
Family Practice Grand Rounds

Meningitis Following Normal Lumbar Punctures

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DR. HENRY M. FEDER, JR (*Associate Professor, Department of Family Medicine*): The case I will discuss today is one frequently encountered by the family physician—a febrile irritable infant without a focus of infection. My purpose is to review the literature and controversies regarding the care of febrile infants who have no focus of infection. Dr. Adelman will present the case.

DR. ALAN ADELMAN (*Assistant Professor, Department of Family Medicine*): A 13-month-old female child was brought to the model unit because of 12 hours of high fever and rhinorrhea. Her past medical history was noncontributory. Physical examination revealed an irritable infant in no acute distress. Her temperature was 105°F. Except for the presence of rhinorrhea, the physical examination was unremarkable. No nuchal signs were present. Her white blood cell count was $48.2 \times 10^6/\text{mL}$ with 80 percent polymorphonuclear cells and 9 percent band forms; urinalysis and a chest roentgenogram were normal. To confirm the initial abnormal count, a repeat white cell count performed two hours later was $53.4 \times 10^6/\text{mL}$ with 64 percent polymorphonuclear cells and 21 percent band forms. No meningeal signs were pres-

ent, but because of her irritability a lumbar puncture was performed. The cerebrospinal fluid contained two lymphocytes per cubic millimeter and two red blood cells per cubic millimeter, and counterimmunoelectrophoresis (CIE) was negative for *Streptococcus pneumoniae*, *Hemophilus influenzae* type B, and *Neisseria meningitidis*. The cerebrospinal fluid glucose was 123 mg/dL (blood sugar 175 mg/dL) and protein was 10 mg/dL. The patient was then admitted for observation. Because of the possibility of occult bacteremia, a blood culture was obtained, and therapy was initiated with 250 mg of ampicillin given orally every six hours. Twenty-four hours after admission the initial blood culture was reported positive for *S pneumoniae*, and both the cerebrospinal fluid and urine cultures were sterile. At this time the patient was febrile, irritable, and vomiting. A second lumbar puncture was performed and contained 990 white blood cells per cubic millimeter (91 percent polymorphonuclear cells) with glucose, 50 mg/dL and protein, 85 mg/100 mL. Gram stain and culture were negative, but counterimmunoelectrophoresis was positive for *S pneumoniae*. The ampicillin was discontinued and intravenous aqueous penicillin G, 500,000 units every four hours was begun. Within 24 hours the patient was afebrile and no longer irritable. She was treated for ten days with intravenous penicillin and made an uneventful recovery. She has now been followed for one year without apparent sequelae.

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DR. FEDER: During this Grand Rounds I would like to discuss two areas of interest to family physicians. First, I will briefly review the literature of occult bacteremias and summarize a practical approach to this problem. Second, I will review the problem of meningitis following a normal lumbar puncture.

In 1967 Belsey¹ reported occult pneumococcal sepsis in three infants hospitalized because of febrile seizures. These infants had no focus of infection except for rhinorrhea. Laboratory studies were negative except for high white blood cell counts, 16 to 23 $\times 10^6$ /mL. Blood cultures were obtained, and no therapy was initiated. All patients had blood cultures positive for *S pneumoniae*. No patient developed a focus of infection, and all patients became afebrile after the initiation of penicillin therapy. Following this study there were more reports of infants with fever and leukocytosis who presented with no focus of infection and had positive blood cultures for *S pneumoniae*.²⁻⁵

Perhaps the best study of occult bacteremia was done by Teele et al,⁶ who prospectively cultured blood from 255 consecutive infants aged less than two years with temperatures of at least 101° F who were seen in the ambulatory clinic of the Boston City Hospital. These infants either had no focus or an upper respiratory tract focus of infection. None of the 201 patients with temperatures less than 102° F or white blood cell counts less than 15 $\times 10^6$ /mL had positive blood cultures. In contrast, five of 54 patients with temperatures greater than or equal to 102° F and white cell counts greater than or equal to 15 $\times 10^6$ /mL had positive blood cultures for *S pneumoniae*. These five patients with occult *S pneumoniae* sepsis were not treated, and when recalled, four were afebrile and well. The fifth was still febrile with persistent positive blood cultures. This patient was treated with intravenous penicillin and did well.

Since these initial studies, the risks and prognosis for occult pneumococcal bacteremia have become well defined. Infants aged between six and 24 months with no focus or only an upper respiratory tract focus of infection and with temperatures greater than or equal to 102° F and white blood cell counts greater than or equal to 15 $\times 10^6$ /mL have about a 10 percent risk for occult sepsis. When seen at follow-up 24 to 48 hours later,⁷ 40 percent

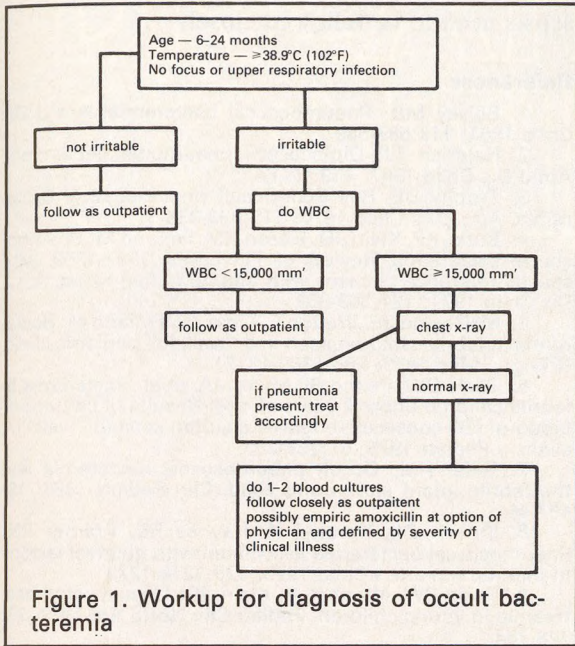
of untreated infants with occult pneumococcal bacteremia had spontaneous resolution of their illness, 29 percent had persistent fever with sterile blood cultures, 21 percent had persistent fever with positive blood cultures, and 10 percent developed meningitis.

Other interesting points concerning occult bacteremia warrant mention. Separate from occult pneumococcal bacteremia are positive pneumococcal blood cultures that are associated with a specific focus of infection, such as meningitis, pneumonia, or septic arthritis. Also, pneumococcal bacteremia can be associated with an oral pneumococcal focus that is characterized by a cystic lesion superimposed on a swollen gingiva.⁸ Also in the differential diagnosis for patients with suspected occult bacteremia is urinary tract infection. Urinalysis, Gram stain, and culture are helpful studies, especially in patients voiding more frequently than usual. The prognosis for these infections is different from that for occult pneumococcal bacteremia. Also occult bacteremias can occur with *H influenzae* type B,⁹⁻¹¹ and *N meningitidis*,¹² both of which have a serious prognosis. Finally, salmonella can also cause occult bacteremia.

Occult pneumococcal bacteremia occurs not only in urban clinic patients but in suburban private patients.^{13,14} In addition to fever, leukocytosis, and age as risk factors for occult bacteremias, persistent irritability appears to be another important risk factor.^{7,15} Empiric therapy with amoxicillin (to cover *S pneumoniae*, *N meningitidis*, and most *H influenzae*) may be beneficial. It should be noted that there are few data dealing with empiric antibiotic therapy; however, in one study¹⁶ penicillin was valuable in resolving occult pneumococcal bacteremia.

Most febrile infants without a focus of infection are not persistently irritable; therefore, I infrequently pursue occult bacteremia with white cell counts and blood cultures. Irritable infants are unsociable and have poor eye contact. A normal white blood cell count does not rule out occult bacteremia. I have listed my workup for the diagnosis of occult bacteremia (Figure 1). The clinician should judge when to do blood cultures and when to prescribe empiric therapy for possible occult bacteremia.

In 1919, Wageforth and Latham¹⁷ reported the



high inoculum pneumococcal bacteremia and that had not received cisternal punctures.

In 1975 Fischer et al²⁰ reported four cases of meningitis following normal lumbar punctures. These cases occurred in infants who were initially hospitalized with sepsis due to H influenzae, Escherichia coli, or N meningitidis. In 1977 I reported in a review of occult pneumococcal sepsis⁷ that five of 38 infants (13 percent) with pneumococemia developed meningitis following normal lumbar punctures, compared with no cases of meningitis in 61 infants with pneumococemia who did not have lumbar punctures. Recently, the association between normal lumbar punctures performed during bacteremia and the development of meningitis has been studied by two groups. Eng and Seligman²² reported three cases of meningitis among 200 adult patients who had normal lumbar punctures performed during bacteremia. It is interesting to note that two of the three patients who developed meningitis initially had traumatic lumbar punctures. In a review of occult bacteremias seen at Boston City Hospital, Teele et al²³ reported the development of meningitis in 7 of 46 (15 percent) children who had normal lumbar punctures done during bacteremia compared with 2 of 231 (1 percent) children who did not have lumbar punctures.

It is not known whether lumbar punctures done during bacteremia cause meningitis or whether sicker patients (who are likely to develop meningitis spontaneously) are selected for lumbar punctures. It is unlikely that a prospective randomized study of lumbar punctures done during bacteremia will be done; therefore, the pathogenesis of meningitis following normal lumbar puncture will remain controversial.

DR. ADELMAN: How should these data concerning lumbar puncture be incorporated into clinical practice?

DR. FEDER: First, good clinical judgment must be exercised when assessing the need for lumbar puncture. It should be emphasized that bacteremia is not a contraindication for performing a lumbar puncture because the risk of not doing a lumbar puncture and delaying the diagnosis of meningitis is potentially more grave than the possible risk of causing meningitis with a lumbar puncture. Second, whenever a lumbar puncture is performed on a child who is at risk for occult bac-

possible causative role of a lumbar puncture done during bacteremia and the later development of meningitis. Six patients had lumbar punctures performed during bacteremia, and five of these patients later developed meningitis.

In 1941 Pray¹⁸ reported on children aged less than two years with bacteremic pneumococcal pneumonia. Seven of 21 (33 percent) developed meningitis following normal lumbar punctures, and 70 of 233 (30 percent) developed meningitis who did not receive lumbar punctures.¹⁸ This pre-antibiotic study has been quoted as evidence that lumbar punctures done during bacteremia do not increase the incidence of meningitis;^{19,20} however, this study was not large enough to show a 15 percent increased incidence of meningitis in patients who had lumbar punctures.

In 1962 Petersdorf et al²¹ demonstrated in dogs that cisternal punctures performed during pneumococcal bacteremia resulted in the later development of meningitis. Forty-two of 71 dogs with high inoculum pneumococcal bacteremia developed meningitis following cisternal punctures. Meningitis did not occur among 50 dogs having

teremia, a blood culture must also be obtained. Third, a possibly bacteremic child who has had a normal lumbar puncture can be treated in two ways: the patient could be hospitalized and treated for meningitis or, if the risk of bacteremia appears slight, the child could be followed closely as an outpatient. It must be realized that in either case oral therapy with amoxicillin would not be expected to cure early meningitis.

DR. PERRY PUGNO (*Assistant Professor, Department of Family Medicine*): How firm are the risk criteria of fever greater than 102° F; white blood cell counts greater than or equal to $15 \times 10^6/\text{mL}$, and age between 6 and 24 months? Do we have to worry about occult pneumococcal bacteremia in adults?

DR. FEDER: The risk criteria for occult bacteremias are not firm. These criteria simply identify the patients at highest risk. However, when these criteria are present, it allows one to justify the use of empiric antibiotic therapy. Finally, occult pneumococcal bacteremia can occur in any age group including adults.²⁴

DR. JOHN DALLMAN (*Associate Professor, Department of Family Practice*): Two final points need to be emphasized. First, I agree that outpatient therapy with amoxicillin is appropriate therapy for patients at risk for occult sepsis. When patients with positive blood cultures return for follow-up, if they are still ill or febrile, they should be hospitalized and treated with parenteral antibiotic therapy. Second, oral amoxicillin may achieve serum levels adequate to resolve low-inoculum pneumococcal sepsis, but amoxicillin and the other oral penicillins poorly penetrate the central nervous system; therefore, oral administration should never be expected to resolve an early meningeal focus of infection.

DR. FEDER: In conclusion, our case of a 13-month-old girl with high fever, irritability, and rhinorrhea is characteristic of many of the published cases of occult pneumococcal bacteremia. Her white blood cell count of $48.2 \times 10^6/\text{mL}$ is higher than most reported cases; however, recently, I have seen three cases of occult bacteremia, all with white blood cell counts greater than $30 \times 10^6/\text{mL}$. Finally, this patient developed meningitis following a normal lumbar puncture, which serves to emphasize that children who have lumbar punctures and who are at high risk of having occult

sepsis need to be followed closely.

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