surgical correction of large diaphragmatic defects.\textsuperscript{1,4} More commonly, the pleural effusion will recur with reintroduction of dialysis.\textsuperscript{5} Therefore, a tension hydrothorax with hemodynamic compromise would likely preclude further use of peritoneal dialysis in any form.

**REFERENCES**


**FIGURE 2.** Massive right pleural effusion with shift of the mediastinal structures.

hour. Her blood pressure rapidly returned to normal, and sinus rhythm was restored. Pleural fluid analysis revealed 1 WBC/cu mm; 6 RBCs/cu mm; glucose, 2,030 mg/dl; protein, 67 mg/dl; and LDH, 14 units/L. A simultaneously drawn serum glucose value was 145 mg/dl, and the serum LDH was 505 units/L. Results from all cultures and cytology of the pleural fluid were negative.

**DISCUSSION**

Hydrothorax is a rare complication of acute, intermittent, and continuous ambulatory peritoneal dialysis.\textsuperscript{1-4} A review of the English literature revealed only 32 reported cases with large pleural effusions of which 27 were women.\textsuperscript{1-4} Detection occurred within 48 hours of acute peritoneal dialysis.\textsuperscript{4} All cases were unilateral and all but one were right sided except for one reported case.\textsuperscript{4}

In the absence of either infection or malignancy, the etiology of this complication is more than likely related to diaphragmatic defects, congenital or acquired, and often microscopic.\textsuperscript{5,7} That this fluid is dialysate and not an ultrafiltrate is suggested by the hypocellularity, markedly elevated glucose and the reported presence of L+ and D— isomers of lactate in the pleural fluid.\textsuperscript{4} The instillation of methylene blue and \textsuperscript{99m}Tc radioisotope into the peritoneal space has confirmed pleuropertitoneal connections in some of the previously reported cases.\textsuperscript{4} With the infusion of large volumes of dialysate solution into the peritoneal space, the intra-abdominal pressure will rise, and associated with a negative intrathoracic pressure, will create a large pressure gradient driving peritoneal fluid into the pleural space.\textsuperscript{7} Interestingly, our case demonstrated rapid accumulation of pleural fluid on positive pressure ventilation.

Management includes discontinuing peritoneal dialysis and possible thoracentesis if respiratory symptoms are severe.\textsuperscript{1} Reinstitution of peritoneal dialysis has occasionally been successful with the use of smaller volumes of dialysate solution, a semi-erect position, tetracycline pleurodesis, and

**Growth and Development of Lungs in Siblings with Nonimmune Hydrops**

ChiMren, F.C.C.P.;\textsuperscript{†} and Daphne deMello, M.D.;\textsuperscript{‡}

Postmortem findings in the lungs of two siblings with nonimmune hydrops and lung hypoplasia are presented. In one, a girl, the hypoplasia was severe, with reduced numbers of airway generations and markedly reduced radial alveolar counts. In the other, a boy, the hypoplasia of both airway and alveolar development was mild. The reason for the difference in the growth of the lungs in these two children is unknown. The additional finding of Noonan's syndrome in the male sibling with mild hypoplasia and in the father is of interest. (Chest 1990; 97:1255-57)

**ECMO = extracorporeal membrane oxygenation**

Immune hydrops was common in the past due to Rh incompatibility, and its association with hypoplasia of the

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lungs has been reported.1 Nonimmune hydrops is still frequently seen, and there are many causes and associations.24 This report describes in detail the lungs of two siblings with nonimmune hydrops and hypoplasia of the lungs. These cases have additional interest in the fact that Noonan's syndrome was present in one of the siblings and also in the father (Fig 1).

**CASE REPORTS**

**CASE 1**

This female infant was delivered vaginally after 32 weeks of gestation to a 22-year-old gravida 2 para 1 mother. The fetal sonogram showed a hydropic baby with pleural effusions and ascites, but neither oligohydramnios nor polyhydramnios. The birth weight was 2,200 g. The Apgar score was 1 and 2 at one and five minutes. The infant was intubated, and pleural effusions were drained with chest tubes. She had pH of 6.8, PCO₂ of 100 mm Hg, and PO₂ of 13 mm Hg. The hemoglobin level was 13.8 g/dl, the hematocrit reading was 40.5 percent, total serum protein level was 2.6 g/dl, and the albumin level was 1.8 g/dl. The mother's blood type was AB, Rh (+); the baby was A, Rh (+). Coombs' test was negative. The infant was edematous, but not dysmorphic, and died at 12 hours of age.

The placenta was normal. At autopsy the infant had marked edema. Her weight was 2,000 g (normal, 1,488 ± 335 g). There was 25 ml of serous ascities and 11 ml of pleural fluid. The heart weighed 12.4 g (normal, 11 ± 3.7 g) and was normal. The lungs were hypoplastic. Together the inflated lung volume was 25 ml (normal, 50 ml) and weighed 14 g (normal, 34 ± 11 g). The ratio of lung weight to body weight was 0.007 (normal, 0.022 ± 0.002). The pulmonary arteries were injected with a barium gelatin suspension at 73 mm Hg, and the lungs were inflated and fixed with 10 percent formalin at 23 cm H₂O. 23 (Fig 2). The posterior basal segment of the bronchial tree was dissected. There were 17 generations (normal mean, 31; maximum, 25; our control, 22 to 23). The alveolar number was reduced, and the radial alveolar count was 1.4 ± 0.5 (normal, 3.2 ± 0.9). Pulmonary arteries on the angiogram were narrower than normals matched for gestational age. *Table 1). There was precocious muscularization of arteries accompanying respiratory bronchioles and increased adventitial collagen around the preacinar arteries. Intra-acinar arteries were of normal size (Table 2). There was also increased collagen around pulmonary veins, which showed mild arteriolarization. The lymphatics were prominent and dilated.

**CASE 2**

Twenty-one months later, a male sibling was born at 34 weeks of gestation by cesarean section. The sonogram showed polyhydramnios and a hydropic fetus with pleural effusions. The infant weighed 2,250 g. He had an Apgar score of 3 at one minute and 5 at five minutes. He was intubated, and chest tubes were inserted. His blood type was A, Rh (+). He had a pH of 7.14. PCO₂ of 86 mm Hg, and PO₂ of 20 mm Hg. The hemoglobin level was 17.8 g/dl, and the hematocrit reading was 51 percent; the serum total protein level was 3.4 g/dl, and the albumin level was 1.5 g/dl. The infant was markedly edematous with low-set ears, depressed nasal bridge, hypertelorism, micrognathia, and a short neck. The testes were small. He was placed on ECMO on the third day. An open lung biopsy on the seventh day revealed medial hypertrophy of pulmonary arteries with intimal proliferation (grade 2 Heath-Edwards

**Table 1.—Right Lower Lobe Axial Arterial Length and Diameter at Selected Distances from Hilum**

<table>
<thead>
<tr>
<th>Data</th>
<th>Total Length, cm</th>
<th>Diameter at Percent</th>
<th>Distance from Hilum, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0%</td>
<td>25%</td>
</tr>
<tr>
<td>Case 1</td>
<td>Actual</td>
<td>3.1</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>Normal*</td>
<td>3.9</td>
<td>3.0</td>
</tr>
<tr>
<td>Case 2</td>
<td>Actual</td>
<td>3.6</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>Normal†</td>
<td>4.8</td>
<td>3.2</td>
</tr>
</tbody>
</table>

*Normal values in fetus with gestational age of 32 weeks.
†Normal values in fetus with gestational age of 33 weeks.

**Table 2.—Intra-acinar Arterial Diameter and Percent Wall Thickness**

<table>
<thead>
<tr>
<th>Data</th>
<th>Arteries Accompanying Respiratory Bronchiole</th>
<th>Diameter of Arteries Accompanying Alveolar Duct, μ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diameter, μ Wall Thickness</td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>54.7 ± 25.3</td>
<td>12.6 ± 6.7</td>
</tr>
<tr>
<td>Case 2</td>
<td>79.6 ± 27.0</td>
<td>16.3 ± 6.5</td>
</tr>
<tr>
<td>Normal*</td>
<td>47.7 (30-77)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

*Mean and range (within parentheses) of arterial diameter in fetus with gestational age of 36 weeks.
proposed
crease
of
in
was
suggested
creased
weighed
classification).
No lymphangiectasia was present. After ten days on ECMO, the infant was weaned but died at 12 days of age.

The placenta was normal. Body weight at autopsy was 2,675 g (normal, 1,583 ± 530 g).1 The facial characteristics were consistent with Noonan's syndrome. There were no pleural effusions. The heart was enlarged and weighed 23.8 g (normal, 13.4 ± 3.9 g).2 There was right ventricular hypertrophy. The lungs together weighed 47.8 g (normal, 40 ± 13 g).3 The increased weight was probably due to edema because the ratio of lung weight to body weight was low at 0.018 (normal, 0.02 ± 0.002).4 Lung volume was not measured. The pulmonary arteries were injected, and the lungs were inflated. Bronchial generations were counted in the right and left lower lobes. The anterior segment of the right lower lobe had 18 generations (normal mean, 19; maximum, 24).5 The posterior basal segment of the left lower lobe had 20 generations (normal mean, 21; maximum, 25).6 Radial alveolar count was low normal at 2.7 ± 0.67 (normal, 3.2 ± 0.9).7 The pulmonary arteries were slightly narrower than normal on the angiogram (Table 1). There was medial hypertrophy of the precapilar and intra-acinar arteries, with increased adventitial collagen. Intra-acinar arteries were of normal size, but there was precocious muscularization of arteries accompanying respiratory bronchioles (Table 2). The veins showed arterio-
ization, with increased adventitial collagen, and the lymphatics were slightly dilated.

The family history of these two siblings was significant in that the father had Noonan's syndrome and pulmonary valvular stenosis. The first child of these parents was born two years before our first patient and also had Noonan's syndrome and pulmonary stenosis, but no hydrops at birth. Both the father and the first son underwent successful pulmonary valvotomy and are well.

**DISCUSSION**

The causes or associations of nonimmune hydrops fetalis are numerous. In Turner's and Noonan's syndromes, the suggested pathogenesis of hydrops is abnormal lymphatic system and interference in drainage of chyle.8,9 Our patient 2 had Noonan's syndrome, but pulmonary lymphangiectasia was not severe and was probably not the cause of hydrops.

The lungs of six hydropic babies who died following Rhesus isoimmunization all showed pulmonary hypoplasia, but the severity varied.1 Whereas airway growth was affected in all, alveolar differentiation was reduced in only two. It was therefore proposed that isoimmunization somehow affected the development of the lungs in the first 16 weeks of gestation when active airway branching occurs. Our patient 1 had severe pulmonary hypoplasia, with both airway and alveolar number reduction,8,11,12 causing a marked decrease in total alveolar number. These findings suggest an interference in the growth of the lungs beginning early and continuing throughout gestation. In patient 2, pulmonary hypoplasia was mild, and both airway number and acinar development were minimally affected. The striking differences in the severity of pulmonary hypoplasia in these two infants, both of whom had a similar degree of hydrops as judged by their birth weight, suggests that the pulmonary hypoplasia was probably not produced solely by the physical effect of small intrathoracic space due to pleural effusion and ascites. It is possible that humoral factors such as those proposed in immune hydrops played a role. This concept supports the finding in both patients of precocious muscularization of intra-acinar arteries, a process indicative of maldevelopment in utero, as seen in other entities.13,14 By contrast, in infants with immune hydrops, there was no precocious muscularization of intra-acinar arteries, even though the pulmonary arteries were small and the numbers reduced commensurate with the reduction in airway number.

The familial occurrence of nonimmune hydrops in our patients is intriguing. In a previous report of three siblings in a family with nonimmune hydrops,2 it was ascribed to abnormal placenta; however, in our children, the placentas were normal. From our observation, it appears that while hydrops and pulmonary hypoplasia could be etiologically related, the role of Noonan's syndrome in hydrops and pulmonary hypoplasia is less certain; however, the possible association of hydrops and abnormal lung development in families with Noonan's syndrome needs to be considered.

**ACKNOWLEDGMENTS:** We thank Professor Lynne Reid, M.D., for her valuable suggestions in the preparation of this manuscript.

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