Diagnosis and Testing in Bronchiolitis

A Systematic Review

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Background: The diagnosis of bronchiolitis is based on typical history and results of a physical examination. The indications for and utility of diagnostic and supportive laboratory testing (eg, chest x-ray films, complete blood cell counts, and respiratory syncytial virus testing) are unclear.

Objectives: To review systematically the data on diagnostic and supportive testing in the management of bronchiolitis and to assess the utility of such testing.

Design: In conjunction with an expert panel, we generated admissibility criteria and derived relevant terms to search the literature published from 1980 to November 2002 in MEDLINE and the Cochrane Collaboration Database of Controlled Clinical Trials. Trained abstractors completed detailed data collection forms for each article. We summarized the data in tables after performing data integrity checks.

Results: Of the 797 abstracts identified, we present evidence from 82 trials that met our inclusion criteria (17 are primary articles on diagnosis of bronchiolitis and 65 are reports of treatment or prevention trials). Numerous studies demonstrate that rapid respiratory syncytial virus tests have acceptable sensitivity and specificity, but no data show that respiratory syncytial virus testing affects clinical outcomes in typical cases of the disease. Seventeen studies presented chest x-ray film data. Abnormalities on chest x-ray films ranged from 20% to 96%. Insufficient data exist to show that chest x-ray films reliably distinguish between viral and bacterial disease or predict severity of disease. Ten studies included complete blood cell counts, but most did not present specific results. In one study, white blood cell counts correlated with radiologically defined disease categories of bronchiolitis.

Conclusions: A large number of studies include diagnostic and supportive testing data. However, these studies do not define clear indications for such testing or the impact of testing on relevant patient outcomes. Given the high prevalence of this disease, prospective studies of the utility of such testing are needed and feasible.

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BRONCHIOLITIS IS THE MOST common lower respiratory tract infection in infants. Virtually all children have been exposed to respiratory syncytial virus (RSV), the cause of most bronchiolitis cases, by their second birthday. Up to 3% of all children are hospitalized with bronchiolitis in their first year of life.[1] The diagnosis of bronchiolitis is based primarily on typical history and results of a physical examination.[2] Despite the high prevalence of bronchiolitis, little consensus exists on the optimal management of the disease.[3] There is significant variation in the use of supportive testing and treatment of bronchiolitis.[4,5]

A variety of laboratory studies can provide supportive data for diagnosis. Examples include chest x-ray films, complete blood cell (CBC) counts, and specific testing to determine the cause of bronchiolitis (eg, viral culture, immunofluorescence, and enzyme-linked immunosorbent assays for RSV). The use of testing is typically justified for 1 of the following reasons: ruling out other diagnoses (eg, congestive heart failure or bacterial pneumonia), first-time wheezing, cohorting of hospitalized patients, deciding on treatment (eg, ribavirin), including patients in research protocols, or performing public health surveillance.

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The clinical utility of specific etiologic testing in cases of bronchiolitis is unclear. Complete blood cell counts have poor test characteristics for determining bacterial disease.[6] Chest x-ray film findings for bronchiolitis and pneumonia are variable and nonspecific.[7,8] Knowing that RSV is the cause of bronchiolitis does little

Table 1. Inclusion and Exclusion Criteria

Category	Criteria
Study population	Humans, infants, and children
Study settings and geography	Inpatient, outpatient, home; all geographical locations subject to publication language and study design criteria
Time period	Systematic reviews, from 1966-2002; individual studies, published from 1980 through 2002*
Publication languages	English only
Admissible evidence (study design and other criteria)	Original research studies that provide sufficient detail regarding methods and results to enable use and abstraction of the data and results
For studies on diagnosis	RCTs with double-blinded, single-blinded, and crossover designs; non-RCTs with prospective cohort designs
For studies on treatment and prophylaxis	RCTs, with double-blinded, single-blinded, and crossover designs; sample size appropriate for the study question addressed (ie, case reports or small case series; with <10 subjects excluded)

Abbreviation: RCT, randomized controlled trial.
*1980 start point was based on consensus of the expert panel.

Table 2. Search Terms

Topic	Search Terms
Exploded terms for diagnosis	Bronchiolitis, diagnosis, differential diagnosis, thoracic radiography, laboratory techniques, and procedures
Exploded terms for treatment	Steroidal anti-inflammatory agents, steroids, bronchodilator agents, antiviral agents, antimicrobial cationic peptides, antibiotics, antimicrobials, and anti-infective agents
Exploded terms for prophylaxis	Primary prevention, immunoglobulins, bronchiolitis (prevention and control), isolation strategies, and patient isolation
Study design for diagnosis	Prospective studies, longitudinal studies, and cohort studies
Study design for treatment and prophylaxis	Randomized controlled trial, single-blind method, double-blind method, random allocation, and meta-analysis
Outcomes for diagnosis	Fatal outcome, outcome and process assessment (health care), outcome assessment (health care), and treatment outcome
Outcomes for treatment and prophylaxis	Morbidity, mortality, and adverse effects or harms
Limiting terms for all	Human, years 1980-2002, newborn infant (age, birth to 1 mo), infant (age, 1-23 mo), or preschool child (age, 2-5 y)

to change the clinical course, the management, or the prognosis. Supportive testing, nevertheless, is common and is associated with significant cost in the care of infants with this disease.[9] Some institutions have developed evidence-based guidelines specifically to decrease the use of RSV enzyme-linked immunosorbent assays and supportive diagnostic testing.[10]

The present study was part of a larger systematic review of the literature on the diagnosis and treatment of bronchiolitis. We herein attempt to determine the effectiveness of diagnostic tools and supportive testing for diagnosing bronchiolitis in infants. A companion report presents the data on the treatment and prevention of bronchiolitis.[11]

METHODS

In conjunction with an expert panel, we generated inclusion and exclusion criteria (**Table 1**) and derived relevant terms (**Table 2**) to search the literature in MEDLINE and the Cochrane Collaboration Database of Controlled Clinical Trials. For all studies, key inclusion criteria consisted of outcomes that were clinically relevant and could be abstracted. Meta-analyses were included in the search to examine their lists of included and excluded studies. We conducted hand searches of the reference lists of relevant included articles to ensure that we did not exclude important work. In addition, we consulted with the technical expert advisory group about any studies that were under way but not yet published. Our search was last updated in November 2002. Two additional studies published during this this article's review process were included.[12,13]

Trained abstractors completed detailed data collection forms for each included study. We summarized the information in tables after reviewing the data collection forms against the articles. Senior study personnel (W.C.B. and V.J.K.) performed data integrity checks by reviewing the articles a second time against the evidence tables.

RESULTS

We reviewed 797 abstracts identified using the search strategy. Of these, 17 are primary articles on diagnosis of bronchiolitis. None of these studies was designed specifically to measure the utility of diagnostic or supportive testing. However, considerable data on diagnosis and testing were found in the 65 treatment and prevention trials identified, so these are also included in our results.

The studies dealing with diagnosis fell into the following 5 categories: (1) case definitions and inclusion criteria used in the clinical trials; (2) viral causes of bronchiolitis when all subjects underwent testing; (3) comparison of various virus isolation techniques; (4) predictors of disease severity, complications, or both; and (5) studies in which standardized tests were performed on all patients as part of their evaluation (eg, chest x-rays and CBC counts).

CASE DEFINITION AND INCLUSION CRITERIA

The challenge of this literature is the fact that bronchiolitis is a clinical diagnosis based on typical history and findings on physical examination. There is no specific diagnostic test or gold standard that confirms the diagnosis or excludes other diseases that may be clinically similar (eg, bacterial pneumonia). We reviewed the case definitions and inclusion criteria used in the clinical trials and found that most definitions were quite similar. Forty-three trials used tachypnea in the case definition or inclusion criteria; 42 used wheezing; 37 used oxygen saturation; and 32 used retractions. However, many studies simply stated that infants with signs and symptoms con-

Table 3. Studies Examining the Accuracy of Virological Tests

Source	Gold Standard	Tests Compared	Results
Ahluwalia et al,[21] 1987	Viral culture of NPA and NPS	EIA, IFA on NPA and NPS specimens	EIA-NPA: Sn = 69%, Sp = 100%; EIA-NPS: Sn = 61%, Sp = 100%; IFA-NPA: Sn = 61%, Sp = 89%; and IFA-NPS: Sn = 52%, Sp = 78%
Chattopadhya et al,[22] 1992	Viral culture	IFA, EIA, EIA by blocking test	IFA: Sn = 89%, Sp = 92%, EIA: Sn = 94%, Sp = 74%; and EIA by blocking test: Sn = 94%, Sp = 77%
Eugene-Ruellan et al,[23] 1998	Viral culture and/or IFA	PCR	97% Concordance
Ong et al,[22] 2001	IFA	PCR	IFA detected 27 cases; PCR detected 28 cases
Warner et al,[25] 1990	Viral culture and/or IFA	EIA	Sn = 86%, Sp = 91%

Abbreviations: EIA, enzyme immunoassays; IFA, direct immunofluorescence assay; NPA, nasopharyngeal aspirate; NPS, nasopharyngeal suction; PCR, polymerase chain reaction; Sn, sensitivity; Sp, specificity.

sistent with bronchiolitis were eligible for inclusion. Many authors referred to the classic historic definition of bronchiolitis by Court.[14]

Eligibility criteria in the clinical trials varied, especially with respect to criteria such as age, duration of symptoms, comorbidities (eg, prematurity and chronic lung disease), history of previous wheezing, and severity of disease. Specific study objectives determined most of these variations (eg, numerous studies included only infants with bronchiolitis due to RSV).

Most trials measured disease severity as a baseline independent variable and as a dependent outcome (ie, change in disease severity resulting from treatment). Disease severity was most commonly measured using clinical scales (43 of the 65 clinical trials), but the variety of scales used made comparing studies difficult. Some studies used clinical scales validated in previous studies such as the Respiratory Distress Assessment Instrument.[15-18] Other research teams created or modified scales for their particular trial.[19,20] Despite these differences, the clinical scales all incorporated measures of respiratory rate, respiratory effort, severity of wheezing, and oxygenation.

IDENTIFICATION OF THE CAUSE OF BRONCHIOLITIS

Many but not all of the included studies attempted to identify the cause of enrolled cases of bronchiolitis. Twenty-nine of the clinical trials enrolled only infants with positive findings for RSV. Of the 56 treatment trials, 46 performed RSV testing on all subjects. In the 21 trials in which all patients underwent testing and were included, regardless of RSV status, the cases caused by RSV ranged from 26% to 95%. In 12 trials, patients underwent testing for other viral causes (eg, parainfluenza viruses) in addition to RSV, but most reported results as the percentage with positive findings for RSV vs other viruses.

The techniques for identifying RSV as the causative agent of bronchiolitis included viral cultures, rapid antigen detection tests (eg, direct immunofluorescence assay and enzyme immunoassays), polymerase chain reaction, and measurements of acute and convalescent antibody titers. Rapid antigen detection tests for RSV were used most frequently. In many studies, investigators performed viral cultures on cases with negative findings for RSV.

COMPARISON OF VIROLOGICAL TESTS

Five studies examined the accuracy of various virological tests for RSV and other causative viruses.[21-25] **Table 3** demonstrates that numerous tests for RSV exist and that their test characteristics vary. The *2000 Red Book* from the American Academy of Pediatrics reports that the overall sensitivity of the rapid antigen detection tests ranges from 80% to 90%.[26] Data presented in Table 3 are consistent with this estimate. Individual test manufacturers likely have additional, unpublished data on their own assays, as they generally report test characteristics in the package insert materials that accompany test kits. Our search strategy would not have identified this unpublished data. In addition to looking at test agreement, Ahluwalia et al[21] compared 2 methods of specimen collection and demonstrated that viral culture, enzyme immunoassays, and direct immunofluorescence assays all yielded positive results more often when performed on nasopharyngeal aspirates than when performed on nasopharyngeal swabs.

We identified no trials that addressed the question of whether knowing RSV is the causative agent in bronchiolitis affects clinical outcomes.

PREDICTORS OF DISEASE SEVERITY OR COMPLICATIONS

Four studies (**Table 4**) measured various predictors of disease severity.[7,27-29] Shaw et al[28] examined historical elements, physical examination findings, and laboratory results and identified the following 5 clinically important predictors of severe disease: ill or toxic appearance, oxygen saturation of less than 95%, gestational age of less than 34 weeks, respiratory rate of greater than 70 breaths per minute, and age younger than 3 months. Mulholland et al[27] correlated clinical findings with disease severity defined by pulse oximetry findings and arterial blood gas measurements. Young age, cyanosis, crackles, and oxygen saturation of less than 90% all predicted more severe disease. Dawson et al[7] studied the relationship between clinical severity based on clinical scales with the degree of radiological changes on chest x-rays. The authors found no correlation. Wright et al[29] examined the relationship between demographic characteristics, viral shedding and antibody responses, and disease severity

Table 4. Studies Measuring Predictors of Disease Severity

Source	Outcome Predicted	Indicators Examined	Predictors
Dawson et al,[7] 1990	Clinical score (mild, moderate, severe, or very severe)	CXR findings (ie, hyperinflation, atelectasis, and infiltrates)	There was no correlation between CXR findings and disease severity
Mulholland et al,[27] 1990	Severity at the time of admission as assessed by means of oximetry and arterial blood gas results; O_2 requirements during admission	Demographics, cyanosis, crackles, chest wall in drawing, RR >50 breaths/min, Liver >2 cm below costal margin, SaO_2 <90%, PaO_2 <60 mm Hg, $PaCO_2$ >45 mm Hg, and RSV status	Indicators of severity at time of admission: young age, cyanosis, and crackles; predictors of oxygen requirement during admission: young age, cyanosis, crackles, high RR, chest wall indrawing, SaO_2 <90%, $PaCO_2$ >45 mm Hg, $PaCO_2$ >45 mm Hg, and PaO_2 <60 mm Hg
Shaw et al,[28] 1991	Mild disease (defined as alert, active, and able to take fluids throughout their disease, no O_2 therapy, etc) vs severe disease (defined as all others without mild disease)	Historical information: cyanosis or apnea, gestational age, age <3 mo, decreased oral intake, perinatal complications, and URI symptoms <3 d; physical examination and observations: ill or toxic appearance, Yale Observation Scale score ≥10, accessory muscle use, clinical asthma score ≥2, RR, and rales; and laboratory: pulse oximetry while quiet, pulse oximetry while sucking, CXR findings of atelectasis or hyperaeration, and isolation of RSV	The following 6 independent clinical and laboratory findings were strongly associated with more severe disease using multiple-factor analysis: ill or toxic appearance, oxygen saturation <95%, gestational age <34 wk, RR ≥70 breaths/min, and age <3 mo
Wright et al[29] (2002)	Illness severity in hospitalized infants with RSV bronchiolitis measured by (1) sum of respiratory illness scores, (2) duration of O_2 therapy (3) length of ventilatory support	Historical information: age; laboratory: serum neutralizing antibody titer; RSV shedding	History of BPD or congenital heart disease and younger age

Abbreviations: BPD, bronchopulmonary disease; CXR, chest x-ray film; RR, respiratory rate; RSV, respiratory syncytial virus; SaO_2, arterial oxygen saturation; URI, upper respiratory tract infection.

using data collected during the 2 RSV immunoglobulin clinical trials.[20,29,30] Their report focused primarily on immunologic responses to RSV, but demonstrated that younger age, history of bronchopulmonary dysplasia, and history of congenital heart disease were independently associated with more severe disease.

Most textbooks cite young age, history of prematurity or other comorbidities, toxic appearance at presentation, and rapid progression of symptoms as risk factors for severe disease. The studies by Shaw et al,[28] Mulholland et al,[27] and Wright et al[29] support these assertions.

UTILITY OF CHEST X-RAYS IN BRONCHIOLITIS

Seventeen studies obtained chest x-ray films on all patients (**Table 5**),[7,12,19,20,28,30-41] but many clinical trials do not report chest x-ray film results. Two studies examined the relationship between x-ray film abnormalities and disease severity. In the trial by Shaw et al,[28] the patients with atelectasis were 2.7 times more likely (95% confidence interval [CI], 1.97-3.70) to have severe disease than those without this x-ray film finding. This association persisted when it was included in a multivariable analysis. In contrast, the data from Dawson et al[7] demonstrated no correlation between chest x-ray film findings and baseline disease severity as measured by a clinical severity scoring system.

Three studies compared chest x-ray films with cultures and management. In a prospective cohort of 128 infants younger than 7 years with clinical lower respiratory tract infections, Friis et al[35] obtained viral and bacterial studies on nasopharyngeal secretions; they compared virus-infected children with or without bacteria in their secretions with data on the corresponding groups without virus infection. The x-ray film findings were normal significantly more often in the virus-positive–bacteria-negative group than in the other groups. Alveolar pneumonia appearing as lobar or segmental consolidations ("lobar" pneumonia) was observed with equal frequency and without relation to bacterial findings in the virus-positive and virus-negative groups. Roosevelt et al[39] showed that the presence of chest x-ray film abnormalities was strongly correlated with the use of antibiotics, but did not examine the effectiveness of antibiotic treatment in these patients. Swingler et al[8] examined the impact of chest x-ray films in acute lower respiratory tract infections on clinical outcomes by randomizing 522 infants aged 2 to 59 months to receive or not to receive a chest radiograph. Children in the chest radiograph group were more likely to be diagnosed as having pneumonia or upper respiratory tract infections and were more likely to be treated with antibiotics; children who did not receive a chest radiograph were more likely to be diagnosed as having bronchiolitis. Despite these differences, the median time to recovery was 7 days in both groups.

UTILITY OF CBC COUNTS IN BRONCHIOLITIS

Ten studies obtained CBC counts on all patients (**Table 6**).[19,31,38,41-47] In most of these studies, however, the CBC results were not reported or used only to demonstrate that the treatment and control groups were similar at baseline. Saijo et al[31] correlated white blood cell counts in 120 RSV-positive infants with radiologically de-

Table 5. Utility of Chest X-ray Films in Bronchiolitis

Source	Purpose of Study	Use of Chest X-ray	Results
Bertrand et al,[32] 2001	RCT of epinephrine vs salbutamol in hospitalized infants	Baseline assessment	CXR results not reported
Can et al,[19] 1998	RCT of salbutamol vs mist in the ED	Baseline assessment	CXR findings "consistent with bronchiolitis" were present in 88%, 69%, and 73% of the infants in the 3 study groups
Dawson et al,[7] 1990	Cohort design specifically to look at the utility of routine CXRs in bronchiolitis by examining the relationship between clinical assessment (ie, mild, moderate, severe, or very severe) and CXR findings (ie, hyperinflation, atelectasis, and infiltrates)	Baseline assessment	No correlation between CXR findings and disease severity
Dobson et al,[34] 1998	RCT of albuterol in hospitalized infants	Baseline assessment	CXR results not reported
Friis et al,[35] 1990	Prospective cohort of children <7 y designed to correlate CXR findings with viral and bacterial studies	Baseline assessment	The results for children with bronchiolitis not reported separately, so no conclusions can be drawn
Luchetti et al,[36] 1998	RCT of porcine-derived surfactant in ventilated infants	Baseline assessment and to document clinical improvement	CXR results not reported
Meert et al,[33] 1994	RCT of ribavirin in ventilated children with RSV	Baseline assessment	CXR results not reported
Nasr et al,[37] 2001	RCT of recombinant human deoxyribonuclease I (rhDNase) in hospitalized infants	Baseline assessment and at study end or time of hospital discharge	CXR improvement was a trial outcome (CXR scores improved in the treatment group but not in the control group); CXR findings were not used to assess disease severity or determine management
Patel et al,[12] 2002	RCT of epinephrine vs albuterol vs saline	Baseline assessment	Pneumonia on CXR: 38% (epinephrine group), 42% (albuterol group), and 29% (placebo group)
Rodriguez et al,[20] 1997	RCT of RSVIg treatment of hospitalized young children at high risk for severe disease	Baseline assessment repeated at time of hospital discharge	CXR results not reported
Rodriguez et al,[30] 1997	RCT of RSVIg treatment of previously healthy hospitalized children	Baseline assessment repeated at time of hospital discharge	CXR results not reported
Rodriguez et al,[38] 1987	RCT of ribavirin in infants with RSV disease (included patients with bronchiolitis, pneumonia, and croup)	Baseline assessment	CXR results for infants with bronchiolitis not reported separately
Roosevelt et al,[39] 1996	RCT of dexamethasone in acute bronchiolitis	Baseline assessment	No data presented correlating CXR findings to disease severity; infiltrates seen in 32% of treatment group and 20% of placebo group, and 90% of infants with visible infiltrates were treated with antibiotics vs 44% of those without these findings
Saijo et al,[31] 1996	Compare laboratory findings (WBC, neutrophil count, ESR, and CRP) to radiographically defined categories of RSV lower respiratory tract infections	Baseline assessment to define disease categories (ie, lobar pneumonia vs bronchopneumonia vs bronchiolitis)	WBC, ESR, and CRP levels were all higher in patients with RSV lobar pneumonia vs bronchiolitis or bronchopneumonia
Schuh et al,[40] 1990	RCT of albuterol in ED	Baseline assessment	CXR results not reported
Shaw et al,[28] 1991	Prospective cohort of 228 infants designed to predict mild disease (defined as alert, active, and able to take fluids throughout their disease, no O_2 therapy, etc) vs severe disease (defined as all others without mild disease)	Baseline assessment	Overall, 58% had hyperaeration, and 9% had atelectasis; findings in patients with severe vs mild disease: atelectasis in 21%; vs 2% (RR, 2.7; 95% CI, 1.97-3.70), hyperaeration in 69% vs 52% (RR, 1.58; 95% CI, 1.03-2.42)
Taber et al,[41] 1983	RCT of ribavirin in hospitalized infants	Baseline assessment	Hyperinflation in 24/26; peribronchial thickening in 25/26

Abbreviations: CI, confidence interval; CRP, C-reactive protein; CRX, chest x-ray film; ED, emergency department; ESR, erythrocyte sedimentation rate; O_2, oxygen; RCT, randomized controlled trial; RR, relative risk; RSV, respiratory syncytial virus; RSVIg, RSV immunoglobulin; WBC, white blood cell count.

fined categories of lung disease (ie, lobar pneumonia vs bronchopneumonia vs bronchiolitis). They found that a white blood cell count of greater than 15000/µL and a neutrophil count of greater than 10000/µL were more likely in children with lobar pneumonia or bronchopneumonia than in children with bronchiolitis. The 3 disease categories were defined radiologically. None of the studies reporting CBC data demonstrated their utility in diagnosing bronchiolitis or guiding therapy.

COMMENT

Evaluating diagnostic tests for bronchiolitis is problematic because it is a disease that is diagnosed clinically. Thus,

Table 6. Utility of CBCs in Bronchiolitis

Source	Purpose of Study	Use of CBC in Study	Results
Barry et al,[42] 1986	RCT of ribavirin in acute bronchiolitis	Baseline assessment, completion of study	CBC results not reported
Can et al,[19] 1998	RCT of salbutamol sulfate vs mist	Baseline assessment	Mean WBC, neutrophil, eosinophil, Hb, and Hct levels similar in 3 study groups
Chipps et al,[43] 1993	RCT of interferon alfa-2a in hospitalized infants	Baseline assessment, day 5 of study	CBC results not reported
De Boeck et al,[44] 1997	RCT of dexamethasone hospitalized infants	Baseline assessment	No difference in leukocyte count and eosinophilia between treatment groups
Friis et al,[45] 1984	RCT of antibiotics in treatment of pneumonia and bronchiolitis	Baseline assessment	CBC results for bronchiolitis vs pneumonia not compared
Kjolhede et al,[46] 1995	RCT of vitamin A in ALRI	Baseline assessment	CBC results not reported
Kong et al,[47] 1993	RCT of Chinese herbs in hospitalized infants	Baseline assessment	CBC results not reported
Rodriguez et al,[38] 1987	RCT of ribavirin in infants with RSV disease (included patients with bronchiolitis, pneumonia, and croup)	Baseline assessment	No differences between treatment groups
Saijo et al,[31] 1996	Finding of lobar pneumonia vs bronchopneumonia vs bronchiolitis in hospitalized infants with RSV ALRI	WBC $>15 \times 10^3/\mu L$; neutrophil count $> 10 \times 10^3/\mu L$; ESR >30 mm/h; and CRP level >3.0 mg/dL	The percentages of all 4 indicators were higher in patients with RSV lobar pneumonia vs bronchiolitis or bronchopneumonia
Taber et al,[41] 1983	RCT of ribavirin in hospitalized infants	Baseline assessment, time of discharge, and follow-up	No differences between treatment groups; no differences from admission to discharge to follow-up

Abbreviations: ALRI, acute lower respiratory tract infection; CBC, complete blood cell; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; RCT, randomized controlled trial; RSV, respiratory syncytial virus; WBC, white blood cell.

there is no gold standard against which to compare testing strategies. Numerous tests for RSV, the leading cause of bronchiolitis, exist, but the clinical utility of RSV testing has not been demonstrated for any category of patients. The question of whether RSV testing is necessary in patients with bronchiolitis is of interest from the clinical and utilization points of view. Although such testing is commonly used to document the cause of bronchiolitis, knowing the cause rarely changes clinical management or outcomes.

Many institutions require RSV testing of all infants admitted to the hospital; the rationale is to allow cohorting of patients to decrease nosocomial infections. However, no direct evidence from randomized, controlled trials shows that this strategy prevents nosocomial transmission of RSV in children.[48] A more logical strategy, followed by many infection control policies, is to isolate all infants with acute lower respiratory tract infection, regardless of the cause.

Data from clinical trials demonstrate that large numbers of infants with bronchiolitis have abnormalities on chest x-ray films. However, chest x-ray films do not discriminate well between bronchiolitis and other forms of lower respiratory tract infection. Although textbooks suggest that chest x-ray films be considered in the management of bronchiolitis, specific indications are lacking.[49] The data in this review suggest that, in mild disease, chest x-ray films offer no information that is likely to affect treatment and should not be routinely performed. Data from the studies by Roosevelt et al[39] and Swingler et al[8] demonstrate that chest x-ray films may lead to the use of antibiotics, although this was not the focus of either of these studies. Given that most children with bronchiolitis or other forms of acute lower respiratory tract infection have

viral infections, it could be argued that chest x-ray films are more likely to lead to inappropriate antibiotic use than to improved clinical outcomes.

Very few data exist on the utility of CBC counts. Although many of the treatment trials collected data on CBC counts, their results were either used to demonstrate that treatment and control groups were similar or not reported at all. Complete blood cell counts are commonly used to assist in determining whether a patient has bacterial disease. The large body of literature on febrile infants demonstrates that the test characteristics for CBC counts vary greatly on the the basis of the cutoff used and that elevated white blood cell counts alone have low specificity and positive predictive value. Three studies have looked at bacteremia in febrile infants with bronchiolitis. Greenes and Harper[50] found that the rate of bacteremia was 1 (0.2%) in 411 for subjects with bronchiolitis. Purcell and Fergie[51] reviewed the medical records of 2396 infants admitted to a single hospital and found that 1.6% had positive findings in cultures of blood, urine, or spinal fluid. Both of these studies were retrospective, and CBC count results were not presented. Kupperman et al[52] prospectively studied 163 infants with bronchiolitis and fever and found a 0% rate of bacteremia (95% CI, 0%-1.9%) and a 1.9% rate of urinary tract infections.

Our review has several limitations. First, all systematic reviews are at risk for publication bias.[53] We searched the largest and most relevant databases for published studies but did not seek unpublished data or data maintained by pharmaceutical companies. Second, no search strategy is guaranteed to return all relevant studies. Additional studies may be indexed under terms not used in our search. To decrease the likelihood of missing important studies, we asked a technical advisory group of

What This Study Adds

Despite the large number of clinical trials and prospective cohort studies of bronchiolitis, evidence-based indications for RSV and other supportive testing do not exist. The data available suggest that such testing does not alter clinical outcome. This systematic review justifies a prospective clinical trial to address these questions that uses clinically relevant outcomes such as hospitalization rates, length of hospital stay, time to complete recovery, costs of care, and consequences of false-positive and false-negative test findings.

content experts to review our final list to identify missing studies. Third, our exclusion of non-English studies may have introduced bias as well, although most systematic reviews published in the United States use similar exclusions. Finally, we were not able to analyze quantitatively the data in this review because of the heterogeneity of the studies.

Despite the high prevalence of bronchiolitis, little consensus exists on optimal management.[3,4,54] Diagnostic and supportive testing is common, but data demonstrating appropriate indications and efficacy of such testing do not exist. Wilson et al[9] demonstrated wide institutional variations in the care of hospitalized infants with bronchiolitis that were not explained by disease severity. These variations correlated significantly with hospital costs and length of stay.

Perlstein et al,[10] Adcock et al,[55] and Kotagal et al[56] have all demonstrated that evidence-based guidelines can be used to decrease the frequency of RSV testing, chest x-rays, and bronchodilator use in infants hospitalized with bronchiolitis. These studies demonstrated significant decreases in length of stay and no changes in readmission rates. These studies did not purport to test the utility of RSV testing, chest x-ray films, or CBC counts, but their findings suggest that the routine use of such testing is unnecessary. Additional prospective trials in emergency departments and other outpatient settings will help to validate these findings.

We recognize that, in some clinical situations, the cause of an infant's illness can significantly affect the need for additional workup; examples include infants younger than 2 months with fever and signs of lower respiratory tract disease. Complete blood cell counts and chest x-rays can be useful in patients with unusual clinical courses or severe disease. However, in most infants with bronchiolitis, the limited evidence available does not support routine use of RSV testing, chest x-ray films, or CBC counts. Given the high prevalence of bronchiolitis, prospective trials of diagnostic and supportive testing are feasible and needed. Clinicians are understandably reluctant to change management practices without high-quality evidence to guide them.

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