Evidence Report/Technology Assessment
Number 69

Management of Bronchiolitis in Infants and Children

Agency for Healthcare Research and Quality

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. Endorsement by the Agency for Healthcare Research and Quality (AHRQ) or the U.S. Department of Health and Human Services (DHHS) of such derivative products may not be stated or implied.

AHRQ is the lead Federal agency charged with supporting research designed to improve the quality of health care, reduce its cost, address patient safety and medical errors, and broaden access to essential services. AHRQ sponsors and conducts research that provides evidence-based information on health care outcomes; quality; and cost, use, and access. The information helps health care decisionmakers—patients and clinicians, health system leaders, and policymakers—make more informed decisions and improve the quality of health care services.

Evidence Report/Technology Assessment
Number 69

Management of Bronchiolitis in Infants and Children

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
2101 East Jefferson Street
Rockville, MD 20852
http://www.ahrq.gov

Contract No. 290-97-0011

Prepared by:
RTI International-University of North Carolina
Evidence-based Practice Center

Meera Viswanathan, Ph.D.
Valerie J. King, M.D., M.P.H.
Clay Bordley, M.D., M.P.H.
Amanda A. Honeycutt, Ph.D.
John Wittenborn, B.A., B.S.
Anne M. Jackman, M.S.W.
Sonya F. Sutton, B.S.P.H.
Kathleen N. Lohr, Ph.D.

AHRQ Publication No. 03-E014
January 2003

This document is in the public domain and may be used and reprinted without permission except for any copyrighted materials noted for which further reproduction is prohibited without the specific permission of copyright holders. AHRQ appreciates citation as to source, and the suggested format is provided below:

Viswanathan M, King V, Bordley C, et al. Management of Bronchiolitis in Infants and Children. Evidence Report/Technology Assessment No. 69 (Prepared by RTI International*-University of North Carolina at Chapel Hill Evidence-based Practice Center under Contract No. 290-97-0011). AHRQ Publication No. 03-E014. Rockville, MD: U.S. Department of Health and Human Services, Agency for Healthcare Research and Quality. January 2003.

(*RTI International is a trade name of Research Triangle Institute.)

ISBN: 1-58763-130-X
ISSN: 1530-4396

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Acting Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

Carolyn Clancy, M.D.
Acting Director
Agency for Healthcare Research and Quality

Jean Slutsky, Acting Director
Center for Practice and
Technology Assessment
Agency for Healthcare Research and Quality

The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

Acknowledgments

This study was supported by Contract 290-97-0011 from the Agency of Healthcare Research and Quality (AHRQ)(Task No. 9). We acknowledge the continuing support of Jacqueline Besteman, J.D., MA, director of the AHRQ Evidence-based Practice Center program and to Marian James, Ph.D., the AHRQ Task Order Officer for this project.

The investigators deeply appreciate the considerable support, commitment, and contributions from RTI staff Nash Herndon, M.A., Linda Lux, M.P.A., Loraine Monroe, and Philip Salib, B.A. In addition, we appreciate the contributions of our data abstractors, Sonya Harris-Haywood, M.D., Mary Maniscalco, M.D., and Laura Sterling, M.D., and our methods abstractor, Cheryl Coon, Ph.D., all of the University of North Carolina at Chapel Hill (UNC). We are also thankful for the research support provided by Joy Harris and Donna Curasi, also of UNC.

In addition, we extend our appreciation to the members of our Technical Expert Advisory Group (TEAG), who served as vital resources throughout our process. They are: Henry L. Dorkin, M.D., Massachusetts General Hospital and Harvard Medical School, Boston, Mass; Bernard Ewigman, M.D., M.S.P.H., School of Medicine, University of Missouri-Columbia, Columbia, Mo; Glenn Flores, M.D., Boston University School of Medicine, Boston, Mass; Anne Haddix, Ph.D., Rollins School of of Public Health, Emory University, Atlanta, Ga; Allan S. Liberthal, M.D., (representing the American Academy of Pediatrics) Southern CA-Permanente Medical Group, Panorama City, Calif; H. Cody Meissner, M.D., New England Medical Center, Boston, Mass; Jonathan L. Temte, M.D., Ph.D., (representing the American Academy of Family Physicians), Department of Family Medicine, University of Wisconsin, Madison Wis; and Steve Wegner, M.D., NC Access, Inc, Morrisville, NC.

We owe our thanks as well to our external peer reviewers, who provided constructive feedback and insightful suggestions for improvement of our report. Other peer reviewers were: Alan H.Cohen, M.D., Senior Director, Medical Affairs, MedImmune Inc. and Johns Hopkins Medical School, Gaithersburg, Md; Jeffrey M. Ewig, M.D., Pediatric Pulmonary Associates, PA, St. Petersburg, Fla; Anne Haddix, Ph.D., Rollins School of Public Health, Emory University, Atlanta, Ga; Elizabeth Susan Hodgson, M.D., Princeton, NJ; Allan S. Liberthal, M.D., Southern CA-Permanente Medical Group, Panorama City, Calif; Michael Light, M.D., University of Miami, North Miami Beach, Fla; H. Cody Meissner, M.D., New England Medical Center, Boston, Mass; Jeff Michael, D.O., University of Missouri-Columbia, Columia, Mo; and Tonse NK Raju, M.D., National Institute of Child Health and Human Development, Washington, DC.

Structured Abstract

Objectives. This systematic review seeks to clarify the existing knowledge base for the management of bronchiolitis and offers directions for future research. Specifically, the review addresses the effectiveness of appropriate diagnostic tools, the effectiveness of pharmaceutical therapies for treating bronchiolitis, the role of prophylactic therapy for prevention of bronchiolitis, and the cost-effectiveness of such prophylactic therapy.

Search strategy. The reviewers in conjunction with an expert panel generated admissibility criteria for each question and derived relevant terms to search the literature in three databases: MEDLINE®, Cochrane Collaboration Library, and Health Economic Evaluations Database (HEED).

Selection criteria. For the key question on diagnosis, the investigators included prospective cohort studies and randomized controlled trials (RCTs). To ensure greater strength of evidence for interventions, the investigators raised admissibility criteria to allow only RCTs for the key questions on treatment and prophylaxis. For the cost-effectiveness of prophylaxis, studies that employed economic analysis were reviewed. For all studies, key inclusion criteria included outcomes that were both clinically relevant and able to be abstracted. The investigators set a minimum sample size of 10; small case series and single case reports were excluded. Studies in languages other than English were not reviewed. The reviewers initially identified 744 abstracts for possible inclusion. Upon full review, a total of 83 articles for this systematic review were retained.

Data collection and analysis. A team of abstractors reviewed and abstracted information on study methodology and results into a data abstraction form. The Study Director entered data from studies on treatment and prophylaxis into evidence tables. The Scientific Directors performed quality control assessments of the evidence tables against the original article and independently assigned quality scores to each article. When they did not agree, the Scientific Directors reviewed the article together and arrived at a consensus.

Results and discussion. The diagnosis of bronchiolitis is primarily clinical; therefore, only limited literature is available on effectiveness of diagnostic tools for diagnosing bronchiolitis in infants and children. Only one study supported the clinical usefulness of diagnostic testing. Thus, the existing data do not support routine laboratory, radiologic, or other types of testing over purely clinical criteria to diagnose bronchiolitis.

The volume of literature is much greater for effectiveness of treatments. Trials included tested 15 classes of interventions (e.g., bronchodilators, steroids, antibiotics). However, the strength of evidence was limited by trials that were underpowered and outcomes that were not comparable across studies. At present, evidence is insufficient to recommend any of the treatments studied over good supportive care of affected infants and children. However, several interventions did show some potential for being efficacious and should be subjected to rigorously designed, adequately sized trials.

This review of the literature on respiratory syncytial virus immunoglobulin (RSVIG) suggests that it is effective for prophylaxis in high-risk infants and children who have underlying

bronchopulmonary dysplasia (BPD) or have been born prematurely and are less than 6 months of age. Use of prophylaxis in at-risk groups that were excluded from prior studies would need to be studied or reported before these agents can be recommended more broadly for other groups of infants and children at increased risk of more severe bronchiolitis.

When all costs of prophylaxis are adjusted to 2002 dollars, previous studies report incremental costs of prophylactic therapy for infants from 32 through 35 weeks' estimated gestational age (EGA) ranging from saving of $46,400 to costs of $535,400. Given these variations, evidence is insufficient at the present time to calculate the cost-effectiveness of administration of a prophylaxis for bronchiolitis in infants in this age group or who are premature with comorbidities.

Future research. Both specific and general recommendations for future research were identified.

Specific recommendations are:

1. Ancillary testing is common practice, but no data demonstrate the utility of such testing. Therefore, prospective trials of the utility of ancillary testing (chest x-rays, complete blood tests, respiratory syncytial virus [RSV] testing) should be considered. These should report clinical outcomes that are important to parents and clinicians, such as the change in physician management.

2. The following interventions should be studied in rigorously designed, adequately powered trials: nebulized epinephrine, nebulized salbutamol plus ipratropium bromide, nebulized ipratropium bromide, oral or parenteral corticosteroids, and inhaled corticosteroids. Despite the lack of evidence on the efficacy of these treatments, clinicians are likely to continue their use unless a large simple trial of the most common interventions is mounted.

3. Better estimates of the cost of palivizumab administration, hospitalization costs for infants who do do not receive palivizumab, and RSV hospitalization rates are needed to assess the cost-effectiveness of RSV prophylaxis. In particular, additional data are needed on the material and time costs of administration for parents and providers, the actual cost of palivizumab to providers and family, the consequences of palivizumab on long-term wheezing and chronic asthma, and the societal costs of morbidity.

General recommendations are:

1. Clinically relevant outcomes should be chosen for future studies. Examples of these types of outcomes for intervention studies are rates of hospitalization, need for more intensive services in the hospital, costs of care, parental satisfaction with treatment, and development of chronic asthma.

2. Studies should be powered to detect meaningful differences in clinically relevant outcomes. Power calculations must include sufficient numbers to account for multiple comparisons if multiple outcomes are to be measured.

3. Future investigations should carefully monitor and report adverse events associated with treatments; without this information determining whether the risks of particular treatments are low enough to support their clinical use is difficult.