Diagnostic Testing for Serious Bacterial Infections in Infants Aged 90 Days or Younger With Bronchiolitis

Erica L. Liebelt, MD; Keqin Qi, PhD; Karanja Harvey, MD

**Objectives:** To describe the different laboratory tests that are performed on young infants aged 90 days or younger with bronchiolitis and to identify historical and clinical predictors of infants on whom laboratory tests are performed.

**Design:** Cross-sectional study whereby information was obtained by retrospective review of medical records from November through March 1992 to 1995 of all infants with a clinical diagnosis of bronchiolitis.

**Setting:** Urban pediatric emergency department.

**Patients:** Two hundred eleven consecutive infants aged 90 days or younger (median age, 54 days) with 216 episodes of bronchiolitis.

**Main Outcome Measures:** Historical and clinical data on each infant in addition to laboratory data that included a white blood cell count, urinalysis, and blood, urine, and cerebrospinal fluid cultures.

**Results:** Two or more laboratory tests (not including chest radiographs) were obtained in 48% of all infants and 78% of febrile infants. Of the 91 infants with a history of a temperature of 38.0°C or more or temperature on presentation of 38.0°C or more, white blood cell counts were obtained in 77%, blood cultures in 75%, urinalyses in 53%, urine cultures in 60%, and analyses-cultures of cerebrospinal fluid in 47%. Febrile infants were 10 times more likely to get at least 2 laboratory tests than afebrile infants (P<.01). All 6 studies were done in 42 (58%) of 72 febrile infants compared with 7 (16%) of 43 afebrile infants (P<.001). Multiple logistic regression analysis identified a history of a temperature of 38.0°C or more or temperature on presentation of 38.0°C or more (odds ratio [OR] 10.0; 95% confidence interval [CI], 4.8%-21.0%; P<.001), oxygen saturation less than 92% on presentation (OR, 4.7; 95% CI, 1.9%-12.1%; P<.01), and history of apnea (OR, 0.1; 95% CI, 0.02 – 0.35; P<.001) as significant clinical predictors of whether laboratory studies were obtained. History of preterm gestation, aged younger than 28 days, previous antibiotic use, and presence of otitis media were not associated with obtainment of laboratory studies. No cases of bacteremia, urinary tract infection, or meningitis were found among all infants with bronchiolitis who had blood, urine, and/or cerebrospinal fluid cultures.

**Conclusion:** There is wide variability in the diagnostic testing of infants aged 90 days or younger with bronchiolitis. The risks of bacteremia, urinary tract infection, and meningitis in infants with bronchiolitis seems to be low. History of a documented temperature of 38.0°C or more; oxygen saturation of less than 92%, and history of apnea were associated with laboratory testing for bacterial infections.

Arch Pediatr Adolesc Med. 1999;153:525-530

---

**Editor’s Note:** These small, sick infants make me nervous. It would be nice if the findings in this study are borne out by others.

*Catherine D. DeAngelis, MD*

BRONCHIOLITIS is an acute viral infection of the lower respiratory tract that typically affects young infants and is most commonly caused by the respiratory syncytial virus (RSV). It is a clinical diagnosis characterized by wheezing, cough, and rhinorrhea, and is sometimes accompanied by prolonged fever. Several studies have demonstrated a viral cause, commonly RSV, for fever in a substantial proportion of febrile young infants younger than 3 months hospitalized for suspected bacterial sepsis. An established clinical practice guideline recommends a laboratory evaluation (white blood cell count, urinalysis, cerebrospinal fluid [CSF] analysis, and blood, urine, and cerebrospinal cultures) for bacterial infection in all febrile infants younger than 28 days and in some infants 2 to 3 months of age. However, it does not address the laboratory evaluation of the febrile infant with an obvious viral infection. Recent studies have demonstrated a
PATIENTS AND METHODS

The study design was a cross-sectional study whereby information was obtained by retrospective review of medical records. The emergency department (ED) patient log was reviewed for all patients aged 90 days or younger seen in the pediatric ED at Yale–New Haven Hospital, New Haven, Conn, during a 5-month period (November through March) for 3 consecutive years, 1992 to 1995. The winter months were chosen because bronchiolitis is more prevalent during this time. Yale–New Haven Hospital is an urban, university-affiliated medical center with a pediatric ED that handles 20,000 to 22,000 children per year and is the primary referral site for the region.

PATIENT SELECTION

All infants aged 90 days or younger presenting with a chief complaint of fever, shortness of breath, wheezing, cough, increased work of breathing, apnea, and/or an ED discharge or admission with a diagnosis of fever, bronchiolitis, pneumonia, apnea, wheezing, or reactive airway disease were identified, and the ED records, hospital records, and clinic records were reviewed. All infants aged 90 days or younger who had documentation of wheezing heard on auscultation of the chest while in the ED and documented history of upper respiratory tract symptoms (eg, rhinorrhea) were included. Infants with a history of bronchopulmonary dysplasia, underlying immunodeficiency, complex congenital heart disease, other bacterial infections (septic arthritis, cellulitis, or osteomyelitis), or other identifiable viral infection (varicella, croup, or stomatitis) were excluded. Infants with multiple ED visits that met the aforementioned criteria were included in the study as separate episodes of bronchiolitis if these visits were separated by 3 weeks or more, when the clinical signs and symptoms had resolved.

MAIN OUTCOME MEASURES

We recorded demographic and historical data such as history of prematurity, apnea, cyanosis, fever, and previous antibiotic use as well as clinical data such as vital signs, oxygen saturation, and physical examination findings including the presence of otitis media. Infants with a history of tactile fever were not recorded as having a history of fever. We recorded whether a white blood cell count, urinalysis, urine culture, blood culture, CSF cell count, or a CSF culture was obtained for each infant. In addition, the results of RSV rapid antigen and viral cultures were documented.

Laboratory results documented in the patients’ medical records were cross-checked for accuracy using the Yale–New Haven Hospital microbiology and hematology computer databases. Additionally, all urine, blood, and CSF cultures obtained from pediatric patients during the study period were cross-referenced with the medical record number of all infants included in the study to ensure that no cultures were overlooked. Diagnostic tests obtained at other health care facilities were recorded for those patients transferred to our ED for evaluation.

A serious bacterial infection was defined as the presence of bacteremia, urinary tract infection (UTI), or bacterial meningitis based on analysis of blood, urine, and CSF cultures. A culture was considered to be a contaminant if coagulase-negative Staphylococcus (or other nonpathogenic bacteria) was grown from an infant who was clinically well-appearing. A UTI was defined as 10,000 or more colony-forming units per milliliter of a single pathogenic organism on a catheterized specimen or 1000 or more colony-forming units per milliliter of a gram-positive coccus or any growth of a gram-negative rod from a suprapubic aspiration. Respiratory syncytial virus was identified either by enzyme immunoassay (EIA) (TestPack EIA; Abbott Laboratories, North Chicago, Ill) obtained from a nasopharyngeal aspirate or viral cultures that were obtained on selected infants at the discretion of the physician.

STATISTICAL ANALYSES

Differences between groups of patients were analyzed using the 2-tailed Student t test for continuous variables (age, vital signs, and pulse oximetry) and χ² analysis for categorical variables. The Fisher exact test was used if a categorical variable had less than 3 results. A forward stepwise multiple logistic regression analysis was performed to identify predictors of whether laboratory tests were obtained. Eight variables were evaluated for each infant for their univariate association with whether laboratory studies were obtained. Variables were chosen for the regression model based on their statistical significance (P < .05) and clinical importance. An internal validation of the model was performed after dichotomizing the sample based on sex. Statistical analyses were done using commercial statistical software (SAS System for Windows, release 6.10; SAS Institute Inc, Cary, NC). An α level of less than .05 was considered statistically significant.

RESULTS

There were 211 consecutive infants who had 216 episodes of bronchiolitis included in the study (5 infants...
had 2 separate episodes of bronchiolitis. The infants ranged in age from 8 to 90 days with a median age of 54 days. One hundred twenty-four (59%) were boys and 87 (41%) were girls. One hundred seventy-nine (78%) were products of a full-term gestation and 87 (41%) were products of a preterm gestation (>37 weeks). Three infants had minor congenital heart lesions. Thirty-five (16%) of 216 infants had been prescribed oral antibiotics prior to presentation to the ED, 22 (10%) had an episode of cyanosis, 20 (9%) had an episode of apnea, and 87 (40%) had a history of irritability.

At least 1 laboratory test was obtained in 115 (53%) of 216 infants and at least 2 were obtained in 103 (48%) of 216 infants. Table 1 gives the proportion of all infants who had laboratory testing performed. Of the 35 infants who received antibiotics before arrival to the ED, 7 (20%) had blood, urine, and CSF cultures; 5 (14%) had a blood culture and CSF or urine cultures; and 1 (3%) had a urine culture.

Infants were stratified into 2 groups based on the presence or absence of fever, defined as a temperature of 38°C or higher. Ninety-one (42%) of 216 infants had a history of fever or fever on presentation that ranged from 38.0°C to 40.7°C, while 125 infants (58%) had no history or temperatures lower than 38.0°C on presentation. There were no significant historical or clinical differences between the 2 groups, including vital signs and pulse oximetry.

Table 2 presents the differences in the laboratory evaluations between the febrile and afebrile infants. All laboratory tests were more likely to be obtained in febrile infants compared with afebrile infants. A white blood cell count, urinalysis, CSF analysis, and blood, urine, and CSF cultures all were obtained in 42 (58%) of 72 febrile infants who received tests compared with 7 (16%) of 43 afebrile infants, \( P < .001 \). Disposition and management outcomes are given in Table 3. Febrile infants were 9.2 times more likely than afebrile infants to be given parenteral antimicrobials and 3.0 times more likely to be hospitalized. One hundred (46%) of 216 infants had antimicrobial therapy initiated in the ED: 60 (28%) received parenteral antimicrobials and 39 (18%) had oral antimicrobials initiated in the ED. Sixty infants had parenteral antibiotics initiated in the ED for the diagnoses of sepsis/apnea (n = 52), pneumonia (n = 7), and otitis media (n = 1). Forty-seven (62%) of 76 febrile infants who were admitted to the hospital were given parenteral antibiotics. There was no statistically significant difference in the rate of RSV isolation between the 2 groups.

Infants with elevated temperatures were further stratified into those with temperatures lower and higher than 39.0°C. There was wide variability in the laboratory test results obtained in those infants with temperatures below 39.0°C. Only 54% of infants with bronchiolitis and a temperature of 38.0°C or higher (but <39.0°C) underwent a lumbar puncture (Table 4).

No cases of serious bacterial infection were found in any of the infants with a clinical diagnosis of bronchiolitis. Of the 100 children in whom blood cultures were obtained, 0 were positive. Thus, the risk of bacteremia in this group was 0% (1-sided 95% confidence interval [CI] 0%-3.6%). None of the 68 urine cultures obtained were positive (risk, 0%; 1-sided 95% CI, 0%-3.5%). The risk of meningitis in the 33 infants in whom CSF cultures were obtained was 0% (1-sided 95% CI, 0%-6.7%). Of the febrile infants, the risk of any serious bacterial infection was 0% (1-sided 95% CI, 0%-8.4%). The risk of bacteremia was 0% (1-sided 95% CI, 0%-5.3%); of UTI, 0% (1-sided 95% CI, 0%-6.5%); and of meningitis, 0% (1-sided 95% CI, 0%-8.2%).

A positive RSV EIA or culture was documented in 120 (82%) of 146 episodes of bronchiolitis that were studied for RSV. There were no significant differences in the frequency at which laboratory tests were obtained be-
between those infants who subsequently had a positive RSV EIA and/or culture and those infants with a negative EIA and/or culture. Those infants in the positive RSV identification group were more likely to be diagnosed with otitis media than those infants in the RSV negative group (25% vs 4%; \( P < .03 \)).

**Table 5** displays the proportion of infants for whom laboratory tests were obtained and were not obtained. A significant relationship was found between history of a temperature or current temperature of 38.0°C or higher (OR, 10.0; 95% CI, 4.8%-21.0%; \( P < .001 \)), oxygen saturation lower than 92% (OR, 4.7; 95% CI, 1.9%-12.1%; \( P < .01 \)), history of apnea (OR, 0.10; 95% CI, 0.02%-0.35%; \( P < .001 \)), and whether laboratory tests were obtained. A significant relationship was found between history of a temperature or current temperature of 38.0°C or higher (OR, 10.0; 95% CI, 4.8%-21.0%; \( P < .001 \)), oxygen saturation lower than 92% (OR, 4.7; 95% CI, 1.9%-12.1%; \( P < .01 \)), history of apnea (OR, 0.10; 95% CI, 0.02%-0.35%; \( P < .001 \)), and whether laboratory tests were obtained.

**COMMENT**

Clinical practice regarding laboratory evaluation of febrile infants younger than 3 months is widely debated and varies greatly among clinicians despite recommended guidelines.\(^8,13,14\) Furthermore, little data exist to support or refute the need for evaluation of bacterial infections in infants with an obvious viral infection. Indeed, in our sample, there was great variability in the number and type of laboratory tests ordered in both febrile and afebrile infants. Some infants with fever or history of fever did not receive any laboratory tests and were sent home without parenteral antibiotics. Other infants without fever received a full sepsis evaluation, hospitalization, and treatment with parenteral antibiotics. The numerous different physicians who are working in the ED can explain much of this variability and, hence, different clinical practice styles. In addition, many of the infants were sent to the ED with particular instructions for laboratory tests from their primary care physicians.

It was not surprising that temperature was a significant predictor of whether laboratory tests were ordered, since this factor alone is generally believed to be one of the most influential factors in the decision to pursue a workup for bacterial infections. It was unexpected that age younger than 28 days was not a significant predictor in whether laboratory tests were obtained. Clinicians probably tend to vary the least from recommended guidelines in this age group. Neither the length of gestation nor previous antibiotic use was associated with obtaining of laboratory tests. Both of these factors have been identified as placing young infants at high risk for serious bacterial infections by previously defined criteria, suggesting that a full sepsis evaluation, hospitalization, and antibiotic therapy may be indicated.\(^15\)

In another retrospective study, Antonow et al\(^8\) found similar variability in the decision to perform sepsis evaluations in hospitalized infants aged 60 days or younger with bronchiolitis. However, temperature was not a significant predictor in their sample. Infants were more likely to receive sepsis evaluations if they had higher levels of respiratory distress and normal chest radiographs and were
less likely if they appeared to have typical bronchiolitis and they were older than 28 days.

No infants in our study who had laboratory testing had a systemic bacterial infection even in the presence of fever. Some investigators have speculated that RSV infections may predispose the respiratory tract to bacterial invasion or may act in synergy with bacteria to produce more serious infection and thus, they advocate for evaluation for bacterial infection in febrile infants despite RSV isolation. Previous studies have reported a 0.02% to 3% incidence of concurrent serious bacterial infection in infants and older children hospitalized with RSV infection. In these studies, RSV infection did not necessarily denote clinical bronchiolitis; some children acquired RSV during hospitalization, and some children developed bacteremia during hospitalization.

Several recent studies of infants with clinical bronchiolitis have demonstrated a low or nonexistent risk of concurrent bacterial infections. Davies et al found no cases of bacteremia in 52 patients aged 6 months or younger hospitalized with bronchiolitis. In a prospective study, Kuppermann et al found a low risk of UTI (1.9%) and 0% risk of bacteremia in infants and children aged 24 months or younger with bronchiolitis and fever evaluated in the outpatient setting. The number of patients younger than 2 months in their study was too small to make statistically significant conclusions. Antenow et al report a 1.8% risk (5/140) of systemic bacterial infection in their hospitalized group of infants.

A large proportion of infants in our study were given parenteral antimicrobial therapy until the cultures were negative. Certainly, infants with bronchiolitis may receive antibiotic treatment because of their young age, severity of their respiratory illness, and difficulty in clinically differentiating RSV pneumonia from bacterial pneumonia. Some investigators have questioned whether prophylactic antibiotic treatment of RSV infection is detrimental and may increase the frequency of secondary bacterial infections. Based on our results and those of previous studies, it appears that withholding of antibiotics may be considered in infants aged 28 to 90 days unless clinical or laboratory findings suggest a bacterial infection.

In our study, oxygen saturation of less than 92% was a significant predictor of whether laboratory tests were obtained. However, only 30 children had an infiltrate on their chest radiograph, 22 of which were in infants that were RSV EIA or culture positive. We purposely did not include pneumonia in our definition of serious bacterial infection despite its customary inclusion in numerous studies. A major problem in this study or any study requiring the diagnosis of bacterial pneumonia is that no sensitive, specific, and feasible method of laboratory diagnosis exists. Our study was not designed to address these issues. The physician's decision to obtain laboratory tests, hospitalize the infant, and/or administer antimicrobial therapy may have depended on the presence of an infiltrate on chest radiograph with or without a fever. Interestingly, the study by Antenow et al demonstrated that a normal chest radiograph was a clinical predictor for performing a sepsis evaluation in their subjects.

Our study differs from others because it looks specifically at infants aged 90 days or younger with a clinical diagnosis of bronchiolitis on presentation to the ED. From a practical standpoint, it is the physician evaluating the infant who must decide if further laboratory testing is necessary. Frequently, by the time the RSV status is known, decisions on evaluation, treatment, and admission have already been made. We found no significant differences between those infants diagnosed with positive RSV detection or culture vs those with negative RSV test results with regard to clinical presentation, laboratory evaluation, or laboratory test results. Based on our study findings, it is not clear whether rapid RSV detection in the ED would be a cost-effective means of determining which previously healthy, well-appearing, young infants may not need further laboratory testing for evaluation of a bacterial infection.

This study has several limitations. Information was obtained by retrospective review of medical records, which relies on documented information and may not always be complete. Second, patient follow-up was assessed using only our hospital and pediatric primary care clinic's medical records. A small proportion of infants who were discharged from the ED (<5% of our subjects) may have been seen at other health care facilities where additional laboratory evaluation could have been done, perhaps biasing the true rate of concomitant bacterial infection. Finally, blood, urine, and CSF cultures were obtained in only 49 (23%) of 216 infants; therefore, it is possible that the rate of bacteremia, UTIs, and/or meningitis could have been higher had bacterial cultures been obtained in all febrile infants.

There is wide variability in the diagnostic testing of both febrile and afebrile infants with bronchiolitis. Significant predictors of whether laboratory tests were obtained included a history or documented temperature of 38.0°C or higher, oxygen saturation of less than 92%, and a history of apnea. Previously defined clinical and laboratory factors that may place a young infant at increased risk for serious bacterial infection (preterm gestation, otitis media, or previous antibiotic use) were not associated with laboratory testing. The risks of bacteremia, UTIs, and meningitis in infants aged 90 days or younger with bronchiolitis and for whom appropriate cultures were obtained was 0%. Our data in conjunction with other published data suggest that previously healthy, well-appearing infants with wheezing and other signs of an upper respiratory infection may not need laboratory testing for bacterial infections even in the presence of a fever. A large randomized prospective clinical trial needs to address all of these challenging issues in this cohort of infants.

Accepted for publication October 7, 1998.


We thank Eugene Shapiro, MD, for his assistance and guidance in the development and preparation of the manuscript.
REFERENCES