Meconium Induces Only Localized Inflammatory Lung Injury in Piglets

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ABSTRACT

Neonatal meconium aspiration often produces severe respiratory distress due to an inflammatory pulmonary injury, but the extension of this damaging reaction to the noncontaminated lung regions is still uncertain. To investigate the presence of generalized pulmonary inflammatory response, 31 anesthetized and ventilated neonatal piglets (1–3 d) were studied. Meconium ($n = 16$) or saline ($n = 15$) was instilled unilaterally into the right lung, and analysis of the lung tissue or bronchoalveolar lavage (BAL) fluid from both lungs was performed after 12 h. Meconium increased the wet/dry weight ratio, histologic tissue injury score and tissue myeloperoxidase activity as well as BAL fluid total cell count in the contaminated lung. Tumor necrosis factor-alfa concentrations in BAL fluid did not however differ significantly. Furthermore, in the meconium-instilled lungs the tissue and lavage fluid catalytic activity of phospholipase A_2 (PLA_2) and tissue PLA_2 group-I and group-II concentrations were significantly elevated. Although BAL fluid catalytic activity of PLA_2 was moderately increased also in the meconium noninstilled lung, significant inflammatory injury in this lung was absent. The results thus indicate that meconium aspiration induces severe local inflammation and lung injury, but significant generalized pulmonary inflammatory damage in the pathogenesis of meconium aspiration syndrome is unlikely. (***Pediatr Res*** **54: 192–197, 2003**)

Abbreviations
MAS, meconium aspiration syndrome
BAL, bronchoalveolar lavage
MPO, myeloperoxidase
TNF-α, tumor necrosis factor alfa
PLA$_2$, phospholipase A_2

Despite aggressive perinatal treatment, meconium aspiration syndrome (MAS) still remains a significant cause of morbidity and mortality in term and postterm infants (1). The clinical syndrome is characterized by fetal or neonatal aspiration of meconium leading to severe respiratory distress with hypoxemia in the newborn, and may be further complicated by air leaks, persistent pulmonary hypertension, hypoxic organ damage and long-term pulmonary sequelae (2). The pathophysiology of MAS is very complex, including early mechanical obstruction of the airways (3), surfactant inactivation (4, 5), ventilation/perfusion mismatch and progressively developing patchy lung injury with areas of atelectasis and hyperexpansion (1, 6, 7). Aspirated meconium may directly damage the alveolar-capillary membrane and also frequently induces pulmonary inflammatory response, common to a variety of experimental lung injury models (8, 9), that are proposed to contribute to the development of the clinical pulmonary dysfunction (6, 7).

Pulmonary inflammatory response with neutrophil accumulation, supposedly initiated by meconium-induced activation of alveolar macrophages (10), seems to be present already within a few hours of exposure to meconium (6, 7, 11). Infiltration of activated neutrophils may initiate a cascade of events, including the release of reactive oxygen metabolites and production of inflammatory mediators, such as cytokines and lipid mediators (12, 13). This inflammatory reaction is associated with increased pulmonary vascular permeability, proteinaceous exudation into the alveolar spaces, inactivation of pulmonary surfactant and decrease in lung compliance, and may thus significantly contribute to the impairment of pulmonary function (6). In contrast to acid aspiration that rapidly leads to generalized inflammatory reaction potentiating the local injury (14, 15), the extension and significance of the pulmonary tissue inflammation in meconium aspiration is poorly known.

We hypothesized that, in addition to local damage, intrapulmonary meconium could induce also generalized pulmonary

inflammatory injury. We therefore developed a newborn piglet model, in which unilateral lung injury was caused by local meconium instillation, and examined both lungs for signs of inflammation and injury.

METHODS

Animal preparation. Thirty-one newborn (1–3 d) piglets weighing 1.6 to 2.4 kg from 17 maternal animals were studied. Animals were sedated with diazepam (1.5 mg/kg) i.m., and anesthetized with sodium pentobarbital (30 mg/kg) i.v. Tracheotomy was performed, a 3.5-mm internal diameter endotracheal tube was inserted with the distal tip located at least 1 cm proximal to the carina, and animals were placed on a pressure-controlled neonatal mechanical ventilator (Baby Bird, Bird Productions Corp., Palm Springs, CA, U.S.A.). The initial respiratory settings were: Fraction of inspired oxygen (FiO_2) 0.21, rate 30 breaths/min, peak inspiratory pressure (PIP) 20 cmH_2O and positive end expiratory pressure (PEEP) 4 cmH_2O. Anesthesia was maintained with a continuous i.v. infusion of sodium pentobarbital (6 mg/kg/h). Paralysis was induced with pancuronium bromide (0.3 mg/kg) i.v. and maintained with a continuous infusion (0.6 mg/kg/h). A polyethylene catheter was inserted through the umbilical or femoral artery into the descending aorta to obtain blood gas samples and to continuously measure the blood pressure.

Experiments were approved by the Committee of Animal Care in Research of the University of Turku. Animals were cared for in accordance to procedures outlined in the "Guide for the Care and Use of Laboratory Animals" (National Institutes of Health Publications No. 85–23).

Meconium preparation. Meconium was collected from the first stools of several healthy term human neonates. The samples were initially frozen and later pooled, lyophilized, and irradiated for sterility. Before the experiment meconium was diluted with sterile saline to a concentration of 65 mg/mL.

Study protocol. After 1 h of stabilization a bolus (1.5 mL/kg) of meconium ($n = 16$) or sterile saline ($n = 15$) was instilled into the lower lobe of the right lung. In a supine position, a roentgenopaque catheter was inserted through the intubation tube under fluoroscopic guidance into the right main bronchus, 2 cm distal from the bifurcation of the trachea. The piglets were then turned to the right lateral position, and meconium or saline was instilled slowly through the catheter. Remaining of meconium in the right lung was confirmed in preliminary roentgenographic studies by unilateral instillation of meconium mixed with barium, and in the present study macroscopically and histologically after each experiment. After 15 min of ventilation the animals were turned back to the supine position for the rest of the study. Oxygen was added, when necessary, to keep Pao_2 >8 kPa and ventilatory frequency adjusted to keep $PaCO_2$ <5 kPa. Body temperature was maintained >38°C with a radiant warmer and a heating blanket. Five percent glucose in saline was infused i.v. at 6 mL/kg/h. After 12 h of follow-up animals were killed with an overdose of potassium chloride.

Tissue samples. Lung tissue wet/dry weight ratio measurement and histologic analysis were performed in nine piglets in the meconium and eight in the saline group. 2×2 cm lung tissue samples were excised in a consistent manner from the lateral region of the lower lung lobes of both lungs, fixed in 10% buffered formalin, dehydrated, cleared and embedded in paraffin according to a routine process. Five-μm sections were stained with hematoxylin and eosin for light microscopic analysis. To determine the extent and severity of the lung tissue injury, a pathologist (H.A.) blinded to the grouping of the piglets examined the samples and assigned a score from 0 to 4 for three different characteristics: *1)* extension of leukocyte infiltration (0 = 0%, 1 = 0% to 25%, 2 = 25% to 50%, 3 = 50% to 75%, 4 = 75% to 100%), *2)* amount of intra-alveolar leukocytes (0 = none, 1 = occasional, 2 = several leukocytes in the alveoli, 3 = alveoli almost full of leukocytes, 4 = alveoli distended by tightly packed leukocytes), and *3)* amount of exudative debris (0 = alveoli open, 1 = exudate scarcely seen, 2 = exudate clearly visible, 3 = alveoli almost full of exudate, 4 = alveoli distended by exudate). The histologic lung injury score is the sum of these scores. Alveolar septal diameter was subsequently measured with a computer software. Five high-power fields from hematoxylin-eosin stained sections were viewed and an average from 50 measurements registered.

Bronchoalveolar lavage (BAL). BAL was performed in seven piglets in the meconium and seven the in the saline group. The heart and lungs were first removed en bloc. Both main bronchuses were alternately tied and lavage of both lungs was performed separately by instillation of 15 mL of 0.9% NaCl 3 times to each lung and immediate aspiration. BAL fluid was centrifuged (350 G, + 4°C for 10 min) and total alveolar cell counts from cellular debris were performed in Bürker chamber. Differential cell counts were performed after cytocentrifugation and May-Grünwald-Giemsa staining. Supernatant was collected, frozen at −70°C, and later used for determinations of total protein concentration with biuret method as well as for biochemical measurements of tumor necrosis factor alfa concentration and catalytic activity of phospholipase A_2.

Myeloperoxidase (MPO). As an indicator of activated neutrophils, MPO activity of the lung tissue was assayed spectrophotometrically after homogenization of the tissue specimen using a method, in which the enzyme catalyzes the oxidation of 3.3'.5..5'-tetramethylbenzidine by H_2O_2 to yield a blue chromogen with a maximum wavelength of 655 nm (16).

Tumor necrosis factor alfa (TNF-α). Pig TNF-α concentration in BAL fluid supernatant was measured with *in vitro* ELISA (Endogen, INC., Woburn, MA, U.S.A.) according to manufacturer's instructions. Absorbance was read at 450 nm on an EIA reader (Spectra II, Wallac, Turku, Finland) with a fitting statistical software (MultiCalc Advanced, version 2.4) to calculate the results.

Catalytic activity and concentrations of phospholipase A2 (PLA2). The catalytic activity of PLA_2 in lung tissue and BAL fluid supernatant were measured according to a modified method described earlier (17, 18). Briefly, lung tissue specimens were homogenized in 50 mM sodium acetate buffer (pH 5.0) with 1 M NaCl and 1 tablet of protease inhibitor cocktail (Complete by Boehringer), 1 g of lung tissue per 4 mL of buffer. Homogenized samples were centrifuged for 20 min at 1000 G, and the supernatant was separated and used for PLA_2

catalytic activity assay. The substrate working solution for the assay was prepared by mixing unlabeled 1.2-dipalmitoylphosphatidylcholine (Sigma Chemical Co., St. Louis, MO, USA) with 1-palmitoyl-2-[^{14}C]-arachidonoylphosphatidylethanolamine (Dupont, Boston, MA, U.S.A.) in a ratio of 6 mM:1.325 μM (250nCi), dissolved in a mixture of chloroform and methanol (2:1), dried under a flow of nitrogen, and redissolved in 10 mL 0.1 M glycine buffer (pH 8.1). Ten-μl samples of lung tissue supernatant or BAL fluid supernatant were then incubated with 100 μL of substrate buffer for 3 h at 40°C. The reaction was stopped by adding 100 μL of Dole's reagent. Released [^{14}C]-arachidonic acid was segmented by SiO$_2$/water/heptane phase extraction, and detected by a liquid scintillation spectrometer (Wallac, Turku, Finland).

The concentrations of human PLA$_2$ group I (PLA$_2$-I, pancreatic type) and group II (PLA$_2$-II, synovial type) were measured in the supernatant of the homogenized lung tissue by time-resolved fluoroimmunoassays (19, 20). PLA$_2$-I immunoassay uses MAb-coated microtitre plates and europium chelate-labeled polyclonal (rabbit) antibody as a tracer. Both antibodies were raised against purified human pancreatic PLA$_2$. PLA$_2$-II immunoassay utilizes a polyclonal antibody, raised in rabbits against human recombinant group II enzyme, both immobilized on the microtitre plate and also detecting tracer antibody. Fluorescence was measured with an Arcus fluorometer (Wallac, Turku, Finland).

Data analysis. Longitudinal data (mean arterial blood pressure and arterial oxygenation index) was first studied with the analysis of variance for repeated measures design, and posthoc comparisons between the groups were made with a nonpaired *t* test. Significance between means of other data were first tested by analysis of variance for repeated measurements with one between factor (group) and one within factor (side). If significant differences were noted, a Bonferroni adjusted paired *t* test was used to compare right and left lungs, and a nonpaired *t* test to compare instilled and noninstilled lungs between the study groups. Association between variables was examined using the Pearson correlation test. A *p*-value <0.05 was considered statistically significant.

RESULTS

Mean arterial blood pressure decreased during the study period ($p < 0.001$), but there were no differences between the study groups (Fig. 1). The effect of time on arterial oxygenation index (Pao$_2$/FiO$_2$) was significant ($p < 0.001$), and there was a significant group by time interaction ($p < 0.001$). The index was significantly lower in the meconium group during the first three hours, but later there were no differences between the groups (Fig. 1).

Intrapulmonary instillation of meconium resulted in increased wet/dry weight ratio, histologic injury score and MPO activity in the instilled lung, when compared with the contralateral lung (Table 1). Saline instillation had no significant effect on these parameters, although no difference in the wet/dry ratio was found between the meconium- and saline-instilled lungs. Alveolar septal diameter was similar in all the studied lungs (Table 1).
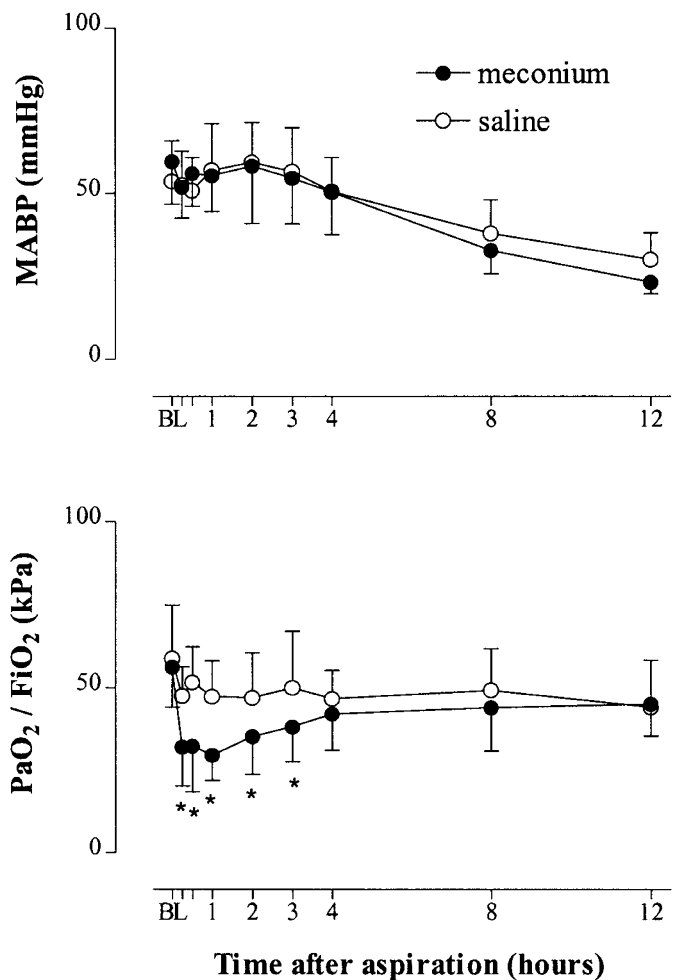

Figure 1. Mean arterial blood pressure (MABP) and arterial oxygenation index (Pao$_2$/FiO$_2$) in newborn piglets after unilateral intrapulmonary instillation of meconium ($n = 16$) or saline ($n = 15$). Mean (SD).

Meconium instillation was associated with increased BAL fluid total cell count ipsilaterally (Table 2). A majority of these cells were neutrophils. BAL fluid protein concentration was increased after intrapulmonary meconium when compared with saline lungs, but no significant difference to the meconium noninstilled lungs was found (Table 2). Despite a tendency toward elevated values in the meconium-instilled lungs, TNF-α concentration in BAL fluid was similar in all studied groups (Table 2). Saline administration had no significant effect on these parameters. There were no correlations ($p > 0.05$) between the BAL total cell or neutrophil count and protein or TNF-α concentration in any of the studied groups.

The catalytic activity of PLA$_2$, measured from BAL fluid and lung tissue, was increased locally in the meconium-instilled lungs, when compared with the noninstilled meconium lungs, and also in BAL fluid from the contralateral lungs (*t* test between noninstilled lungs, $p = 0.0052$). Lung tissue PLA$_2$ group-I and group-II concentrations were similarly elevated in the meconium-instilled lungs, group-I also in the noninstilled meconium lungs (Table 3). Saline instillation had no effect on the PLA$_2$ activity or concentrations. The lung tissue catalytic activity or concentrations of PLA$_2$ did not relate

Table 1. *Wet/dry lung weight ratio, histological lung injury score, alveolar septal diameter (μm) and myeloperoxidase (MPO) activity (units/mg prot) in newborn piglets 12 h after unilateral intrapulmonary instillation of meconium* (n = 9) *or saline* (n = 8). *Mean ± SD (range)*

	Wet/dry lung weight ratio	Histological lung injury score	Alveolar septal diameter	MPO activity
Meconium				
Instilled lung	5.5 ± 0.4*	7.6 ± 1.7*†	7.5 ± 1.9	0.79 ± 0.22*†
	(5.0–6.3)	(5–10)	(4.3–10.6)	(0.35–1.07)
Non-instilled lung	5.0 ± 0.5	0.6 ± 1.0	6.9 ± 2.8	0.45 ± 0.19
	(4.6–5.9)	(0–3)	(3.5–12.8)	(0.25–0.79)
Saline				
Instilled lung	5.1 ± 0.2	0.8 ± 0.9	7.9 ± 2.6	0.51 ± 0.17
	(4.8–5.4)	(0–2)	(4.7–11.9)	(0.32–0.77)
Non-instilled lung	5.0 ± 0.3	0.9 ± 2.1	6.7 ± 1.6	0.43 ± 0.09
	(4.6–5.4)	(0–6)	(5.1–10.0)	(0.33–0.56)
	Group, $p = 0.173$	Group, $p < 0.001$	Group, $p = 0.923$	Group, $p = 0.045$
	Side, $p < 0.001$	Side, $p < 0.001$	Side, $p = 0.131$	Side, $p < 0.001$
	Interaction, $p = 0.006$	Interaction, $p < 0.001$	Interaction, $p = 0.608$	Interaction, $p = 0.016$

* $p < 0.05$ vs. contralateral lung.
† $p < 0.05$ vs. saline instilled lung.

Table 2. *Total cell count* ($\times 10^6$/L), *polymorphonuclear neutrophils (PMN) (%), protein (g/L) and tumor necrosis factor alfa (TNF-α) concentration (pg/ml) in bronchoalveolar lavage fluid of newborn piglets 12 h after unilateral intrapulmonary instillation of meconium* (n = 7) *or saline* (n = 7). *Mean ± SD (range)*

	Total cell count	PMN	Protein	TNF-α
Meconium				
Instilled lung	5 240 ± 3 500*†	58.2 ± 31.3	2.6 ± 0.4†	157 ± 33
	(1 380–10 120)	(5.0–85.0)	(1.8–3.1)	(109–215)
Non-instilled lung	1 210 ± 750	59.0 ± 16.6	2.2 ± 0.4	111 ± 44
	(410–2 210)	(46.5–89.5)	(1.3–2.6)	(35–160)
Saline				
Instilled lung	710 ± 330	74.1 ± 19.7	1.4 ± 0.7	121 ± 20
	(310–1 180)	(48.5–96.0)	(0.5–2.3)	(80–137)
Non-instilled lung	370 ± 180	66.7 ± 22.9	1.5 ± 1.1	128 ± 8
	(140–630)	(35.5–95.0)	(0.2–2.5)	(114–136)
	Group, $p = 0.005$	Group, $p = 0.238$	Group, $p = 0.015$	Group, $p = 0.465$
	Side, $p = 0.002$	Side, $p = 0.690$	Side, $p = 0.348$	Side, $p = 0.057$
	Interaction, $p = 0.007$	Interaction, $p = 0.622$	Interaction, $p = 0.196$	Interaction, $p = 0.014$

* $p < 0.05$ vs. contralateral lung.
† $p < 0.05$ vs. saline instilled lung.

to the injury score or wet/dry-ratio, and similarly the bronchoalveolar PLA$_2$ activity had no correlation to the cell count or protein or TNF-α concentrations.

DISCUSSION

In experimental meconium aspiration, inflammatory lung changes with ultrastructural signs of cellular injury have been observed within 6 h (7, 11, 21), with a maximum at 12 to 48 h after exposure (6). In contrast to experimental acid aspiration with marked generalized inflammatory response and significant lung injury manifesting as early as 3 h after instillation (14, 15), our present data suggest that these alterations are and remain mainly local, restricted to areas of meconium contamination. Since the meconium concentration of 65 mg/mL, used in the present study, clinically corresponds to thick meconium in amniotic fluid, and after bilateral instillation induces severe persistent hypoxemia and progressive vascular hypertension in neonatal lungs (22), it is apparent that generalized pulmonary inflammatory reaction unlikely has a significant contribution to the pathogenesis of the clinical MAS. The early period of hypoxemia even after unilateral meconium insufflation may be

a reflection of an initial ventilation/perfusion mismatch, frequently associated with pulmonary surge of smooth muscle contracting agents, like thromboxane A$_2$, which may increase the resistance of the lung vascular bed and airways (9, 22, 23).

Influx of neutrophils into the airspaces is a consistent feature of acute lung injury after various direct and nondirect insults (8, 12, 13), as also evident in the meconium-contaminated lungs in our study. The mechanism underlying the local meconium-induced neutrophil migration is still unclear, but is supposedly triggered through stimulation of alveolar macrophages by constituents of meconium (10). Furthermore, in contrast to acid aspiration, the previously observed meconium-induced up-regulation of adhesion receptors may occur only locally (10, 15). Human meconium itself appears to have some neutrophil chemotactic activity, presumably due to the presence of potently chemotactic cytokines, such as IL-8 (24). Aspirated meconium may further induce intrapulmonary production of proinflammatory cytokines and prostaglandins (25, 26). Our results however indicate that alveolar TNF-α release is not significantly increased in the meconium-contaminated lungs. Thus, although TNF-α is a potent activator of neutrophils and

Table 3. *Catalytic activity of phospholipase A$_2$ (CA-PLA$_2$) (units/liter) in bronchoalveolar lavage (BAL) fluid supernatant and lung tissue, and lung tissue PLA$_2$ group-I and group-II concentrations (PLA$_2$-I and PLA$_2$-II) (ng/ml) in newborn piglets 12 h after unilateral intrapulmonary instillation of meconium (n = 9 for lung tissue, n = 7 for BAL) or saline (n = 8 for lung tissue. n = 7 for BAL). Mean ± SD (range)*

	CA-PLA2 (BAL fluid)	CA-PLA2 (lung tissue)	PLA2-I	PLA2-II
Meconium				
Instilled lung	401 ± 91*†	379 ± 140*†	1511 ± 246*†	12.2 ± 3.3*†
	(289–566)	(235–667)	(1120–1930)	(8.0–18.0)
Non-instilled lung	15.3 ± 5.2‡	10.6 ± 1.6	48.2 ± 33.0‡	1.5 ± 0.7
	(9.4–23.0)	(8.6–13.1)	(8.7–94.0)	(0.5–2.6)
Saline				
Instilled lung	8.3 ± 6.3	9.9 ± 1.1	18.6 ± 30.7	1.3 ± 0.5
	(0.4–17.4)	(7.6–10.9)	(0.9–93.0)	(0.1–1.7)
Non-instilled lung	4.8 ± 4.0	9.7 ± 1.6	10.8 ± 11.3	1.4 ± 0.3
	(0.5–12.7)	(7.6–12.8)	(0.6–31.0)	(1.0–1.8)
	Group, $p < 0.001$	Group, $p < 0.001$	Group, $p < 0.001$	Group, $p < 0.001$
	Side, $p < 0.001$	Side, $p < 0.001$	Side, $p < 0.001$	Side, $p < 0.001$
	Interaction, $p < 0.001$	Interaction, $p < 0.001$	Interaction, $p < 0.001$	Interaction, $p < 0.001$

* $p < 0.05$ vs. contralateral lung.

† $p < 0.05$ vs. saline instilled lung.

‡ $p < 0.05$ vs. saline non-instilled lung.

may up-regulate neutrophil/endothelial adhesion receptors, it is probably not markedly responsible for the early local extravasation and accumulation of leukocytes within the alveolar spaces (8, 12). Previous experimental data indeed suggest that pulmonary TNF-α synthesis and release is time-dependent and peaks only at 24 h after meconium insult (25).

A bulk of clinical and experimental evidence indicates that neutrophils, when stimulated, are involved in the pathogenesis of the acute lung injury of various origin (8). Activated neutrophils release a wide variety of mediators, including reactive oxygen metabolites, cytokines and proteolytic enzymes, which may play an important role in the alveolocapillary injury with subsequent protein leak and edema formation (8, 12). Proteinaceous exudation into the alveolar spaces can further inactivate the pulmonary surfactant, decrease the lung compliance and intensify the respiratory failure (6, 27). On the other hand, since neutrophils may also migrate into the alveolar spaces without substantially altering the permeability of the lung epithelial barrier (28), the precise role of invading neutrophils in the pathogenesis of meconium-induced lung tissue injury still remains unclear. Alternatively, aspirated meconium may directly cause damage of the respiratory epithelium and thereby significantly increase the alveolar epithelial permeability to protein. Previous data indeed showed morphologic evidence of epithelial and endothelial injury already at 6 h after meconium instillation in piglets (21).

A number of observations have suggested that phospholipid-degrading enzyme, PLA$_2$ plays an exacerbating role in the pathogenesis of acute inflammatory lung injury (29–31). PLA$_2$-induced lipolysis can generate biologically active mediators, like lysophospholipids and FFA (8, 32), which may induce both damage to the alveolocapillary membrane and intrapulmonary sequestration of neutrophils (33). In accordance to findings in humans and experimental models with acute lung injury, we found elevated catalytic activity of PLA$_2$ in the bronchoalveolar fluid from the meconium-instilled lungs (30,

31, 34). This enzyme may have been released from the activated neutrophils and macrophages accumulated in the alveolar space, or may be produced endogenously in the fixed pulmonary cells. Alternatively, human meconium is known to contain high concentrations of pancreatic (group-I) PLA$_2$ that may, similar to intratracheal PLA$_2$ group-II (synovial) administration, induce acute functional and morphologic alterations in the air spaces (21, 29, 33). Pancreatic PLA$_2$ is further identified to be present in lung tissue and may additionally induce group-II PLA$_2$ secretion that may at least partly explain the high enzyme concentrations in the meconium-instilled lungs (34, 35). Although the possibility of some contamination of the noninstilled lungs with meconium cannot be totally ruled out and the conclusive evidence of the pathogenetic role of PLA$_2$ still remains unsettled, the observed challenge of the meconium-instilled lung with high activity of PLA$_2$, both exogenous and endogenous, may contribute to the local tissue injury and surfactant dysfunction after meconium aspiration also in neonatal lungs (4, 34, 36).

Treatment of meconium-induced respiratory dysfunction with corticosteroids, potent anti-inflammatory agents, has yielded conflicting results (37–40). Despite of some improvement in oxygenation and hemodynamics after experimental meconium instillation, corticosteroid treatment does not seem to have any clear effect on the inflammatory reaction in the lung tissue (39). This further strengthens the present finding of lacking generalized pulmonary inflammatory injury after meconium insult. However, since local inflammatory lung injury after meconium instillation is significant, combined obstetric and pediatric suctioning of the airways remains as a critically important therapeutic approach in deliveries with meconium-stained amniotic fluid (2). Once meconium has entered the lungs, treatments aimed to ameliorate the local pulmonary tissue damage, such as intratracheal surfactant lavage, might be more beneficial than systemic anti-inflammatory treatments.

CONCLUSION

In conclusion, meconium instillation induces severe localized lung inflammation, but significant generalized lung injury is lacking. Thus, the extension of the localized effects in the lungs, and hence the amount of aspirated meconium, seem to be critical in the pathogenesis of MAS, and the therapeutic efforts should be directed accordingly.

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