospital, Hobart, Australia; bNeonatal Research Group, Murdoch Children’s Research Institute, Melbourne, Australia; cDepartment of Neonatology, Royal Children’s Hospital, Melbourne, Australia

The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVE. We sought to examine, in a large cohort of infants within a definable population of live births, the incidence, risk factors, treatments, complications, and outcomes of meconium aspiration syndrome (MAS).

DESIGN. Data were gathered on all of the infants in Australia and New Zealand who were intubated and mechanically ventilated with a primary diagnosis of MAS (MASINT) between 1995 and 2002, inclusive. Information on all of the live births during the same time period was obtained from perinatal data registries.

RESULTS. MASINT occurred in 1061 of 2 490 862 live births (0.43 of 1000), with a decrease in incidence from 1995 to 2002. A higher risk of MASINT was noted at advanced gestation, with 34% of cases born beyond 40 weeks, compared with 16% of infants without MAS. Fetal distress requiring obstetric intervention was noted in 51% of cases, and 42% were delivered by cesarean section. There was a striking association between low 5-minute Apgar score and MASINT. In addition, risk of MASINT was higher where maternal ethnicity was Pacific Islander or indigenous Australian and was also increased after planned home birth. Uptake of exogenous surfactant, high-frequency ventilation, and inhaled nitric oxide increased considerably during the study period, with 50% of infants receiving ≥1 of these therapies by 2002. Risk of air leak was 9.6% overall, with an apparent reduction to 5.3% in 2001–2002. The duration of intubation remained constant throughout the study period (median: 3 days), whereas duration of oxygen therapy and length of hospital stay increased. Death related to MAS occurred in 24 infants (2.5% of the MASINT cohort; 0.96 per 100 000 live births).

CONCLUSIONS. The incidence of MASINT in the developed world is low and seems to be decreasing. Risk of MASINT is significantly greater in the presence of fetal distress and low Apgar score, as well as Pacific Islander and indigenous Australian ethnicity. The increased use of innovative respiratory supports has not altered the duration of mechanical ventilation.
Meconium aspiration syndrome (MAS) is a disease of the term and near-term infant that is associated with considerable respiratory morbidity. The disease is characterized by early onset of respiratory distress in a meconium-stained infant, with poor lung compliance and hypoxemia clinically and patchy opacification and hyperinflation radiographically. At least one third of infants with MAS require intubation and mechanical ventilation, and newer neonatal therapies, such as high-frequency ventilation (HFV), inhaled nitric oxide (iNO), and surfactant administration are often brought into play.

In previous epidemiologic studies, some important risk factors for the development of MAS have been identified, either within the general birth population or among infants born through meconium-stained amniotic fluid (MSAF). The presence of fetal compromise, indicated by abnormalities of fetal heart rate tracings and/or poor Apgar scores, is known to increase the risk of MSAF and of MAS in the meconium-stained infant. Cesarean delivery is also associated with a heightened incidence of MAS. There is an apparent relationship between maternal ethnicity and risk of MSAF and the suggestion in several reports of an increased risk of MAS in black Americans and Africanans and Pacific Islanders. Advanced gestation has also been recognized as a risk factor, both for MSAF and of MAS.

Therapy for infants with MAS, in particular, those requiring intubation, is evolving rapidly. There is, however, a paucity of longitudinal data examining the proportional uptake of newer therapies in ventilated infants with MAS. Similarly, whereas it is clear that severe MAS is associated with a relatively high risk of pneumothorax and a relatively long duration of respiratory support and oxygen therapy, the specific factors that predict severe disease and long ventilator course are incompletely characterized. The mortality has been quoted as lying between 5% and 37%, with the marked disparity in published figures being attributable to the difficulties in identifying the cause of death (respiratory versus non-respiratory) and the skewed populations in which the mortality risk is calculated.

A complete understanding of the epidemiology of MAS has been hampered by the lack of population-based studies and by difficulties in assembling large cohorts of infants with confirmed disease. We have sought to remedy this situation using the database of the Australian and New Zealand Neonatal Network, supplemented by data from perinatal data registries. Our aims with this study were to examine current indicators and longitudinal trends for (1) the incidence of MAS, (2) the risk factors for MAS among all live births, (3) the treatments applied to ventilated infants with the disease, and (4) the complications and outcomes. In view of the difficulty in reliably recognizing cases of mild to moderate MAS, this investigation focused on infants with relatively severe disease in whom intubation and mechanical ventilation were required.

METHODS

Data on infants with MAS were obtained from the database of the Australian and New Zealand Neonatal Network (ANZNN). This is a voluntary collaboration between all 28 level III NICUs that was established in 1994 to monitor the care of high-risk newborns. A minimum data set has been developed, with any infant satisfying any of the following criteria being included in the database: (1) need for assisted ventilation either through an endotracheal tube or via nasal/nasopharyngeal continuous positive airway pressure (nCPAP), (2) need for major surgery, (3) gestation <32 weeks, and (4) birth weight <1500 g. Data are supplied to ANZNN in identified form by the individual units and are checked for errors. For each infant, a primary respiratory diagnosis is entered.

For this study, the ANZNN database for the years 1995–2002 was searched for infants >35 weeks’ gestation with a primary respiratory diagnosis of MAS. The ANZNN defines MAS in a meconium-stained infant as respiratory distress within 12 hours of age, displaying symptoms such as hypoxia, tachypnea, gasping respirations, and signs of underlying asphyxia, with a chest radiograph showing overexpansion of the lungs with widespread coarse infiltrates. It is important to note that the diagnosis of MAS is ascribed by the clinicians responsible for supplying data to the ANZNN database. This analysis focused on cases of MAS requiring intubation and mechanical ventilation (MAS$_{int}$). Infants with MAS treated with nCPAP only were excluded; such infants, although meconium-stained, may have other diagnoses as the predominant cause of respiratory distress, for example, transient tachypnea of the newborn. All of the available antenatal and intrapartum data and information pertaining to severity of the disease and medical management, were extracted from the identified records. The presence of intrauterine growth retardation was noted, defined as birth weight less than the 10th percentile derived from Australian normative data. For infants who died, the cause of death was classified as being respiratory or nonrespiratory (ie, directly related or not related to the aspiration of meco-
nium) based on the International Classification of Diseases code numbers and additional diagnostic information entered in the ANZNN database.

Information regarding the total birth population in Australia and New Zealand was also obtained for the years 1995–2002. Data were gathered on the total numbers of live births and the incidence of potential risk factors for MAS that could be matched to the ANZNN MAS\textsubscript{INT} cohort. These factors included maternal ethnicity, gender, place of birth, mode of delivery, gestational age, and condition at birth as indicated by 5-minute Apgar score. Australian data were obtained from the annual reports of the Australian Institute of Health and Welfare.\textsuperscript{30} Where variables were reported in terms of the number of confinements, the same percentage was used to project the number of live births. Variables treated in this manner were indigenous births, home births, delivery by cesarean section, and instrumental deliveries. Where data were stated to be missing or incomplete from some states or territories (eg, the classification of cesarean section as “emergency” or “elective”), the national average and previous trends were used to calculate the totals.

For New Zealand, the total number of live births for each year and data on maternal ethnicity and infant gender were obtained from electronic documents made available by Statistics New Zealand.\textsuperscript{31} Data on type of delivery between 1999 and 2002 and numbers of instrumental vaginal deliveries between 1995 and 1998 were obtained from the Ministry of Health reports on maternity (eg, refs 32 and 33). Numbers of emergency and elective cesarean section deliveries were not separately reported in the years 1995-1998, and estimates have been made from subsequent trends. No reliable data on home births in New Zealand were available. Summary statistics on gestational age and 5-minute Apgar score were reported differently from Australian data and could not be included in the overall data set. For both countries, numbers of infants born in tertiary hospitals were obtained from the annual reports of the ANZNN.\textsuperscript{26}

Summary statistics were generated for all variables in the MAS data set. The duration of intubation and nCPAP were summed to give duration of respiratory support. No assumptions were made about the distribution of continuous variables. For binary and continuous variables, simple comparisons were made with $\chi^2$ and Mann-Whitney tests, respectively; longitudinal trends in these variables were examined using the $\chi^2$ test for trend and linear regression, respectively. For all tests, a $P < .05$ was considered statistically significant. Within the MAS\textsubscript{INT} cohort, predictors of duration of respiratory support were sought using multiple linear regression analysis, with addition of all of the relevant variables to the model in a stepwise manner. Binary variables were entered as 1 or 0. Multivariate analysis could not be applied to the entire birth population because of lack of access to specific data from each individual without MAS\textsubscript{INT}.

**RESULTS**

Between 1995 and 2002, 1061 infants were admitted to a level III NICU in Australia or New Zealand with MAS\textsubscript{INT}, with the number ranging between 109 and 150 annually. An additional 107 infants with MAS treated with nCPAP only were excluded along with 2 infants with a primary diagnosis of MAS in whom no respiratory support was required. Median gestation for infants with MAS\textsubscript{INT} was 40 weeks (interquartile range: 39–41 weeks), median birth weight was 3400 g (interquartile range: 3000–3700 g), and 52.4% were male. Overall, 42% of infants with MAS\textsubscript{INT} were born in a tertiary hospital, with the proportion being higher in New Zealand than Australia (64% vs 31%; $P < .001$).

During the study period, there were 2 490 862 live births in the 2 countries, giving an overall rate of MAS\textsubscript{INT} of 0.43 per 1000 live births. In Australia, there were 894 infants with MAS\textsubscript{INT} in 2 038 666 live births and in New Zealand, 167 cases in 452 196 live births, yielding rates of MAS\textsubscript{INT} of 0.44 and 0.37 per 1000 live births, respectively. Combined longitudinal data from both countries revealed an overall decrease in the incidence of MAS\textsubscript{INT} to a low of 0.35 per 1000 in 2002 ($P = .0087$). Analysis by country shows a steady decrease in incidence in Australia between 1995 and 2002, with considerable fluctuation but no clear trend in incidence in New Zealand.

Figure 1 shows the rate of MAS\textsubscript{INT} per 1000 live births at each week of gestation (Australian data only). Between 36 and 40 weeks, the rate varied between 0.24 and 0.46 per 1000, with the lowest rate occurring at 38 weeks, and rose thereafter to a high of 1.42 per 1000 at

**FIGURE 1**

Incidence of MAS\textsubscript{INT} according to gestational age. Plot of incidence of MAS\textsubscript{INT} at each week of gestation; Australian data only. See text for comparisons between gestational age groups.
42 weeks and beyond. Thirty-four percent of the MAS\textsubscript{INT} cohort were at >40 weeks’ gestation and 6.5% at >41 weeks’ gestation compared with 16% and 2.0% of the total birth population (P < .001 in both cases). Figure 2 shows the trends in incidence of MAS\textsubscript{INT} by gestational age grouping during the study period. A decrease in incidence was noted over time at gestations >40 weeks but not at gestational ages between 36 and 40 weeks.

Antecedents of MAS\textsubscript{INT}, with analysis by year and by country, are shown in Table 1. More than half of the infants were noted to have fetal distress prompting obstetric intervention; 70% of these went on to deliver by cesarean section or assisted vaginal delivery. Cesarean section was the mode of delivery for 42% of the MAS\textsubscript{INT} infants overall. Fully 9.7% of the entire MAS\textsubscript{INT} cohort were delivered by cesarean section without labor, preceded by the recognition of fetal distress in 77% of cases and of intratamnit growth restriction in an additional 6%. The proportion of assisted vaginal deliveries decreased during the study period. The number of MAS\textsubscript{INT} infants with 5-minute Apgar score <7 and the number requiring intubation in the delivery room also decreased. Median Apgar scores at 5 minutes were lower among infants born in New Zealand (6 vs 7; P = .0012), and intubation in the delivery room for resuscitation was more commonly required (59% vs 43%; P < .001).

The impact of selected antecedents on the risk of MAS\textsubscript{INT}, using combined data from all years, is shown in Fig 3. There was a striking association between low 5-minute Apgar score and risk of MAS\textsubscript{INT}, with an odds ratio of 52. Among the demographic variables, infants born to Pacific Islander mothers in New Zealand and Aboriginal/Torres Strait Islander mothers in Australia were 3 times more likely to develop MAS\textsubscript{INT}, whereas infants born to Maori mothers had no increased risk. Gender of the infant was not a significant factor. All forms of assisted delivery increased the risk of MAS\textsubscript{INT} to some extent, with infants undergoing emergency cesarean section being at the highest risk, almost sixfold higher than other modes of delivery. Planned home birth was associated with a 2.7-fold increase in risk of MAS\textsubscript{INT}.

Figure 4 shows longitudinal trends in odds ratios for selected risk factors during the study period. There was considerable fluctuation in the odds ratio for most risk factors, with no clear trend over time. The risk for infants born to Aboriginal/Torres Strait Islander mothers did, however, increase markedly from 1998, such that in 2002 the risk of MAS\textsubscript{INT} was >7 times that of the non-indigenous population in Australia. Both emergency cesarean section and birth in a tertiary center showed a downward trend over the study period but continued to be associated with an increased risk of MAS\textsubscript{INT}. The odds ratio for an assisted vaginal delivery decreased rapidly and was <1 after 1997.

With the knowledge of the antecedents of MAS\textsubscript{INT} in the birth population overall, we sought to identify changes in the demography of live births that might explain the decrease in incidence of MAS\textsubscript{INT} in the latter years of the study period. Compared with 1995, in 2002, there were fewer deliveries beyond 41 weeks’ gestation (1.6% vs 2.8%; P < .001) and fewer infants with a 5-minute Apgar score <7 (1.4% vs 1.7%; P < .001). These factors combined account for 62% of the reduction in MAS incidence noted in this time period.

Table 2 shows the therapies received by infants with MAS\textsubscript{INT}. More than half of infants overall received either surfactant, HFV or iNO, with upward trends in the use of all of these therapies during the study period. Infants receiving $\geq$1 of surfactant, HFV, or iNO were intubated for a median of 5 days and required respiratory support for a median of 6 days, compared with 2 and 3 days, respectively, for infants who received none of these therapies. Only 1.1% of the MAS\textsubscript{INT} cohort required treatment with extracorporeal membrane oxygenation; all infants treated with this therapy survived.

Table 3 shows the complications and outcomes for the ANZNN MAS\textsubscript{INT} cohort. Although no clear trend was discernible for the whole study period, the incidence of air leak seemed to decrease in 2001–2002, being significantly lower for these 2 years compared with all of the other years (5.3% vs 10.8%; P = .013). Infants who developed air leak required respiratory support for a median of 5 days compared with 3.2 for those without this complication. In the MAS\textsubscript{INT} cohort overall, the duration of intubation and of respiratory support remained relatively constant during the study period; however, the duration of oxygen therapy and the length of hospital stay increased. The overall mortality was 6.6% (70 of 1061), with the majority of these deaths...
being because of perinatal asphyxia \((n = 33)\) or congenital anomalies \((n = 6)\). Death directly attributable to aspiration of meconium occurred in 24 infants, equivalent to 2.5% of the total MAS\textsubscript{INT} cohort and 0.96 per 100 000 live births. Mortality rates seemed to remain constant during the study period. Of the 24 infants whose death was directly related to MAS, 7 (29%) were in relatively good condition at birth, not requiring immediate intubation, and with a 5-minute Apgar \(\geq 7\). Air leak occurred in 42% of MAS-related deaths compared with 13% of infants dying from other causes \((P = .037)\) and 8.6% of survivors \((P < .001)\). Infants dying of MAS were more likely to have received surfactant, HFV, or iNO \((P = .037)\), but 5 infants received none of these therapies.

Forty-nine infants received home oxygen, with requirement for this therapy increasing during the study period. These infants had a longer duration of respiratory support, with a median of 7 days, compared with 3.8 days for infants who did not require home oxygen \((P < .001)\). They were also more likely to receive surfactant \((P < .001)\), HFV \((P = .038)\), and iNO \((P < .001)\), and were less likely to require assisted vaginal delivery \((P = .038)\). Mortality rates for these infants were higher than for those who did not receive surfactant \((P = .001)\), HFV \((P < .001)\), or iNO \((P = .003)\), but lower than for those who received all three therapies \((P = .001)\).

### TABLE 1: Antecedents of MAS Among the ANZNN MAS\textsubscript{INT} Cohort

|----------|-----------|-----------|-----------|-----------|-----------------
| Fetal distress noted, % of total | 51.1 | 45.3 | 55.5 | 54.0 | ↑ (0.19)
| All CS, % of total | 41.8 | 40.4 | 39.9 | 47.1 | Nil
| CS in labor, % of total | 32.0 | 30.6 | 31.9 | 34.8 | Nil
| Assisted vaginal delivery, % of total | 11.1 | 16.1 | 7.8 | 7.9 | ↓ (<.001)

**Appgar scores**
- At 1 min, median, IQR: 4 (2–6) to 4 (2–6) to 5 (2.5–6)  \(↑ (0.017)\)
- At 5 min, median, IQR: 7 (5–8) to 7 (5–8) to 7 (5–8)  \(↑ (0.029)\)
- < 7 at 5 min, % of total: 46.7 to 47.2 to 39.2  \(↓ (0.017)\)

**Intubated in delivery room, % of total:** 46.1 to 45.5 to 38.2  \(↓ (0.006)\)

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\(\text{TSI indicates Torres Strait Islander; } \text{“All CS,” all cesarean-section deliveries.}\)

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**FIGURE 3**
Risk factors for MAS\textsubscript{INT} within the total birth population: plot of odds ratios (\(\bigcirc\)) and 95% confidence interval (--- and ----) for selected risk factors for MAS\textsubscript{INT}. Odds ratio (95% confidence interval) also indicated as text.\(^a\) Australian data only; \(^b\) New Zealand data only. 

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**FIGURE 4**
Longitudinal trends in odds ratio for selected risk factors. Plot of odds ratio by year for ethnicity (A), place and mode of delivery (B), and 5-minute Apgar score (<7) are shown. 

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\(\text{TSI indicates Torres Strait Islander; } \text{“All CS,” all cesarean-section deliveries.}\)
In multiple linear regression analysis, duration of respiratory support in MAS\textsubscript{INT} survivors was found to be predicted by the following binary variables: cesarean section in labor (coefficient: 1.33; \( P = 0.003 \)), fetal distress (coefficient: 1.05; \( P = 0.012 \)), indigenous Australian or Pacific Islander ethnicity (coefficient: 1.38; \( P = 0.019 \)), and male gender (coefficient: 0.82; \( P = 0.040 \)). Gestational age, intrauterine growth restriction, and 5-minute Apgar score did not independently predict duration of respiratory support when added to the model.

**DISCUSSION**

In this study we investigated the epidemiology of MAS in a large cohort of ventilated infants, with reference to available data for the entire birth population during the same period. We found that during the period 1995–2002, there was a reduction in the incidence of MAS\textsubscript{INT} to <0.40 cases per 1000 live births, a strong association of MAS\textsubscript{INT} with low 5-minute Apgar score, a clear increase in risk in Pacific Islander and indigenous Australian pregnancies, and a similar association with advanced gestation to that noted previously. A heightened risk of MAS\textsubscript{INT} was also noted after planned home birth. Our data show a median duration of respiratory support of 4 days, with 31%, 19%, and 30% of cases receiving exogenous surfactant, HFV, and iNO, respectively. Mortality directly attributable to MAS was 2.5% in the MAS\textsubscript{INT} cohort.

A strength of this study lies in the large numbers of infants with MAS\textsubscript{INT} in the ANZNN cohort (1061 infants), in whom a relatively large individual data set has been assembled. In addition, ANZNN data entry allows only 1 primary respiratory diagnosis, with MAS being a clearly defined and distinct entity. This allows exclusion of meconium-stained infants with minimal evidence of parenchymal disease in whom the main diagnosis is PPHN. We have also had the advantage of obtaining data from large perinatal data registries in both countries, meaning that the findings in the ANZNN cohort can be placed in the context of the total population of 2 490 862 live births in which the cases of MAS\textsubscript{INT} occurred.

The low incidence of MAS\textsubscript{INT} and its apparent reduction during the study period confirm that modern obstetric practices can, for the most part, interrupt the chain of events that results in significant aspiration of meconium. The reduction in incidence cannot be ascribed to more zealous delivery room management, in particular, tracheal suctioning. Indeed, in the latter part of the study period, routine intubation of the trachea after MSAF was largely abandoned in Australia and New Zealand, contemporaneous with the publication of a randomized, controlled trial finding no benefit from this intervention in the vigorous infant.\textsuperscript{15} The decrease in incidence parallels the findings of Yoder et al.,\textsuperscript{8} who, in selected birth cohorts from the same time period, found a reduction in risk of MAS, attributed to avoidance of postmaturity and more aggressive management of suspected fetal distress. The reduced incidence of MAS\textsubscript{INT} over time in the present study would seem to relate to similar factors, with advanced gestation and the propor-

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Therapies Received by the ANZNN MAS\textsubscript{INT} Cohort</th>
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<tbody>
<tr>
<td>Surfactant, any type</td>
<td>30.8</td>
</tr>
<tr>
<td>HFV</td>
<td>19.1</td>
</tr>
<tr>
<td>INO</td>
<td>29.5</td>
</tr>
<tr>
<td>ECMO</td>
<td>1.1</td>
</tr>
<tr>
<td>Surfactant or HFV</td>
<td>42.4</td>
</tr>
<tr>
<td>Surfactant or HFV or INO</td>
<td>50.6</td>
</tr>
<tr>
<td>NCPAP used\textsuperscript{b}</td>
<td>24.2</td>
</tr>
</tbody>
</table>

Data shown are % of total in each case. ↑ indicates increased over time; ↓, decreased over time.

\( * \) Data on HFV and INO were not collected in 1995; all year percentages for these therapies, therefore, slightly underestimate the actual figures.

\( { }^{b} \) Either before or after the period of intubation and mechanical ventilation.

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<table>
<thead>
<tr>
<th>Table 3</th>
<th>Respiratory Outcomes and Complications in the ANZNN MAS\textsubscript{INT} Cohort</th>
</tr>
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<tbody>
<tr>
<td>Air leak, % of total</td>
<td>9.6</td>
</tr>
<tr>
<td>Duration of intubation, median (IQR), d</td>
<td>3 (2–6)</td>
</tr>
<tr>
<td>Duration respiratory support, median (IQR), d</td>
<td>4 (2–7)</td>
</tr>
<tr>
<td>Duration oxygen therapy, median (IQR), d</td>
<td>6 (3–15)</td>
</tr>
<tr>
<td>Length of hospital stay, median (IQR), d</td>
<td>13 (8–24)</td>
</tr>
<tr>
<td>Death, % of total</td>
<td>6.6</td>
</tr>
<tr>
<td>MAS-related death, % of total</td>
<td>2.5</td>
</tr>
<tr>
<td>Home oxygen, % of total</td>
<td>4.7</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; ↑, increased over time; ↓, decreased over time; “duration respiratory support,” the duration of intubation plus duration of nCPAP.
tion of infants having a 5-minute Apgar score <7 being seen to decrease from 1995–2002.

Our data analysis allowed the computation of odds ratios for a number of potential risk factors for MAS\(_{\text{NT}}\) in the total birth population. In Australian live births, we noted a very strong association with a 5-minute Apgar score <7, with an overall odds ratio of 52. This is, to our knowledge, the first population-based study to quantify the risk of MAS in relation to the condition of the infant at birth. The implication is that ~1.3% of all live-born infants with a 5-minute Apgar score <7 will subsequently be ventilated with MAS compared with 0.025% of those with a 5-minute Apgar score ≥7. Other cohort studies have documented the importance of condition at birth in determining the risk of MAS developing in the context of MSAF. For this latter association, Wiswell et al.\(^1\) using stepwise linear regression, reported an odds ratio of 21; others have found the risk to be approximately fourfold.\(^6,12\) There remains some dispute about how this effect is mediated; the presence of fetal distress requiring obstetric intervention in >50% of the ANZNN MAS\(_{\text{NT}}\) cohort suggests exaggerated fetal respiration and in utero aspiration of meconium as a possible mechanism.

The ethnology of MAS has been explored in this study, with the finding of a 3 times greater risk of MAS\(_{\text{NT}}\) in Pacific Islanders and indigenous Australians and, in the latter group, an apparent upsurge in risk in 2001 and 2002. These findings complement those of other investigators in identifying ethnic groups of heightened risk of MSAF and MAS. Black Americans and Africans have been found to have a risk of MSAF 1.5 to 2.6 times that of other ethnic groups,\(^7,10,17,19\) the explanation for which may lie in earlier attainment of fetal maturity and is not related to longer gestation.\(^19\) Pacific Islanders in New Zealand have a 1.8-fold increase in risk of MSAF.\(^18\) There are no published data regarding risk of MSAF or MAS in indigenous Australians. Our population-based estimate of the risk of MAS in Pacific Islanders (odds ratio: 2.7) is similar to that noted previously within a single hospital (odds ratio: 3.6)\(^20\) and cannot be entirely explained by the increase in the risk for MSAF noted in this group. At least within the MAS\(_{\text{NT}}\) cohort, we could not identify any other possible explanatory factors, with fetal distress, Apgar score, and gestation being equivalent among Pacific Islanders, indigenous Australians, and others (data not shown). The mechanism by which ethnicity imparts additional risk of MAS requires additional study. We found, as have others,\(^18\) no increase in the risk of MAS among the New Zealand Maori population.

The risk of MAS\(_{\text{NT}}\) among live-born infants was increased beyond 40 weeks’ gestation, with a 3.4-fold increase in risk at >41 weeks. Only 1 other population-based study has examined the relationship between gestation and risk of MAS, reporting an odds ratio of 2.9 for the risk of MAS beyond 41 weeks.\(^24\) The propensity to develop MAS at advanced gestation would seem to be related both to a higher risk of MSAF\(^10,17,21,23\) and an increased likelihood that MAS will occur in the presence of MSAF,\(^6,11,21\) independent of other risk factors, such as fetal distress and low Apgar scores.\(^8\)

We found that place of birth was a predictor of MAS\(_{\text{NT}}\) with a higher risk for infants born in tertiary centers (odds ratio: 1.65) and for planned home births (odds ratio: 2.74). This latter finding is in contrast to the reported outcome for planned home birth in Canada, where no apparent increase in the risk of either MSAF or MAS was noted.\(^34\) We also found cesarean delivery to be associated with MAS\(_{\text{NT}}\), as has been documented previously in a smaller birth cohort.\(^16\) The need for cesarean delivery is also known to be associated with a higher risk of subsequent MAS in the setting of MSAF.\(^11,12,15\) Fetal growth restriction has been linked previously to MAS,\(^24\) and we found a doubling of risk for MAS\(_{\text{NT}}\) in growth-restricted infants. Most infants with MAS\(_{\text{NT}}\) were, however, well-grown, with average birth weight being between the 25th and 50th percentile for gender and gestation.\(^29\)

A weakness of our investigation is that within the total birth population it was not possible to ascertain the incidence of MSAF, a requisite intermediary in the pathogenesis of MAS. This limits, to some degree, our capacity to distinguish whether the risk factors we defined within the population exert their effect by increasing the rate of MSAF, the risk of MAS in the presence of MSAF, or both. Similarly, for this study we did not have access to data from each individual in the total birth population and, thus, can perform only univariate data analysis. In the absence of multivariate regression analysis, it is not possible to define clearly whether the heightened risks of MAS\(_{\text{NT}}\) related to ethnicity and gestation are subsumed in a final common pathway of fetal distress or low Apgar score. These questions clearly need additional investigation in population-based epidemiologic studies.

Despite limited data to support the use of HFV and exogenous surfactant in MAS, both of these treatments were applied with increasing frequency over the study period. Anecdotally, HFV in the form of oscillatory or jet ventilation has been found to be effective in supporting infants with MAS\(^15,36\) and may be a contributing factor to the low requirement for extracorporeal membrane oxygenation in the ANZNN MAS\(_{\text{NT}}\) cohort. In a national survey of neonatal units in continental France, Nolent et al.\(^17\) found high-frequency oscillatory ventilation to be used for MAS in 27 of 29 units; a similar situation exists in Australia and New Zealand (P.A.D., unpublished data).

Of the trials of bolus surfactant therapy published during the study period,\(^38,39\) only that of Findlay et al.\(^38\) show clear benefits beyond an improvement in oxygen-
ation. It is, therefore, somewhat surprising that exogenous surfactant therapy has found such a prominent place in the treatment of MAS\textsubscript{INT}. In the latter years of the study period, exogenous surfactant was administered to \(\sim 40\%\) of all infants with MAS\textsubscript{INT}. No data are available in this study concerning surfactant dose and retreatment.

Among the ANZNN MAS\textsubscript{INT} cohort, 51\% of infants received \(\geq 1\) HFV, iNO, and exogenous surfactant, with a documented increase in this proportion from 1996 to 2002. The uptake of these newer therapies over the study period seems to have had no effect on the duration of intubation, and the duration of oxygen therapy and length of hospital stay have increased in the MAS\textsubscript{INT} cohort overall. These findings emphasize the supportive rather than curative nature of these therapies in infants with MAS\textsubscript{INT}.

The mortality risk for ventilated infants with MAS in Australia and New Zealand remains significant. Overall mortality was 6.6\%, with deaths directly attributable to the respiratory illness occurring in 2.5\% of the entire MAS\textsubscript{INT} cohort and 0.96 per 100 000 live births. This latter figure compare favorably with other population-based estimates of MAS-related mortality. Sriram et al\textsuperscript{7} found a mortality of 2.0 per 100 000 live-born infants in the United States in 1998–2000; Nolent et al\textsuperscript{37} report 1.03 deaths per 100 000 births in France in 2000–2001, but incomplete ascertainment of MAS\textsubscript{INT} cases in this study may limit the reliability of this estimate. These population-based estimates of mortality from MAS are generally markedly lower than those derived from hospital birth cohorts. The largest of these, studying cases of MAS in 7 hospitals in the United States during the years 1973–1987 (total birth population: 176 790), found a mortality rate of 28 per 100 000 live births.\textsuperscript{4} Another study found a mortality rate of 22 per 100 000 among 85 562 live births in 1 hospital in Saudi Arabia during the period 1989–1994.\textsuperscript{40} The apparent high mortality in hospital-based studies is a reflection of the high-risk birth populations from which the estimates are made and can be presumed to also be related to the time period in which the studies were done, before the advent of a number of newer therapies that seem to have improved outcome in MAS. Other more recent studies of smaller hospital-based cohorts have shown lower mortality, including, in several instances, no MAS-related deaths.\textsuperscript{8,41}

Pneumothorax remains an important complication of MAS, occurring in 9.6\% of the MAS\textsubscript{INT} cohort overall, with an apparent reduction to \(\sim 5\%\) in 2001–2002. Other recent studies have reported an incidence of pneumothorax in intubated infants of 8\%,\textsuperscript{38} 14\%,\textsuperscript{42} and 20\%,\textsuperscript{43} although this last study selected infants with more severe disease. Despite the advances in respiratory support for MAS, pneumothorax remains an important indicator of disease severity, being present in 42\% of infants who ultimately died of MAS in the ANZNN cohort.

Durations of intubation and respiratory support did not alter throughout the study period, although more infants received nCPAP either before or after mechanical ventilation. Disconcertingly, the duration of oxygen therapy and length of hospital stay increased during the study period, reaching a median of 8 and 17 days, respectively, in 2002. These figures emphasize the considerable burden that MAS continues to place on afflicted infants, their families, and the health care system.

CONCLUSIONS

We found in this study that the incidence of MAS requiring intubation in 2 countries in the developed world is low and seems to be decreasing. The risk of MAS\textsubscript{INT} is significantly greater in the presence of fetal distress and low Apgar score, as well as Pacific Islander and indigenous Australian ethnicity. MAS is now frequently treated with newer therapeutic modalities, such as HFV, iNO, and exogenous surfactant, but the duration of ventilation and oxygen therapy have not been improved as a result. Mortality for MAS\textsubscript{INT} is low, but there remains a significant risk of pneumothorax.

ACKNOWLEDGMENTS

We thank Deborah Donoghue and Samantha Abeywardana, past and current Australian and New Zealand Neonatal Network Project Officers, and the Directors and participating units of the Australian and New Zealand Neonatal Network: Australia: Professor John Whitehall (Women’s and Children’s Health Institute, the Townsville Hospital); Professor David Tudehope (Mother’s Hospital, Brisbane); Dr David Cartwright (Neonatology, Royal Women’s Hospital, Brisbane); Dr Chris Wake (NICU, John Hunter Hospital, Newcastle); Associate Professor Nick Evans (the John Spence Nurseries, Royal Prince Alfred Women and Infants, Sydney); Dr Robert Guaran (Newborn Care, Liverpool Health Service, Liverpool); Dr Robert Halliday (Neonatology, Children’s Hospital at Westmead, Sydney); Dr Kei Lui (Newborn Care, Royal Hospital for Women, Sydney); Dr Barry Duffy, PICU, Sydney Children’s Hospital, Sydney); Dr Lyn Downe (NICU, Nepean Hospital); Professor William Tarnow-Mordi (Neonatal Medicine, Westmead Hospital, Sydney); Associate Professor Graham Reynolds (Pediatrics and Child Health, Canberra Hospital, Canberra); Dr Andrew Watkins (Neonatology [Medical], Mercy Hospital for Women, Melbourne); Dr Andrew Ramsden (NICU, Monash Medical Centre, Melbourne); Dr Peter McDougall (Neonatal Services, Royal Children’s Hospital, Melbourne); Dr Neil Roy (Neonatal Services, Royal Women’s Hospital, Melbourne); Dr Chris Bailey (Pediatrics, Launceston General Hospital, Launceston); Associate Professor Peter Marshall (Centre for Perinatal Medicine, Flinders Medical Centre, Adelaide); Dr Ross
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HELMET USE AND RISK OF HEAD INJURIES IN ALPINE SKIERS AND SNOWBOARDERS

“Context: Although using a helmet is assumed to reduce the risk of head injuries in alpine sports, this effect is questioned. In contrast to bicycling or inline skating, there is no policy of mandatory helmet use for recreational alpine skiers and snowboarders.

Objective: To determine the effect of wearing a helmet on the risk of head injury among skiers and snowboarders while correcting for other potential risk factors.

Design, Setting, and Participants: Case-control study at 8 major Norwegian alpine resorts during the 2002 winter season, involving 3277 injured skiers and snowboarders reported by the ski patrol and 2992 non-injured controls who were interviewed on Wednesdays and Saturdays. The controls comprised every 10th person entering the bottom main ski lift at each resort during peak hours. The number of participants interviewed corresponded with each resort’s anticipated injury count based on earlier years.

Results: Head injuries accounted for 578 injuries (17.6%). Using a helmet was associated with a 60% reduction in the risk for head injury (odds ratio [OR], 0.40; 95% confidence interval [CI], 0.30–0.55; adjusted for other risk factors) when comparing skiers with head injuries with uninjured controls. The effect was slightly reduced (OR, 0.45; 95% CI, 0.34–0.59) when skiers with other injuries were used as controls. For the 147 potentially severe head injuries, those who were referred to an emergency physician or for hospital treatment, the adjusted OR was 0.43 (95% CI, 0.25–0.77). The risk of head injury was higher among snowboarders than for alpine skiers (adjusted OR, 1.53; 95% CI, 1.22–1.91).

Conclusion: Wearing a helmet is associated with reduced risk of head injury among snowboarders and alpine skiers.”


Noted by JFL, MD
The Epidemiology of Meconium Aspiration Syndrome: Incidence, Risk Factors, Therapies, and Outcome
Peter A. Dargaville, Beverley Copnell and for the Australian and New Zealand Neonatal Network
Pediatrics 2006;117;1712-1721
DOI: 10.1542/peds.2005-2215

This information is current as of June 15, 2006

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