done in other developing countries, hand in hand with vaccine development efforts, with the goal of early vaccine introduction where the burden of illness is greatest.

Eric A. F. Simões, MB BS, DCH, MD
Department of Pediatrics
Section of Infectious Diseases
University of Colorado
Denver and Children's Hospital Colorado
Aurora, CO
Health Research Unit
Faculty of Medicine
Padjadjaran University/Hasan
Sadikin General Hospital
Bandung, West Java, Indonesia

Cissy B. Kartasasmita, MD, PhD
Health Research Unit
Faculty of Medicine
Padjadjaran University/Hasan
Sadikin General Hospital
Bandung, West Java, Indonesia

REFERENCES

1. Simões EA, Mutyara K, Soh S, et al. The epidemiology of respiratory syncytial virus lower respiratory tract infections in children less than 5 years of age in Indonesia. *Pediatr Infect Dis J*. 2011;30:778–784.
2. Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *Lancet*. 2010;375:1545–1555.
3. Stockman LJ, Curns AT, Anderson LJ, et al. Respiratory syncytial virus-associated hospitalizations among infants and young children in the United States, 1997–2006. *Pediatr Infect Dis J*. 2012;31:5–9.
4. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. *N Engl J Med*. 2009;360:588–598.
5. Graham BS. Biological challenges and technological opportunities for respiratory syncytial virus vaccine development. *Immunol Rev*. 2011;239:149–166.
6. Nair H, Verma VR, Theodoratou E, et al. An evaluation of the emerging interventions against respiratory syncytial virus (RSV)-associated acute lower respiratory infections in children. *BMC Public Health*. 2011;11 (suppl 3):S30.

Reply:

We thank Cooper and colleagues for their comments on our article and that by Simões and co-workers.[1,2] They bring up the highly interesting question what incidence should be considered substantial. Simões found that the incidence of respiratory syncytial virus (RSV) lower respiratory tract infection (LRI) in patients with age 0–2 months, 3–5 months and 6–8 months is 0, 50 and 198, respectively, per 1000 child-years.[1] These numbers are in-line with the accumulated cohort data from the Utrecht RSV Research group.[2] These studies allow for the conclusion that RSV bronchiolitis is relatively rare during the first months of life, but when it occurs, the course of disease is severe. It seems obvious that both incidence and severity of RSV LRI during infancy determine the burden of disease. Thus, we agree with Cooper and colleagues that the burden of RSV LRI in children 3–6 months is quite substantial despite the consistent observation that incidence is lower than in children 7–12 months.

Louis Bont, MD, PhD
Michiel L. Houben, MD
Department of Pediatrics
Utrecht RSV Research Group
University Medical Center Utrecht
Utrecht, The Netherlands

REFERENCES

1. Bont L, Houben ML. Commentary: why are young healthy term infants protected against respiratory syncytial virus bronchiolitis? *Pediatr Infect Dis J*. 2011;30:785–786.
2. Simões EA, Mutyara K, Soh S, et al. The epidemiology of respiratory syncytial virus lower respiratory tract infections in children less than 5 years of age in Indonesia. *Pediatr Infect Dis J*. 2011;30:778–784.

L.B. has received fees for advisory activities and funding for investigator initiated studies from Abbott Laboratories. The authors have no other funding or conflicts of interest to disclose.

The Need to Capitalize on New Recommendations

Stimulating Tuberculosis Diagnostic Research in Children

To the Editors:

This year, the focus for World Tuberculosis (TB) day was children, a neglected area despite the fact that TB causes an estimated 70,000 childhood deaths each year.[1] The starting point for this neglect is the lack of appropriate diagnostic tests for TB in children, which means that the disease is underdetected and underreported. Using a conservative estimate of children representing 5% of the adult prevalence of 9.97 million, then the gap between the numbers expected and cases actually reported, shows a potential 341,365 cases not diagnosed or reported in children during 2010.[2]

Existing diagnostic tests are not adapted for children, and thus it is difficult to confirm active TB. Sputum-based tests, the usual approach to confirm active TB in adults, have far less yield in children who often struggle to produce sputum. There is a desperate need for rapid, accurate, non-sputum-based diagnostic tests for children, suitable for implementation in resource-limited settings. Research into diagnostic tests for children has been hampered by the lack of a unanimously recognized standard for pediatric TB diagnosis. This has contributed to a reluctance to enroll children in studies involving new diagnostic technologies. Of the promising new methods: Gene Xpert Mtb/Rif, microscopic observation drug-susceptibility assay, nitrate reductase assay, colorimetric redox indicator assay, line-probe assay and loop-mediated isothermal amplification, studies are either limited or completely lacking in children. The comparison of existing pediatric diagnostic studies is extremely difficult, with little or no standardization of the definitions.[3]

In March 2012, a consensus statement on critical aspects of TB diagnostic research in children was published. This represents a significant advance toward improved diagnostics for pediatric TB. The expert panel consensus was reached in a National Institutes of Health–sponsored meeting of pediatric TB experts in June 2011 "Critical Issues in Pediatric Tuberculosis Diagnostics Research in HIV-Infected and Uninfected Children." The meeting had 2 key outcomes: consensus on clinical case definitions of intrathoracic TB in children, and methodologic approaches to apply for the evaluation of TB diagnostics in children.[4,5] The consensus agreed on 5 clinical case definitions with further details regarding microbiologic confirmation, clinical signs and symptoms, interpretation of chest radiographs, TB exposure and response to treatment to support these case definitions.

Research into TB diagnostics is grossly underfunded with the only 13% of the $340 million recommended by the Global plan raised in 2011 and only 8% of total research and development investment committed to diagnostics.[6] This funding gap needs to be addressed, and it is essential that this particularly challenging and neglected area of TB diagnostics should not suffer from cutbacks in this period of financial austerity. Dedicated funding streams for research into diagnostics in children are needed, and children should be routinely included in research.

The authors have no funding or conflicts of interest to disclose.

These new consensus statements mean that there is no longer an excuse to continue to exclude children from TB diagnostic research. It is vital that these recommendations are endorsed by funding agencies, research organizations and diagnostic developers.

Grania Brigden, MB ChB, MRCP
Médecins Sans Frontières –
Access Campaign
Geneva, Switzerland

REFERENCES

1. No More Crying, No More Dying. Towards Zero Deaths in Children. Geneva: WHO; 2012.
2. Du Cros P, Nyang'wa BT, Gale M, Venis S, Ford N. Counting children: comparing reporting for paediatric HIV and tuberculosis. *Bull World Health Organ*. 2011;89:855.
3. Graham S. Research into tuberculosis diagnosis in children. *Lancet Infect Dis.* 2010;10:581–582.
4. Graham S, Ahmed T, Amanullah F, et al. Evaluation of TB diagnostics in children: 1. Proposed clinical case definitions for classification of intrathoracic tuberculosis disease. Consensus from an expert panel. *J Infect Dis.* 2012;205(suppl 2): S199–S208.
5. Cuevas L, Browning R, Bossuyt P, et al. Evaluation of TB diagnostics in children: 2. Methodological issues for conducting and reporting research evaluation of TB diagnostics for intrathoracic TB in children. Consensus from an expert panel. *J Infect Dis.* 2012;205(suppl 2):S209–S215.
6. Jimenez-Levi E. 2011 Report on Tuberculosis Research Funding Trends, 2005–2010. 2nd Edition. March 2012. Treatment Action Group.

Does Solely Clinical Diagnostics Lead to Overdiagnoses and Overtreatments?

Pneumonia in Children

To the Editors:

British Thoracic Society (BTS) and Infectious Disease Society of America have recently published their evidence-based guidelines for the management of pediatric community-acquired pneumonia (CAP).[1,2] In this journal, the members of CAP Paediatric Research Initiative of European Society for Paediatric Infectious Diseases published a review on antibiotic therapy for pediatric CAP.[3] The authors concluded that their review is a discussion paper with an aim of stimulating further debate and research.[3]

Both BTS and Infectious Disease Society of America guidelines recommend that the diagnosis of CAP in children be based solely on clinical criteria. Chest radiographs are indicated only in severe cases treated in hospital or when complications are suspected.[1,2] According to the BTS guidelines, bacterial pneumonia should be considered in children when there is persistent or repetitive fever >38.5°C accompanied with chest retractions and a raised respiratory rate.[1] Most children with CAP should be treated with antibiotics, with only a few exceptions, such as <24 months (BTS)[1] or <6 years (Infectious Disease Society of America)[2] old children with mild symptoms.[1,2] The guidelines remind that pneumonia is uncommon in wheezing children though other presentations are similar, such as fever, chest retractions and raised respiratory rate.

Esposito et al[3] conclude in their review that there is no standard for establishing the diagnosis of CAP, but chest radiograph still is the best available mean of diagnosing pneumonia. The presence of alveolar infiltration is, more often than interstitial infiltration, associated with bacterial pneumonia. Despite this, the authors do not suggest confirming presumed pneumonia cases by radiology. Children with mild CAP for whom all of the available epidemiologic, clinical, laboratory and radiologic data clearly suggest a viral infection can be treated with symptomatic therapy alone.[3] A history of conjugate pneumococcal vaccination gives greater confidence in the decision to withhold antibiotics.[1]

An alternative way is to diagnose CAP by chest radiograph and treat only radiologically confirmed CAP cases.[4] The goal is to treat only "true pneumonia" cases with antibiotics. A short, 12–48 hours inpatient treatment using intravenous administration ensures rapid effect and close monitoring, and even enables the use of narrow-spectrum antibiotics such as penicillin G. According to the guidelines, improvement should begin within 48 hours after the start of antibiotics.[1] In both developing and developed countries, pneumonia cannot be confirmed by radiology in >80% of children with a clinical suspicion of pneumonia,[4] and these children are treated unnecessarily with antibiotics. On the other hand, taking more radiographs may lead to more findings which are mistakenly considered as pneumonia. To avoid overdiagnostics, only clear pulmonary consolidations should be interpreted as pneumonic changes.[4]

Physicians prescribe antibiotics for children with respiratory infection for many reasons which are not medically justified, because of diagnostic uncertainty, parental wish and fear of complications. Diagnosing pediatric CAP by clinical symptoms and signs alone probably increases the use of unnecessary antibiotics. Focusing antibiotic treatment to those who really benefit from the treatment and using narrow-spectrum antibiotics prevent emerging antibiotic resistance in the population. If the radiologic or clinical findings are mild or nonspecific, antibiotic therapy is usually not needed.

Matti Korppi, MD, PhD
Paediatric Research Centre
Tampere University and
University Hospital
Tampere University
Finland

REFERENCES

1. Harris M, Clark J, Coote N, et al.; British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. *Thorax*. 2011;66(suppl 2): ii1–iis23.
2. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53:e25–e76.
3. Esposito S, Cohen R, Domingo JD, et al. Antibiotic therapy for pediatric community-acquired pneumonia: do we know when, what and for how long to treat? *Pediatr Infect Dis J*. 2012;[Epub ahead of print].
4. Korppi M. Diagnosis and treatment of community-acquired pneumonia in children. *Acta Paediatr*. 2012;[Epub ahead of print].

The authors have no funding or conflicts of interest to disclose.