Long-term Outcome After Neonatal Meconium Obstruction

Julie R. Fuchs, MD, and Jacob C. Langer, MD

ABSTRACT. Objective. It is unclear whether children with cystic fibrosis (CF) who present with neonatal meconium ileus have a different long-term outcome from those presenting later in childhood with pulmonary complications or failure to thrive. We examined a cohort of patients with meconium ileus, and compared their long-term outcome with children who had CF without meconium ileus and neonates who had meconium obstruction without CF (meconium plug syndrome).

Study Design. Comparative study using retrospective and follow-up interview data.

Patients. Group 1 consisted of 35 surviving CF patients who presented with meconium ileus between 1966 and 1992. Two control groups were also studied: 35 age- and sex-matched CF patients without meconium ileus (group 2), and 12 infants presenting with meconium plug syndrome during the same time period (group 3).

Outcome Measures. Pulmonary, gastrointestinal, nutritional, and functional status were reviewed, and surgical complications were recorded.

Results. Mean follow-up was 12.6 ± 6, 12.6 ± 6, and 9.3 ± 4 years in groups 1, 2, and 3, respectively. Patients without CF (group 3) demonstrated better growth and functional status, and had a lower incidence of pulmonary and gastrointestinal problems. Although the presence of meconium ileus among CF patients was associated with an earlier diagnosis, there were no significant differences between groups 1 and 2 with respect to hepatobiliary, nutritional, functional, or respiratory status. Meconium ileus was associated with a higher risk of meconium ileus equivalent (20% vs 6%), although this difference was not statistically significant. Long-term surgical complications (adhesive small bowel obstruction and blind loop syndrome) were seen in 27% of children with meconium ileus; there were no long-term surgical complications in groups 2 or 3, because these infants did not have any neonatal surgical procedures. Children presenting with complicated meconium ileus had a higher rate of long-term surgical complications than those with uncomplicated meconium ileus (36% vs 17%), and those managed with resection or enterostomy had more complications than those treated by enterotomy and lavage (33% vs 0%).

Conclusions. Long-term outcome is similar in CF patients who present with meconium ileus and those who do not, except for a slightly higher incidence of meconium ileus equivalent, and a significantly higher rate of surgical complications. The risk of surgical complications is highest in those presenting with complicated meconium ileus and those undergoing resection or enterostomy. Patients with meconium obstruction who do not have CF have an excellent long-term prognosis. This information will be useful in counseling the families of infants presenting with neonatal meconium obstruction. Pediatrics 1998;101(4). URL: http://www.pediatrics.org/cgi/content/full/101/4/67; cystic fibrosis, meconium ileus, meconium plug syndrome.

ABBREVIATION. CF, cystic fibrosis.

Meconium obstruction in the neonate is a spectrum of disease that includes meconium ileus and meconium plug syndrome.\(^1\) Meconium ileus is characterized by extremely viscid, protein-rich inspissated meconium causing terminal ileal obstruction, and accounts for approximately 20% of neonatal intestinal obstructions.\(^2\) Although meconium ileus can rarely occur in otherwise normal children,\(^3\) the majority of patients with meconium ileus have cystic fibrosis (CF). Meconium ileus is the presenting symptom in 10% to 15% of these patients.\(^4\) Meconium plug syndrome is more commonly seen in premature infants, is characterized by colonic obstruction, and is only rarely associated with CF.

Approximately half of neonates with meconium ileus present with uncomplicated intestinal obstruction. In many of these children, the obstruction can be relieved using a water-soluble contrast enema, and surgery is reserved for those who fail nonoperative management. Patients presenting with complicated meconium ileus, including volvulus, atresia, gangrene, perforation, and meconium peritonitis always require operative intervention.\(^5\) A variety of procedures have been described, including enterotomies and lavage, placement of a T-tube, resection with primary anastomosis, and various types of enterostomies, including the Bishop-Koop ileostomy, Mikulicz double-barreled enterostomy, Santulli proximal chimney enterostomy, and the double enterostomy (proximal enterostomy and mucus fistula).\(^6\) In contrast, virtually all infants with meconium plug syndrome are cured of their obstruction after a water-soluble contrast enema.

Survival of neonates with meconium ileus has improved over the last few decades because of improved surgical technique, neonatal intensive care, nutritional support, and medical management of the pulmonary complications of CF.\(^7\) In addition, it is increasingly being recognized that CF is a heterogeneous disease. The characteristics and severity of gastrointestinal and pulmonary complications vary considerably among patients in long-term follow-up.
studies. It would be helpful for both families and clinicians if it were possible to predict the likelihood of long-term problems at the time of diagnosis. This study was designed to determine whether neonates with CF who present with meconium obstruction have a different long-term outcome than those who do not. To control for the effect of CF itself on outcome, we also sought to determine long-term outcome in patients presenting with neonatal meconium obstruction who did not have CF.

MATERIAL AND METHODS

Charts of all newborns presenting with meconium ileus between 1966 and 1992 were reviewed (group 1). Two control groups were also studied: CF patients without meconium ileus (group 2), and infants presenting with meconium plug syndrome (group 3). Group 2 was generated by randomly matching each of the meconium ileus patients by sex and age to a patient being followed in the CF clinic who had not presented with meconium ileus. Group 3 included infants with a diagnosis of meconium plug syndrome presenting between 1966 and 1992. For the purposes of this study, obstruction was defined as meconium ileus if the meconium obstruction was ileal, and as meconium plug syndrome if the obstruction was primarily colonic.

For each patient, the hospital and clinic charts (if available) were reviewed. Information gleaned included sex, date of birth, gestational age, birth weight, associated anomalies, initial presentation, and radiologic or surgical procedure. All patients or families were also contacted by telephone, and all families contacted agreed to participate in the study. Gastrointestinal complaints and abdominal symptomatology were discussed in detail, with specific questions regarding meconium ileus equivalent, recurrent diarrhea, constipation, abdominal pain, rectal prolapse, and gastrointestinal bleeding. Meconium ileus equivalent was strictly defined for our purposes as partial or complete intestinal obstruction with evidence of impacted feces in the right colon or terminal ileum on radiographic examination, necessitating treatment by either an enema or intestinal lavage solution by mouth. Diarrhea, constipation, and abdominal pain were recorded as positive if they were severe enough to negatively impact the patient’s quality of life, or if the symptoms were recurrent over many years.

Nutritional status and general health were determined by assessing current height and weight, both of which were expressed as population percentile using standard National Center for Health Sciences growth curves. Placement of a gastrostomy tube and the use of nutritional supplements for poor weight gain were recorded. The severity of a patient’s pulmonary course was gauged by the number of pulmonary-related hospital admissions. Existence of other medical complications and procedures related to CF such as diabetes mellitus and biliary cirrhosis, as well as unrelated conditions and procedures were also recorded. Social and emotional status was assessed with a series of questions relating to school or work attendance and performance, quality of life as described by the patient, and activity level that included exercise tolerance and general fatiguability. Patients were rated on a scale from 0 to 2, where 0 = no limitations (similar to siblings without CF), 1 = mild limitations, and 2 = severe limitations.

RESULTS

Characteristics of Patient Groups

Of the 82 patients coded with a diagnosis of meconium ileus, 17 did not have meconium ileus, 12 had incomplete records, and 6 could not be located for long-term follow-up. Of the remaining 47 patients with well-documented follow-up, 12 had died, leaving 35 surviving patients for analysis. These patients were classified as group 1. Group 2 consisted of 35 age- and sex-matched patients chosen randomly from the CF clinic population, who had not presented in the newborn period with meconium ileus. Of the 28 patients coded with a diagnosis of meconium plug syndrome, 3 had died from complications of prematurity, 4 did not have confirmed meconium plug syndrome, and 9 patients could not be located for long-term follow-up, leaving 12 patients for analysis in group 3.

Characteristics of the three groups are shown in Table 1. Gestational age at birth was significantly higher in group 2 compared to group 1. Although the same trend was present for birth weight, the difference was not statistically significant. Children in group 1 were significantly younger when the diagnosis of CF was made than those in group 2.

In group 1, meconium ileus was uncomplicated in 60% (n = 21) and complicated in 40% (n = 14). The complicated cases included patients with proximal volvulus (n = 7), jejunal atresia (n = 6), ileal atresia (n = 2), perforation (n = 7), meconium peritonitis (n = 7), and ascites (n = 2). Some cases had multiple complications. In group 1, 33 of 35 patients had CF diagnosed by sweat chloride, and the other 2 had meconium ileus with normal sweat chloride levels; 1 of these presented with complicated meconium ileus, and the other was uncomplicated. Sweat chlorides were elevated in all group 2 patients and in none of the group 3 patients.

Of the 21 patients with uncomplicated meconium ileus, 9 (43%) were successfully treated by contrast enema alone, and 12 (57%) required surgical intervention [intestinal resection with Mikulicz ileostomy (n = 2), intestinal resection and Bishop-Koop ileostomy (n = 3), enterotomy with N-acetylcysteine or saline lavage (n = 4), resection with primary anastomosis (n = 2), and milking of meconium into the colon without enterostomy (n = 1)]. There was one early postoperative complication in this group, consisting of an anastomotic leak requiring revision.

The 14 patients with complicated meconium ileus all underwent surgery [resection with primary anastomosis (n = 6), resection with Mikulicz ileostomy (n = 1), resection with Bishop-Koop enterostomy (n = 2), and enterostomy with mucus fistula (n = 5)]. There was one early postoperative complication, consisting of enterostomy stenosis treated by resection and primary anastomosis. The various nonoperative and surgical procedures were evenly distributed over time.

All group 3 patients presented with mild abdominal distention and failure to pass meconium at 24 to 48 hours of life. In 3 of 12 patients, thick meconium plugs were eventually passed spontaneously. In the remaining 9 patients, a contrast enema showed nu-

<table>
<thead>
<tr>
<th>TABLE 1. Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
</tr>
<tr>
<td>(n = 35)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
</tr>
<tr>
<td>Gestational age at delivery (wk)</td>
</tr>
<tr>
<td>Positive sweat chloride</td>
</tr>
<tr>
<td>Age at diagnosis of CF (mo)</td>
</tr>
<tr>
<td>Age at follow-up (y)</td>
</tr>
</tbody>
</table>

* P < .05, Student’s t test.
numerous filling defects in the colon with free reflux of contrast into the terminal ileum, followed by spontaneous passage of one or more thick meconium plugs. Hirschsprung’s disease was ruled out by rectal biopsy in 4 patients. In all 12 patients, prompt relief of abdominal distention occurred after the passage of the meconium plugs. None of the patients in group 3 required neonatal abdominal surgery.

Long-term Follow-up

Mean length of follow-up was 12.6 ± 6 years in group 1, 12.6 ± 6 years in group 2, and 9.3 ± 4 years in group 3. Sixty-six percent of the patients received all of their care at our institution. The other patients were initially treated elsewhere, and were subsequently cared for by us. Only 30% of the latter group received more than half of their follow-up care at another hospital.

General Medical Status

General medical status is summarized in Table 2. There was no significant difference between groups 1 and 2 with respect to height and weight. Group 3 patients were taller and heavier, and were close to the 50th percentile for the general population.

Pulmonary Status

Mean number of admissions for pulmonary exacerbations was 4.2 ± 4 in group 1 and 5.1 ± 4 in group 2. Two patients in group 1 have undergone lung transplantation, and 1 additional patient is on the transplant list. None of the patients in group 2 have undergone lung transplantation, and 1 additional patient is on the transplant list. None of these differences were statistically significant. None of the patients in group 3 have had pulmonary problems.

Gastrointestinal and Nutritional Status

Recurrent abnormalities in liver function tests and hepatosplenomegaly were present in 2 group 1 patients (6%) and in 5 group 2 patients (14%). Two of these 5 patients have progressed to cirrhosis; 1 has undergone liver transplantation, and 1 is on the transplant list. Liver problems were not present in any of the group 3 patients.

Incidence of pyloric stenosis, meconium ileus equivalent, recurrent abdominal pain, constipation, diarrhea, rectal prolapse, and rectal bleeding or melena are shown in Table 3, along with the need for nutritional supplementation. The differences among groups with respect to meconium ileus equivalent did not reach statistical significance (P = .15). Within group 1, meconium ileus equivalent was reported by 14% of those with complicated meconium ileus and 24% of those with uncomplicated meconium ileus (P = .80). There were no significant differences between group 1 and group 2 with respect to other gastrointestinal symptoms or need for nutritional support, and these issues were rarely seen in group 3.

Social and Functional Status

The mean social/functional status rating was 0.514 in group 1 and 0.417 in group 2 (P = .7743, Mann Whitney U test). In group 1, 19 patients were rated 0, 14 were rated 1, and 2 were rated 2. In group 2, 20 patients were rated 0, 14 were rated 1, and 1 was rated 2. In group 3, 10 of 12 patients were rated 0 (highest functioning). A patient with Down syndrome had mild limitation (rating of 1), and a patient with chromosomal translocation was severely limited (rating of 2).

Long-term Surgical Complications

Long-term surgical complications are summarized in Table 4. There were seven complications in group 1 (long-term complication rate of 26.9%). Complications occurred between 1.5 months and 18.5 years of age, and included 5 small bowel obstructions and 2 blind loop syndromes. There were no long-term surgical complications in groups 2 or 3, because these

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**TABLE 2.** General Medical Status

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 35)</th>
<th>Group 2 (n = 35)</th>
<th>Group 3 (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean height percentile</td>
<td>30.6 ± 34</td>
<td>30.1 ± 35</td>
<td>42.5 ± 34</td>
</tr>
<tr>
<td>Mean weight percentile</td>
<td>26.1 ± 24</td>
<td>30.3 ± 32</td>
<td>47.1 ± 29</td>
</tr>
<tr>
<td>Insulin-dependent diabetes</td>
<td>3 (9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Attention deficit disorder</td>
<td>2 (6%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Allergic bronchopulmonary aspergillosis</td>
<td>2 (6%)</td>
<td>2 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Periortbial cellulitis</td>
<td>2 (6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>1 (3%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>1 (3%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>0</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Hip synovitis</td>
<td>0</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Genetic anomalies</td>
<td>0</td>
<td>0</td>
<td>3 (25%)</td>
</tr>
</tbody>
</table>

**TABLE 3.** Gastrointestinal and Nutritional Status

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 35)</th>
<th>Group 2 (n = 35)</th>
<th>Group 3 (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver dysfunction</td>
<td>2 (6%)</td>
<td>5 (14%)</td>
<td>0</td>
</tr>
<tr>
<td>Hypertrophic pyloric stenosis</td>
<td>2 (6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Meconium ileus equivalent</td>
<td>7 (20%)</td>
<td>2 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Recurrent abdominal pain</td>
<td>21 (60%)</td>
<td>22 (63%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>5 (14%)</td>
<td>6 (17%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Recurrent diarrhea</td>
<td>18 (51%)</td>
<td>12 (34%)</td>
<td>0</td>
</tr>
<tr>
<td>Rectal prolapse</td>
<td>6 (17%)</td>
<td>4 (11%)</td>
<td>0</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>5 (14%)</td>
<td>4 (11%)</td>
<td>0</td>
</tr>
<tr>
<td>Feeding gastrostomy</td>
<td>3 (9%)</td>
<td>1 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Nutritional supplements without gastrostomy</td>
<td>5 (14%)</td>
<td>4 (11%)</td>
<td>0</td>
</tr>
</tbody>
</table>
infants did not have any neonatal surgical procedures.

When analyzed according to original operation, long-term complications were seen in 1 of 5 patients undergoing Bishop-Koop ileostomy, 2 of 3 patients undergoing Mikulicz enterostomy, 2 of 8 patients undergoing resection and primary end-to-end anastomosis, and 1 of 5 patients undergoing double enterostomy. There were no complications among the 4 patients who underwent enterotomy and lavage. Long-term surgical complication rate was 36% in the patients with complicated meconium ileus, and 17% in the patients with uncomplicated meconium ileus.

Mortality

At the time of our study, 12 group 1 patients had died. These patients ranged in age from 1 month to 26 years at the time of death, with a mean age of 8.14 years. Nine patients had uncomplicated (75%), and 3 had complicated (25%) meconium ileus. In 2 patients, the cause of death was not documented. In the remaining 10 children the causes of death included: staphylococcal sepsis and pulmonary interstitial emphysema in a 1-month-old, aspiration pneumonia and *Pseudomonas* sepsis after anastomotic leak in a 6.5-month-old, bronchopneumonia and pulmonary sepsis in a 7-month-old, fungal sepsis in a 1-year-old, asphyxiation secondary to a displaced tracheostomy tube in a 4-year-old, respiratory failure and cor pulmonale in 3 patients aged 8, 24, and 26 years, and complications of lung transplantation in 2 patients aged 11.5 and 12 years. Therefore, only one death was directly related to the presence of meconium ileus.

**DISCUSSION**

A number of authors have reported a decrease in morbidity and mortality for patients with meconium ileus in recent decades.7-11 The present study was stimulated by a desire to provide more accurate information about long-term prognosis for families with a child afflicted with CF. We were particularly interested in whether the earlier diagnosis that resulted from meconium ileus would result in a better outcome because of more prompt treatment of pulmonary disease, as reported in some series,12-17 and whether the presence of meconium obstruction would be associated with a higher rate of gastrointestinal complications. Finally, we wished to document the degree to which the natural history of neonatal meconium obstruction was significantly affected by the presence of CF.

Our data showed that the major cause of morbidity and mortality in children with meconium ileus remained the pulmonary complications of CF. These complications were unrelated to the presence or absence of meconium ileus, despite the fact that children with meconium ileus were diagnosed at a significantly younger age. This finding is consistent with the several other groups, who noted that early diagnosis of CF prevented serious deterioration and death at a young age from pulmonary disease, but did not affect the long-term progression of lung disease or survival when excluding infants presenting and dying at an age of 6 months or less.18,19 Meconium ileus was related to the cause of death in only 1 of the 12 group 1 patients who died in our series, providing further evidence that meconium ileus does not affect long-term prognosis in patients with CF.

We also found that meconium ileus did not affect long-term functional or social status in children with CF. Quality of life seemed to be directly related to the extent of pulmonary involvement, because the patients with the most significant limitation (missed days of school, time spent bedridden, severity of exercise intolerance), were those with the most severe pulmonary disease, particularly those listed for and awaiting lung transplantation. The lack of effect of meconium ileus on height and weight percentiles or the need for nutritional supplementation supports the observation that the presence of meconium ileus does not adversely affect the long-term nutritional outcome in patients with CF.11,20

There have been conflicting opinions as to whether patients with meconium ileus experience more frequent or severe episodes of long-term gastrointestinal dysfunction than CF patients without meconium ileus.21-24 This issue has never been the central focus of a study, and a group of CF patients has never been included as a control. Although our study did not document any adverse effect of meconium ileus on most gastrointestinal problems, we did note statistically insignificant increases in hypertrophic pyloric stenosis and meconium ileus equivalent. An association of meconium ileus with hypertrophic pyloric stenosis has been noted by one group in the past, but our numbers are too small to draw a definitive conclusion.

Meconium ileus equivalent, also known as distal intestinal obstruction syndrome, is most often de-

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**TABLE 4. Long-term Surgical Complications in Group 1**

<table>
<thead>
<tr>
<th>Original Procedure</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Mikulicz enterostomy</td>
<td>SBO requiring adhesiolysis and resection</td>
</tr>
<tr>
<td>2† Mikulicz enterostomy</td>
<td>Multiple SBOs, one requiring adhesiolysis and resection</td>
</tr>
<tr>
<td>3 Bishop-Koop ileostomy</td>
<td>SBO requiring adhesiolysis</td>
</tr>
<tr>
<td>4 Resection and anastomosis</td>
<td>SBO requiring adhesiolysis and resection</td>
</tr>
<tr>
<td>5 Resection and anastomosis</td>
<td>SBO requiring adhesiolysis</td>
</tr>
<tr>
<td>6 Double enterostomy</td>
<td>Blind loop syndrome requiring resection</td>
</tr>
<tr>
<td>7† Mikulicz enterostomy</td>
<td>Blind loop syndrome requiring resection</td>
</tr>
</tbody>
</table>

Abbreviation: SBO, small bowel obstruction.

* There were no surgical complications in group 2.
† Same patient.
fined as partial or complete intestinal obstruction occurring in CF patients beyond the neonatal period, resulting from abnormally thick, viscid material in the terminal ileum and right colon. The reported incidence of meconium ileus equivalent in CF patients ranges from 2.1% to 41.3%, depending on the specific definition used. In uncontrolled studies, some authors have found no increase in meconium ileus equivalent in patients who presented with meconium ileus, and others have found an increased incidence of meconium ileus equivalent.

In our study, using an age- and sex-matched control group, there was a higher, although statistically insignificant, incidence of meconium ileus equivalent in group 1. It is unclear whether the lack of statistical significance represents a type II error because of small numbers, or why meconium ileus patients would experience meconium ileus equivalent more often. Possible factors include more tenacious intestinal mucus, more viscous intestinal mucoproteins, greater acidity in the small intestine leading to precipitation of undigested dietary protein, altered motility (perhaps related to the original intestinal obstruction or secondary to subsequent surgery), dehydration, or a greater degree of pancreatic insufficiency.

It is also possible that meconium ileus patients have a form of CF in which intestinal mucus glands are more severely affected. There is some controversy regarding whether these patients represent a distinct clinical or genetic entity when compared with CF patients without meconium ileus. Reports on haplotypic variability for the CF mutation between meconium ileus and nonmeconium ileus patients have yielded conflicting results.

The meconium plug syndrome is a distinct form of neonatal colonic obstruction characterized by inspissated, immobile meconium and associated with the presence of meconium plugs or casts. The pathophysiology is unclear, although bowel hypomotility and hyperviscosity of meconium may both play a role. Meconium plug syndrome is usually associated with prematurity, although associations with hypermagnesemia, hypotonia, Hirschsprung’s disease, hypothyroidism, maternal diabetes, and CF have all been described, and in some cases there is no clear predisposing factor. Most authors feel that meconium plug syndrome is a distinct disease entity from meconium ileus and in most cases is associated with an excellent long-term prognosis. Our data support this view, and underscore the importance of a sweat test in all patients presenting with neonatal meconium obstruction.

Our study is the first to report long-term surgical complications after treatment for meconium ileus. The complication rate was 26.9%, and because follow-up was relatively short for some of the patients, we may have actually underestimated the true incidence. There were no long-term complications in patients with uncomplicated disease who were treated nonoperatively, which reinforces the desirability of this approach if at all possible. Long-term problems were more common after surgery for complicated meconium ileus, which likely reflects a higher incidence of peritonitis and intestinal ischemia. Surgical complications occurred after a wide range of procedures, although none of the infants undergoing enterotomy and irrigation had long-term surgical morbidity. These data suggest that resection and stoma formation should be avoided if possible, and that families and pediatricians must be counseled about the risk of long-term morbidity after surgical intervention for meconium ileus.

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