

fungal cell membrane, which produces a disruption of its integrity and transport characteristics, resulting in the loss of intracellular potassium.^{4, 6}

The major side effects of amphotericin B are transient nephrotoxicity, hepatotoxicity and bone marrow suppression.⁷ Baley et al.⁴ reported that 7 of 10 VLBW infants with systemic candidiasis treated with a combination of amphotericin B (1 mg/kg/day) and flucytosine (100 to 150 mg/kg/day) had severe nephrotoxicity manifested by oliguria or anuria and marked increases in blood urea nitrogen and creatinine. The deaths of 6 of the 7 infants were attributed in part to amphotericin B-induced nephrotoxicity. However, several of the infants had confounding factors such as multiple drug therapies and preexisting poor renal function. In contrast all 5 VLBW infants treated by Johnson et al.,² with a smaller dosage of amphotericin B (0.5 to 1 mg/kg/day) and a similar dosage of flucytosine (50 to 150 mg/kg/day), tolerated therapy well and all survived. Since the report of Baley et al., the pharmacokinetics of amphotericin B in neonates has been studied and most of the treated infants have had more favorable outcomes.^{2, 8}

In this series little evidence of toxicity was observed despite some infants having abnormalities of renal, hepatic or hematopoietic function before receiving amphotericin B. The one infant with evidence of worsening renal function was probably affected by urinary tract obstruction. The transient occurrence of oliguria in sick VLBW infants is weak evidence of renal toxicity. We believe that the transient renal and hepatic abnormalities and thrombocytopenia are more likely related to the systemic infection or other preexisting problems rather than amphotericin B toxicity. Although it is not possible to exclude amphotericin B as a contributory factor in the deaths of four infants, overwhelming disseminated *Candida* infection was the likely cause. Our experience supports the opinion of others who have reported that unlike adults and older children who experience fever, chills, nausea and vomiting, infants tolerate amphotericin B well.^{2, 9, 10}

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SERRATIA MARCESCENS PNEUMONIA, EMPYEMA AND PNEUMATOCELE IN A PRETERM NEONATE

Neonatal pneumonia has been associated with many infectious agents. *Staphylococcus aureus* is the most common cause of pneumonia associated with empyema and pneumatocele formation in the newborn.¹ Neonatal pneumonia with empyema caused by *Serratia marcescens* has not to our knowledge been described in the English literature. We describe such a case in a preterm neonate and present a review of similar neonatal infections caused by Gram-negative aerobic bacilli.

Case report. The patient was a 755-g male neonate born at 26 weeks of gestation by precipitous vaginal delivery to a 18-year-old primigravida after an uncomplicated pregnancy. The initial course was complicated by hyaline membrane disease, bilateral grade III intraventricular hemorrhage, a persistent ductus arteriosus that was treated with indomethacin and multiple blood transfusions for anemia. From Day of Life (DOL) 7 until DOL 15 the infant was extubated and reintubated for continuing respiratory problems, had blood, urine and tracheal aspirate cultures and received vancomycin and amikacin for 72 h. A 5-day weaning course of dexamethasone (initial dose, 0.5 mg/kg/day) was started on DOL 10.

On DOL 15 the patient was reintubated for hypoxemia, bradycardia, hypotension and decreased urine output. Blood, tracheal aspirate and urine cultures were obtained and treatment with vancomycin and amikacin was begun. A spinal tap was unsuccessful. A chest roentgenograph showed a large pneumatocele on the right. Twelve hours later a repeat chest roentgenograph revealed a tension pneumothorax on the right, and a thoracotomy tube was placed with no evidence of fluid at that time. The pneumothorax reaccumulated and serosanguinous fluid was noted in the chest tube on DOL 17. Two new chest tubes were inserted for drainage of the empyema. The Gram-stained pleural fluid showed many leukocytes and Gram-negative bacilli. Cefotaxime was added to the antibiotic regimen, and on DOL 20 a right thoracotomy with decortication was performed and the empyema was drained. Multiple ruptured pneumatoceles were discovered and sutured, and two new chest tubes were inserted.

Three blood cultures (DOL 17, 19 and 21), tracheal aspirate (DOL 15) and preoperative (DOL 17) and operative (DOL 20) empyema fluid grew *S. marcescens* susceptible to all the aminoglycosides and to cefotaxime. The urine and a previous tracheal aspirate culture from DOL 10 were sterile. Blood

TABLE 1. Characteristics of seven neonates with Gram-negative empyema and pneumatocele formation

Reference	Age (Days/Sex)	Wt (g)	Underlying Illness	Radiologic Features	Organism	Source	Treatment	Outcome
2	0/NA	NA	Prematurity	NA	<i>Klebsiella pneumoniae</i> , <i>Enterobacter</i>	Pleural fluid	Antibiotics	D
3	9/F	1000	Prematurity	Bilateral P, Pc, Px and E	<i>Klebsiella pneumoniae</i>	Blood	Antibiotics and chest tube	S
4	2/M	4200	Infant of diabetic mother	Right P, Pc	<i>Escherichia coli</i>	Blood, CSF, stool, throat	Antibiotics	S
4	2/NA	3500	None	Right P, Pc	<i>Escherichia coli</i>	Blood, stool, throat, nasopharynx	Antibiotics	S
4	2/M	2700	None	Left P, Pc	<i>Escherichia coli</i>	Blood, urine, throat	Antibiotics	S
5	0/M	3347	None	Right P, Pc, E, Px	<i>Escherichia coli</i>	Pleural fluid	Antibiotics and chest tube	S
This report	14/M	755	Prematurity	Right P, Px, Pc, E	<i>Serratia marcescens</i>	Blood, pleural fluid	Antibiotics, chest tube, decortication	S

NA, not available; P, pneumonia; Pc, pneumatocele; Px, pneumothorax; E, empyema; CSF, cerebrospinal fluid; S, survived; D, died.

(DOL 23, 29), cerebrospinal fluid (DOL 29) and ventricular fluid (DOL 30) cultures were sterile. The infant was treated with cefotaxime and gentamicin and the other antibiotics were discontinued. The infant improved slowly, the chest tubes were removed on DOL 28 and the infant was extubated on DOL 39. Routine cultures failed to identify other infants in the neonatal intensive care unit that were colonized with *S. marcescens*. However, surveillance cultures were not done.

The chest roentgenograph continued to show a persistent right pneumatocele that resolved after 8 weeks. The total duration of antibiotics was 21 days postdecortication. The infant is now 7 months old and has hypertonia, developmental delay and a ventriculoperitoneal shunt for hydrocephalus.

Review of literature. We found reports of seven neonates with Gram-negative empyema and pneumatocele formation with pneumonia, including our patient (Table 1).²⁻⁵ One neonate with *Escherichia coli* empyema was excluded because no other information was available.⁶ Four were full term neonates and three were preterm (age 0 to 14 days). Radiographically all had pneumatocele formation; four had associated empyema and three had pneumothorax as well. The etiologic agents were *E. coli* in four, *Klebsiella pneumoniae* in one, *K. pneumoniae* and *Enterobacter cloacae* in one and *S. marcescens* in our patient. All were treated with antibiotics and three of the four with empyema required thoracotomy tube drainage. One infant died. Only our patient had decortication. The pneumatoceles persisted asymptotically among these infants for 1 to 10 months. One patient had recurrence of pneumothorax at ages 42 and 73 days.³

Discussion. In neonates, including those born prematurely, empyema is uncommon and when described usually has been associated with *Staphylococcus aureus*.^{1, 2, 6-8} Gram-negative organisms less commonly cause empyema or pneumatocele formation. *S. marcescens* has not been described as a cause of empyema, with or without pneumatocele formation, in neonates. However, it has been described as a cause of pneumonia, lung abscess and empyema in older children with underlying immunodeficiency.⁹ In adults *S. marcescens* pleural empyema is also uncommon.¹⁰

S. marcescens is a recognized pathogen in neonates and has been associated with neonatal intensive care unit outbreaks.¹¹⁻²⁰ These outbreaks affect primarily preterm neonates, and the clinical manifestations have included bacteremia, pneumonia, soft tissue infection, urinary tract infection and meningitis.¹¹⁻²⁰ Case fatality rates have been as high as 69%.¹¹⁻²⁰ None of the neonates with pneumonia had empyema or pneumatocele formation. In one outbreak two premature infants with *S. marcescens* septicemia had bilateral

pneumothoraces.¹⁸ It is difficult to say whether bilateral pneumothoraces were a result of the severe idiopathic respiratory distress syndrome these infants had or occurred before the development of empyema given that both infants died.

Contributing factors for invasive disease caused by *S. marcescens* include exposure to contaminated instruments and fluids, peripheral intravenous catheters, use of steroids and broad spectrum antibiotics and prior colonization. Colonization rates of 95% in uninfected infants and 10% in hospital staff may occur early in hospitalization during these outbreaks.^{19, 20} In our case the infant had received steroids and antibiotics. There was no documentation that this neonate was colonized with *S. marcescens* earlier than the tracheal aspirate culture on DOL 15.

The diagnosis of empyema is suspected on chest roentgenographs and confirmed by examination and culture of pleural fluid. The yield for a positive empyema culture is 50 to 66% in children after the newborn period.^{2, 8} Treatment can be guided by results of Gram-stained smears of pleural fluid and when uncertain consist of antimicrobial agents active against *Staphylococcus aureus* and Gram-negative organisms. A thoracotomy tube with closed drainage is initially used to drain the empyema, hasten recovery and decrease complications. Decortication through thoracoscopy,²¹ a noninvasive procedure, has been successful in older children but experience with this procedure in the newborn period is limited. Decortication should be considered if there is evidence of loculated fluid or fluid too viscous to be adequately drained by thoracotomy tube.

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