Research Highlights

Highlights from the latest papers in pediatric emergency medicine

Wendy L Woolley[†] *& John H Burton*
[†]*Author for correspondence*
Department of Emergency Medicine
Albany Medical College
43 New Scotland Avenue, MC 139,
Albany, NY 12208, USA
woollew@mail.amc.edu
Tel.: +1 518 262 4050
Fax: +1 518 262 3236

Effect of pneumococcal vaccine on pneumococcal bacteremia in febrile infants

Evaluation of: Carstairs KL, Tanen DA, Johnson AS *et al.*: Pneumococcal bacteremia in febrile infants presenting to the emergency department before and after the introduction of the heptavalent pneumococcal vaccine. *Ann. Emerg. Med.* 49(6), 772–777 (2007).

Fever is one of the most common complaints of children younger than 3 years of age presenting to the emergency department (ED). The appropriate evaluation and management of these children has been evolving secondary to research advances and the implementation of vaccinations.

After the introduction of the vaccine against *Haemophilus influenzae* type B, there was still approximately a 2% incidence of occult bacteremia in the nontoxic-appearing, febrile child, with more than 90% of the bacterial isolates identified as *Streptococcus pneumoniae* [1,2]. The current American College of Emergency Physicians clinical policy states, "Once the pneumococcal vaccine becomes broadly included within pediatric practice, future studies will be necessary to determine whether empiric antibiotic treatment of children suspected of harboring occult bacteremia is warranted" [2]. A heptavalent pneumococcal vaccine has recently become available and is widely used. This study was designed to determine the incidence of positive blood cultures in febrile infants and children younger than 36 months after the initiation of routine pneumococcal vaccination [3].

This study is a nonconcurrent prospective observation cohort using standardized medical record review to gather data from all febrile children presenting to the ED at a tertiary care military hospital. Patients under 36 months of age with a temperature greater than 100.4°F in the ED or reported from home were included. Data were abstracted from chart review for patient age, temperature and whether blood cultures were obtained in the ED. Heptavalent pneumococcal vaccination status and blood culture results were obtained from an independent review of the computerized medical record to limit subjective bias.

There were a total of 3562 patient visits reviewed, with a total of 1383 being eligible for study inclusion. The only exclusion criteria were for those children whose immunization status could not be determined, or those children who did not have blood cultures drawn during their ED visit.

Study patients were divided into two groups, those without heptavalent pneumococcal vaccination and those who had received at least one dose of vaccine. There were 833 patients who had received at least one dose of the vaccine, and 550 patients who had not been vaccinated. A positive blood culture was determined to be in one of three categories: *Pneumococcus*, other pathogen, and probable contaminant.

Positive blood cultures were found in 4.2% of the children in the study (58/1383). There were 17 positive blood cultures in the immunized group, which included no *Pneumococcus*, two other

pathogens (*Enterococcus*) and 15 probable contaminants. There were 41 positive blood cultures in the nonimmunized group, which included 13 *Pneumococcus*, no other pathogens and 28 probable contaminants.

As with any study, there were limitations to this review. This study does provide some evidence that febrile children who have received at least one dose of the heptavalent pneumococcal vaccine may be protected from pneumococcal bacteremia. This study had a strong advantage of being performed at the time of the introduction of the vaccine, so that there were large comparable groups of infants who had not received the vaccine to be used as a control.

The rate of pneumococcal positive blood cultures in the nonimmunized group was 2.4%, compared with 0% in the group that had received at least one vaccination. The suggestion offered by this study is that the vaccination is protective against invasive pneumococcal disease, and this may change the approach to the evaluation of the well-appearing febrile child aged 3–36 months presenting to the ED.

References

1. Kupperman N: The evaluation of young febrile children for occult bacteremia: time to reevaluate our approach? *Arch. Pediatr. Adolesc. Med.* 156, 855–857 (2002).
2. American College of Emergency Physicians: ACEP Clinical Policy for children younger than three years presenting to the emergency department with fever. *Ann. Emerg. Med*. 42, 530–545 (2003).
3. Carstairs KL, Tanen DA, Johnson AS *et al.*: Pneumococcal bacteremia in febrile infants presenting to the emergency department before and after the introduction of the heptavalent pneumococcal vaccine. *Ann. Emerg. Med.* 49(6), 772–777 (2007).

Clinical and laboratory predictors of occult pneumonia

Evaluation of: Murphy CG, van de Pol AC, Harper MB, Bachur RG: Clinical predictors of occult pneumonia in the febrile child. *Acad. Emerg. Med.* 14(3), 243–249 (2007).

Fever is one of the most common chief complaints for children presenting to the ED. Among these patients, there will be a subset of well-appearing, febrile children who have an underlying serious bacterial infection. The inability to reliably identify these children through the bedside clinical examination alone has led to empiric testing and treatment practices.

The diagnosis of pneumonia remains challenging. There is not at present a reliable prediction rule to identify those children presenting to the ED without respiratory findings with the diagnosis of clinically occult pneumonia. Many studies have shown that empiric chest radiographs (CXR) are not indicated in the routine evaluation of the febrile infant less than 3 months of age without leukocytosis or respiratory symptoms [1,2]. There are limited data regarding the use of the CXR in the evaluation of the older infant (greater than 3 months of age) with fever.

In the past, the presence of leukocytosis has been used as a guide to identify children who have a higher incidence of occult pneumonia [2]. However, the introduction of the pneumococcal vaccine is changing the evaluation of the febrile infant, and physicians may be obtaining fewer white blood cell counts in the evaluation of these patients. The pneumococcal vaccine is also effective in reducing the risk of pneumococcal pneumonia in vaccinated infants [3].

This study sought to investigate the prevalence of occult pneumonia in the post-pneumococcal vaccine era and to identify variables in the history and physical examination that predict the presence of occult pneumonia [4].

This study was a retrospective cross-sectional study conducted over the course of a calendar year at a pediatric medical center. All patients aged 10 years or less who presented with a fever at the time of evaluation or within the preceding 24 h and had a CXR obtained in the ED were reviewed.

Pertinent history and physical examination findings were abstracted from the physician documentation, and patients were classified into one of two groups: those with 'signs of pneumonia' and those with 'no signs of pneumonia' (no visual signs of respiratory distress, no tachypnea, no hypoxia and no lower-respiratory-tract findings on physical examination). The CXR results were based on an attending radiologist's interpretation, and were divided into three groups: positive, negative or equivocal. The CXRs in the equivocal category were excluded from analysis. Statistical comparison of the patients with positive versus negative CXR within the 'no signs of pneumonia' subgroup was performed to identify predictors of occult pneumonia.

There were 2128 eligible patients who presented during the study period. Of these, 1084 were in the 'no signs of pneumonia' group, and 5.3% (95% CI: 4.0–6.8%) had positive CXRs and were classified as having occult pneumonia. There was a 12.6% (95% CI: 10.7–14.8%) prevalence of positive CXRs in the 'signs of pneumonia' group. Analysis performed of the 'no signs of pneumonia' group demonstrated that the individuals with occult pneumonia were significantly older in age (3.14 vs 2.50 years; $p = 0.05$) and had a higher white blood cell count (21.5 vs 14.6; $p < 0.01$).

Historical variables were further examined within the 'no signs of pneumonia' group, and either positive (occult pneumonia) or negative CXRs. The presence of cough (95.7 vs 77.3%; $p < 0.01$) and a duration of cough of more than 10 days (27.3 vs 12.1%; $p = 0.03$) were found to be statistically significant. Duration of fever for more than 3 days reached statistical significance (41.7 vs 25.8%; $p = 0.03$) for association with occult pneumonia, although there was no significant difference in the magnitude of the fever.

In this study, the prevalence of occult pneumonia was 5.3%, with the presence of cough found to be a significant indicator of a positive CXR. The rate of occult pneumonia in patients with a temperature of 39°C or higher and a white blood cell count of 20,000/mm^3 or more was found to be 14.2% in this study, an observation that is decreased from the 26% demonstrated in studies from the pre-pneumococcal vaccine era [2].

Although there appears to be a decrease in the overall incidence of occult pneumonia since the introduction of the pneumococcal vaccine, occult pneumonia remains prevalent to a degree that radiographic pneumonia can be identified in a subset of febrile children, regardless of the presence of lower respiratory symptoms. These occult pneumonias appear to be common in children with prolonged fever and cough, as well as those with a documented leukocytosis. In the absence of cough or leukocytosis, an empiric CXR in patients without respiratory signs likely has limited diagnostic value.

References

1. American College of Emergency Physicians: ACEP Clinical Policy for children younger than three years presenting to the emergency department with fever. *Ann. Emerg. Med.* 42, 530–545 (2003).
2. Bachur R, Perry H, Harper MB: Occult pneumonias: empiric chest radiographs in febrile children with leukocytosis. *Ann. Emerg. Med.* 33(2), 166–173 (1999).
3. Black, SB, Shinefield HR, Ling S *et al.*: Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than five years of age for prevention of pneumonia. *Pediatr. Infect. Dis. J.* 21, 810–815 (2002).
4. Murphy CG, van de Pol AC, Harper MB, Bachur RG: Clinical predictors of occult pneumonia in the febrile child. *Acad. Emerg. Med.* 14(3), 243–249 (2007).

When is a shunt series necessary?

Evaluation of: Pitetti R: Emergency department evaluation of ventricular shunt malfunction: is the shunt series really necessary? *Ped. Emerg. Care* 23(3), 137–141 (2007).

Ventricular shunt placement is one of the most common neurosurgical interventions for the treatment of hydrocephalus. A malfunction of the ventricular shunt is one of the most common clinical problems encountered in pediatric neurosurgery [1]. The malfunction of the shunt can result in increased hydrocephalus, clinical symptoms, or both. Patients with a malfunctioning ventricular shunt will often present to the ED with complaints that may include headache, nausea, vomiting, drowsiness, altered mental status, bulging fontanelle, or other signs of increased intracranial pressure [2]. There is a high morbidity and mortality associated with shunt malfunction. Therefore, the identification of these patients in the setting of common pediatric illness is of high importance.

The standard ED evaluation of possible shunt malfunction includes a head CT study to evaluate ventricular size, as well as a shunt series (plain radiographs of the skull, neck, chest and abdomen) to assess the shunt line for mechanical kinks, breaks or disconnections of the shunt tubing.

This study sought to evaluate whether the shunt series was necessary, or whether the cranial CT scan alone was adequate to predict the presence of shunt malfunction [3].

The study involved a retrospective chart review conducted on all patients younger than 18 years of age with a ventricular shunt who presented to an urban, tertiary pediatric ED during the study period. If the patient had signs or symptoms suggestive of possible shunt malfunction they were enrolled in the study. A standardized questionnaire was used to abstract data from patient charts. The results of radiographic studies, either shunt series or CT, were classified as either normal or abnormal based on the attending radiologist's interpretation. A shunt malfunction was defined as a requirement for shunt revision within 1 week of evaluation. An abnormal radiographic study alone was not sufficient for the diagnosis of malfunction to be made.

During the study, there were 461 evaluations for shunt malfunction in 291 children. There were 360 shunt series obtained and 410 CT scans. Those children presenting with headache were more likely to have a CT scan, while those presenting with a history of seizure or closed head injury were less likely to have radiographic studies ordered. The incidence of abnormal studies was 5.6% for the shunt series and 19.4% for the CT scan. The only significant demographic characteristic was that children with an abnormal shunt series tended to be older than their counterparts with normal shunt radiographs (163.2 months vs 83.8 months; $p < 0.001$).

A total of 71 patients (15.4%) were ultimately diagnosed with shunt malfunction and underwent surgical repair.

These patients were more likely to be older and have a history of vomiting or headache, whereas patients presenting with fever or seizure were less likely to have shunt malfunction. There were 22 patients with shunt malfunction who had a normal CT scan and six of them had an abnormal shunt series. There were 14 patients with a shunt malfunction who had both a normal CT scan and a normal shunt series.

This study demonstrated that a shunt series and a head CT should both be necessary components of the evaluation of any child with suspected shunt malfunction, although this observation is limited by a small dataset with six patients requiring revision based on the shunt series results, despite a negative cranial CT scan. The study also suggests that radiographic testing alone can not be relied upon to diagnose shunt malfunction. Those patients presenting with headache or vomiting were more likely to have shunt malfunction as opposed to those presenting with fever or seizure in their presenting symptoms. In the context of normal radiographic imaging in a patient with clinical signs and symptoms of shunt malfunction, neurosurgical consultation should be obtained.

References

1. Iskandar BJ, McLaughlin C, Mapstone TB *et al.*: Pitfalls in the diagnosis of ventricular shunt dysfunction: radiology reports and ventricular size. *Pediatrics* 101, 1031–1036 (1998).
2. Lee TT, Uribe J, Ragheb J *et al.*: Unique clinical presentation of pediatric shunt malfunction. *Pediatr. Neurosurg.* 30, 122–126 (1999).
3. Pitetti R: Emergency department evaluation of ventricular shunt malfunction: is the shunt series really necessary? *Ped. Emerg. Care* 23(3), 137–141 (2007).

Risk stratification of children with cerebrospinal fluid pleocytosis

Evaluation of: Nigrovic LE, Kuppermann N, Macias CG *et al.*: Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *JAMA* 297(1), 52–60 (2007).

Most children with cerebrospinal fluid (CSF) pleocytosis are admitted to the hospital and placed on broad-spectrum antibiotics, awaiting negative cultures after 2–3 days of incubation to exclude bacterial meningitis. This practice pattern exists despite the fact that the majority of these children have aseptic, rather than bacterial, meningitis [1]. The use of a highly accurate decision-support tool that could allow reliable identification of children with a near-zero risk of bacterial meningitis by ED clinical and laboratory parameters might enable clinicians to avoid unnecessary hospital admissions and prolonged antibiotic use in these children.

Previously, the Bacterial Meningitis Score had been developed as a clinical decision tool to identify patients at very low risk of bacterial meningitis. This tool has shown that a patient was at very low risk of bacterial meningitis if they lacked all of the following criteria: positive CSF Gram stain, CSF absolute neutrophil count (ANC) of 1000 cells/µl or more, CSF protein level of 80 mg/dl or greater, peripheral blood ANC of 10,000 cells/µl or more, and a history of seizure before or at the time of presentation. The Bacterial Meningitis Score had a negative predictive value of 100% (95% CI: 97–100%) and a sensitivity of 100% (95% CI: 91–100%) for the identification of bacterial meningitis patients (presence of ≥1 prediction rule risk factor) in the initial validation set [2].

Clinical decisions tools should be externally validated using a different patient population and clinical setting before widespread use, as they are often less accurate in a different setting from where they were derived [3]. Since the derivation and validation of the Bacterial Meningitis Score, there has been widespread use of the heptavalent pneumococcal vaccine in children. This study was designed to externally validate the Bacterial Meningitis Score in the post-pneumococcal vaccine era [4].

This was a retrospective chart review study using a network of 20 academic centers as part of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. The medical records of all patients aged 29 days to 19 years who received a diagnosis of meningitis at each of the participating sites during the study period were reviewed. Only those patients who had a lumbar puncture in the ED were included in the analysis (n = 4369). Children with CSF pleocytosis (CSF white blood cells ≥10 cells/µl, corrected for the presence of CSF red blood cells using a 1:500 ratio of leukocytes to erythrocytes) or a positive CSF culture for a bacterial pathogen were included in the study. Patients who required admission to the hospital regardless of the risk of bacterial meningitis were excluded, as were those patients who had received antibiotics in the 72 h prior to their lumbar puncture. Patients were defined as having bacterial meningitis or aseptic meningitis. The performance of the Bacterial Meningitis Score was then evaluated and an attempt was made to refine the Bacterial Meningitis Score.

After the exclusion criteria were applied, 3295 patients with CSF pleocytosis remained, of which 121 (3.7%; 95% CI: 3.1–4.4%) had bacterial meningitis and 3174 (96.3%; 95% CI:

95.5–96.9%) had aseptic meningitis. The Bacterial Meningitis Score was applied to 2903 (88%) of the study patients, and the frequency of bacterial meningitis increased with the greater number of additional Bacterial Meningitis Score risk factors. In those patients with no Bacterial Meningitis Score risk factors, the rate of bacterial meningitis was 0.1%, and in those patients with four or more risk factors, the rate of bacterial meningitis was 95%.

In the 1714 patients who were 'very low risk', as categorized by the Bacterial Meningitis Score, two (0.1%) had bacterial meningitis and 1712 (99.8%) had aseptic meningitis (negative predictive value: 99.9%; 95% CI: 99.6–100%). In the 1189 patients who were not 'very low risk' as categorized by the Bacterial Meningitis Score, 119 (10%) had bacterial meningitis and 1070 (90%) had aseptic meningitis. The sensitivity for bacterial meningitis was 98.3% (95% CI: 94.2–99.8%) and the specificity was 61.5% (95% CI: 59.7–63.3%). The Bacterial Meningitis Score failed to identify two patients with bacterial meningitis; both were infants between 1 and 2 months of age with *Escherichia coli* meningitis and urinary tract infections with negative urinalysis at the time of presentation.

An attempt was made to refine the Bacterial Meningitis Score to a simpler model that only relied upon three variables. However, this revision misclassified an additional patient with meningitis. The authors surmised that the original variables of the Bacterial Meningitis Score are easily applied and objectively measurable. When this rule was applied to children over 2 months of age, the sensitivity of the Bacterial Meningitis Score was 100% (95% CI: 96.9–100%) with a specificity of 63.5% (95% CI: 61.4–65.6%) and a negative predictive value of 100% (95% CI: 99.8–100%).

In conjunction with a careful clinical assessment, the Bacterial Meningitis Score can serve as an assistive clinical prediction rule to help guide clinical decision making. In children aged over 2 months with a Bacterial Meningitis Score of zero, the clinician could consider the options of admission for observation without antibiotics, or, if adequate follow-up is available, outpatient management. Due to the devastating consequences of the failure to identify a bacterial meningitis patient, administration of a long-acting parental antibiotic should be strongly considered if a patient is to be discharged from the ED.

References

1. Fleisher GR: Central nervous system infections. In: *Textbook of Pediatric Emergency Medicine. 5th edition.* Fleisher GR, Ludwig SL, Henretig FM (Eds), Lippincott Williams & Williams, PA, USA, 788–795 (2006).
2. Nigrovic LE, Kuppermann N, Malley R: Development and validation of a multivariable predictive model to distinguish bacterial from aseptic meningitis in children in the post-*Haemophilus influenzae* era. *Pediatrics* 110, 712–719 (2002).
3. Wasson JH, Sox HC, Neff RK, Goldman L: Clinical prediction rules: applications and methodological standards. *N. Engl. J. Med.* 313, 793–799 (1985).
4. Nigrovic LE, Kuppermann N, Macias CG *et al.*: Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *JAMA* 297(1), 52–60 (2007).

Oral ondansetron for pediatric vomiting

Evaluation of: Freedman SB, Adler M, Seshadri R, Powell EC: Oral ondansetron for gastroenteritis in a pediatric emergency department. *N. Engl. J. Med.* 354(16), 1698–1705 (2006).

Gastroenteritis remains a common illness among infants and children, with significant morbidity and mortality [1]. The recommendation for the management of mild-to-moderate dehydration in children is oral rehydration therapy [1]; however, oral rehydration therapy remains widely underutilized.

One of the rate-limiting steps to oral rehydration therapy is vomiting. Many clinicians in the ED are more likely to choose intravenous over oral rehydration when vomiting is a major presenting symptom [2].

In a previous study, Ramsook *et al.* evaluated the effect of oral ondansetron administered every 8 h for 2 days versus placebo in pediatric ED patients with vomiting due to gastroenteritis [3]. Although these investigators found a decrease in the rate of vomiting associated with the use of odansetron, the patients in the ondansetron group had significantly more diarrhea in the 48 h following discharge than those patients receiving placebo. The study by Freedman *et al.* was conducted to determine if a single dose of orally disintegrating ondansetron tablet given in the ED to patients with vomiting and dehydration could control vomiting with minimal side effects [4].

This was a prospective, double blind, randomized comparison of ondansetron and placebo in vomiting children aged 6 months to 10 years. Children with at least one episode of nonbloody, nonbilious vomiting, at least one episode of diarrhea, and mild-to-moderate dehydration were considered eligible for inclusion in the study.

Patients in the study were randomly assigned to receive a single weight-based dose of ondansetron or placebo. A total of 15 min after medicine administration, a 1-h period of oral rehydration therapy was initiated. After the oral rehydration therapy period, the treating physician resumed management and was responsible for the disposition of the patient. Follow-up phone calls determined whether the patients had returned to an ED, had received intravenous fluids or required hospital admission. Statistical analysis of all data was performed.

Data were collected and analyzed for 214 patients, 107 in each of the ondansetron and placebo groups. The amount of vomiting during the oral rehydration therapy period was significantly decreased in the ondansetron group, 14 versus 35% ($p < 0.001$). This finding remained significant after adjusting for the type of physician providing care (relative risk: 0.40; 95% CI: 0.26–0.61).

The number of episodes of vomiting was also reduced in the ondansetron group when compared with those receiving placebo (0.18 vs 0.65; $p < 0.001$). A total of 15 children in the ondansetron group went on to receive intravenous hydration (14 vs 31%; $p = 0.003$) and, overall, the children in the ondansetron group received a smaller volume of intravenous fluid and had a shorter stay in the ED. Admission rates were similar between the two groups. At follow-up, children who received ondansetron had more episodes of diarrhea (1.4 vs 0.5; $p < 0.001$), but there were no additional adverse events identified.

The investigators concluded that a single dose of orally disintegrating ondansetron was well tolerated, and resulted in a reduction in vomiting episodes. Treatment with ondansetron also reduced the number of children who were administered intravenous fluids in this study. The number needed to treat with ondansetron to reduce vomiting was five (95% CI: 3.2–10.6), and to prevent intravenous hydration was six (95% CI: 3.6–17.0).

Other anti-emetics have been used in the treatment of pediatric gastroenteritis. However, these agents are not well studied and have a higher rate of adverse effects. Ondansetron is easy to administer in the orally dissolving tablet form, and has minimal side effects. The use of orally disintegrating ondansetron tablets may be a useful therapy in the ED management of children with vomiting and mild-to-moderate dehydration as a result of acute, uncomplicated gastroenteritis.

References

1. King CK, Glass R, Bresee JS, Duggan C: Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. *MMWR Recomm. Rep.* 52, 1–16 (2003).
2. Ozuah PO, Avner JR, Stein RE: Oral rehydration, emergency physicians, and practice parameters: a national survey. *Pediatrics* 109, 259–261 (2002).
3. Ramsook C, Sahagun-Carreon I, Kozinetz CA, Moro-Sutherland D: A randomized clinical trial comparing oral ondansetron with placebo in children with vomiting from acute gastroenteritis. *Ann. Emerg. Med.* 39, 397–403 (2002).
4. Freedman SB, Adler M, Seshadri R, Powell EC: Oral ondansetron for gastroenteritis in a pediatric emergency department. *N. Engl. J. Med.* 354(16), 1698–1705 (2006).

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.