

# APSR Respiratory Research Review

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Issue 6 - 2007

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## Welcome to the 6th edition of APSR Respiratory Research Review.

This month we present several state-of-the-art reviews of diagnostic and staging techniques for non-small cell lung cancer, plus an intriguing new study which assesses the measurement of pleural viscosity as a means to determine the aetiology of pleural exudative effusions.

Also, of particular interest to us here in the Asia Pacific region, compelling evidence for the benefits of infant immunisation with pneumococcal conjugate vaccine in the developing countries.

I hope you enjoy the latest edition and welcome your comments and feedback.

Kind regards,

**Richard Beasley**

Chair, Education Committee, APSR

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## Intensive smoking cessation intervention reduces mortality in high-risk smokers with cardiovascular disease

**Authors:** Mohiuddin SM et al

**Summary:** The impact of different interventions on smoking cessation in 209 smokers hospitalised with acute cardiovascular disease was assessed in this study. Patients were randomised to treatment with intensive antismoking intervention (comprising a minimum of 12 weeks of behaviour modification counselling plus individualized pharmacotherapy provided at no cost to the participant) or usual care consisting of counselling and printed educational material provided prior to hospital discharge. At 24 months, rates of continuous smoking cessation amongst subjects in the intensive intervention group were 33% versus 9% in the control group ( $p < 0.001$ ). There were significant reductions in hospitalisations (RRR 44%;  $p = 0.007$ ) and all-cause mortality in the study group (RRR 77%;  $p = 0.014$  vs controls). The absolute risk reduction in mortality was 9.2% (NNT 11). The authors conclude that hospitalised smokers, especially those with cardiovascular disease, should receive intensive smoking cessation interventions.

**Comment:** The crucial feature of this study is the implementation of the smoking cessation programme at a time when motivation is likely to be at its highest – during an admission for acute coronary syndrome or heart failure. If these findings are extrapolated to other acute medical conditions, it is likely that a similar opportunity may exist for smokers admitted for acute respiratory conditions, such as pneumonia or exacerbations of COPD. <http://www.chestjournal.org/cgi/content/abstract/131/2/446>

**Reference:** *Chest*. 2007; 131:446-52



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## Prevalence of viral respiratory tract infections in children with asthma

**Authors:** Khetsuriani N et al

**Summary:** The aim of this case control study was to assess the contribution of respiratory viruses to asthma exacerbations in children aged 2 to 17 years. Cases with asthma exacerbations (n = 65) were matched with subjects with well-controlled asthma (n = 77). Respiratory specimens were analysed by PCR to determine the presence or absence of respiratory viruses including rhinoviruses, enteroviruses, respiratory syncytial virus, human metapneumovirus, coronaviruses 229E and OC43, parainfluenza viruses 1 to 3, influenza viruses, adenoviruses, and human bocavirus. Rhinovirus was the most prevalent infection, occurring in 60% of cases and 18.2% of controls. Asthma exacerbations were associated with respiratory viral infections overall (OR 5.6; 95% CI 2.7-11.6) and rhinovirus infection (OR 6.8; 95% CI 3.2-14.5). The prevalence of asymptomatic rhinovirus infection was similar in both cases (29.2%) and controls (2.34%;  $p > 0.05$ ). In conclusion the authors suggest that symptomatic rhinovirus infections contribute significantly to asthma exacerbations in children.

**Comment:** Further evidence that rhinovirus infections are the most common cause of exacerbations of asthma in children. The development of safe and effective drugs against rhinovirus represents a priority to reduce the frequency and severity of asthma exacerbations and associated risk of mortality.

<http://www.jacionline.org/article/PIIS0091674906021294/abstract>

**Reference:** *J Allergy Clin Immunol.* 2007; 119:314-21

## Role of pleural viscosity in the differential diagnosis of exudative pleural effusion

**Authors:** Yetkin O et al

**Summary:** In this prospective study, the viscosity of pleural exudative effusions was examined in an attempt to discriminate between various different aetiologies. Measurements of pleural fluid and plasma viscosity were performed on samples from 70 consecutive patients with exudative pleural effusion due to pneumoniae, tuberculous pleurisy and lung cancer. Pleural viscosity  $\geq 1.57$  predicted tuberculous pleurisy (sensitivity 100%, specificity 95%) and pleural viscosity  $< 1.39$  predicted lung cancer (sensitivity 100%, specificity 94%). There were significant associations between pleural viscosity and pleural albumin, protein and plasma viscosity. The authors concluded that there were significant differences between pleural effusions of different etiologies, with tuberculous effusions having the highest viscosity, and malignant effusions from lung cancer the lowest.

**Comment:** Intriguing study of the use of pleural viscosity to help determine the cause of exudative pleural effusions. Pleural viscosity can be measured quickly and cheaply and if these findings are validated in larger studies then it may well become one of the standard methods of assessment of pleural effusions.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2006.01041.x>

**Reference:** *Respirology.* 2007; 12:267-71

## LABAs plus ICS versus ICS for asthma control and exacerbations

**Authors:** Gibson PG et al

**Summary:** This systematic review assessed the efficacy and safety of adding LABAs to ICS versus various different ICS strategies, using data from relevant Cochrane systematic reviews. Outcomes including asthma exacerbations, asthma control, and adverse effects. Adding LABA to ICS significantly reduced exacerbations vs a similar ICS dose alone (NNT 18), but was not more effective than a higher ICS dose, or a similar ICS dose in steroid-naïve patients. Asthma control was significantly improved with LABA added to ICS compared to all three ICS groups. There was a significantly increased risk of tremor with LABA added to ICS as initial therapy (NNH 21) and versus higher ICS doses (NNH 74). In conclusion, the authors found that; "The greatest benefit and least harm of LABAs comes when they are added to a similar ICS dose in adults with symptomatic asthma."

**Comment:** A novel approach utilising a composite measure of asthma control in addition to exacerbations. The greatest benefits with LABA therapy and asthma appear to occur when given to a patient already on ICS therapy. This study does not support the preferential use of LABA/ICS therapy in steroid naïve patients.

<http://www.jacionline.org/article/PIIS0091674906030259/abstract>

**Reference:** *J Allergy Clin Immunol.* 2007; 119:344-50

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## Imaging in the diagnosis and treatment of non-small cell lung cancer

**Authors:** Hicks RJ et al

**Summary:** The authors of this review discuss the benefits of different techniques for diagnosing and staging lung cancer patients. Their focus is on non-invasive techniques (including CT and PET) and minimally invasive techniques (endoscopic approaches) as opposed to invasive (surgical) approaches. For patients with non-small cell lung cancer who would be considered for treatment with curative intent, tests with a high sensitivity and specificity for detection of both systemic metastases and mediastinal nodal involvement are required. The standard of care with regard to diagnosis and staging is now combined PET/CT (using fluorine-18 fluorodeoxyglucose). Nodal abnormalities can be further evaluated (including obtaining pathological samples) using endoscopic endobronchial ultrasound. In patients requiring surgical resection, diagnostic CT may also have an important role. Diagnostic CT may also be useful as the initial investigation in patients who would not be considered for curative treatment on medical grounds.

**Comment:** Please see Yasufuku study, adjacent to the right.

**Reference:** *Respirology*. 2007; 12:165-172

**PMID:** 17298447

## The pre-test probability of lung cancer in patients with solitary pulmonary nodules

**Authors:** Gould MK et al

**Summary:** Multiple logistic regression analysis was used to identify independent clinical predictors of malignancy and to develop a clinical prediction model to estimate pre-test probability of malignancy. Data were obtained from a sample of 375 veterans (mean age 65.9 years) with solitary pulmonary nodules (SPNs) and a malignancy rate of 54%. Most study subjects were previous (n = 177) or current (n = 177 smokers). The risk of malignancy was predicted by positive smoking history (OR 7.9), older age (OR 2.2 per 10-year increment), larger nodule diameter (OR 1.1 per 1mm increment), and time since smoking cessation (OR 0.6 per 10-year increment). The accuracy of the clinical prediction model was good, and the authors suggest that its use may facilitate clinical decision making, for example with regard to selecting and interpreting the results of diagnostic tests such as PET imaging.

**Comment:** The Bayesian approach of first determining the pretest probability to enable interpretation of the results of subsequent diagnostic tests, and then the use of decision analysis to determine the preferred therapeutic intervention. This approach is well established in respiratory medicine, particularly pulmonary embolism (the article by Perrier and Junod, *Respiratory Medicine* 1995; 89: 241-51 is well worth reading). This approach to determine the pre-test probability of malignancy in patients with solitary pulmonary nodules can be recommended in clinical practice.

<http://www.chestjournal.org/cgi/content/abstract/131/2/383>

**Reference:** *Chest*. 2007; 131:383-8

## Staging and diagnosis of non-small cell lung cancer: invasive modalities

**Authors:** Yasufuku K

**Summary:** In this review, the authors discuss the benefits of different invasive staging tests for lung cancer, in terms of both staging and obtaining a diagnosis. The techniques reviewed in relation to mediastinal lymph node staging include mediastinoscopy, thoracoscopy, transbronchial needle aspiration, transthoracic needle aspiration, endoscopic ultrasound-guided fine-needle aspiration and newer techniques such as endobronchial ultrasound-guided transbronchial needle aspiration. Advances in diagnostic bronchoscopy for lung cancer are also reviewed.

**Comment:** Two complimentary state of the art reviews on imaging and staging in the diagnosis and treatment of non-small cell lung cancer. If the necessary resources are available, following the recommendations provided should result in few patients reaching the point of definitive treatment without clear definition of the extent of their disease.

**Reference:** *Respirology*. 2007; 12:173-83

**PMID:** 17298448

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by Professor Richard Beasley*

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## Is childhood immunisation associated with atopic disease?

**Authors:** Nakajima K et al

**Summary:** This retrospective study used immunisation data from school medical records linked to the Tasmanian Asthma Study to examine associations between childhood immunisation and the risk of atopic disease. An increased risk of asthma by age 7 years was weakly associated with diphtheria (OR 1.3, 95% CI 1.1-1.7) but no other vaccinations. A small increase in risk for eczema and food allergies (by age 7) was associated with vaccination for diphtheria, tetanus, pertussis and polio but not small pox. Risk of hay fever or later onset atopic outcomes were not associated with immunisation history. The authors note that the effects observed in this study are small and age-dependent, and support the data from previous studies which found no effect of vaccination on asthma.

**Comment:** Hopefully this prospective 30 year cohort study will be reassuring to both parents and doctors. Based on these findings the fear of their child developing atopic disease should not deter parents from immunising their children, especially when weighed against the benefits.

<http://thorax.bmj.com/cgi/content/abstract/62/3/270>

**Reference:** *Thorax*. 2007; 62:270-5

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**Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

## Cost-effectiveness of pneumococcal conjugate vaccination for prevention of child mortality

**Authors:** Sinha A et al

**Summary:** A decision analysis model was used to provide an economic analysis comparing pneumococcal vaccination of infants to no vaccination in the 72 developing countries eligible for financial support from the Global Alliance for Vaccines & Immunization as of 2005. Estimates of child mortality, effectiveness of vaccination, and immunisation rates were calculated using both published and unpublished data. In children aged 3 to 29 months, vaccination was estimated to prevent 262,000 deaths each year (7%) across the countries studied. This would prevent 8.34 million disability-adjusted life years (DALYs) each year. The cost of vaccination would be \$838 million (\$5 per dose) ie approximately \$100 per DALY averted. In 68 of 72 countries this would be highly cost effective.

**Comment:** The economic and public health argument for purchasing the pneumococcal conjugate vaccine in the developing world is compelling. This must represent a priority for the Asia/Pacific region, and respiratory physicians need to provide the advocacy to ensure its availability.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673607601950/abstract>

**Reference:** *Lancet*. 2007; 369:389-96

## Patterns of community-acquired pneumonia (CAP) in hospitalized Singaporean children

**Authors:** Chiang WC et al

**Summary:** This retrospective study aimed to examine the clinical characteristics, complications, spectrum of pathogens and patterns of antimicrobial resistance associated with hospitalized cases of childhood CAP in Singapore. 1,702 children, median age 4.2 years were studied over a period of 3 years. Causative pathogens included *Mycoplasma pneumoniae* (20.3%), typical respiratory bacteria (10.3%; 64.6% *Streptococcus pneumoniae*; 21.7% non-typeable *Haemophilus influenzae*), viruses (5.5%) and mixed bacterial/viral infections (2%). Most *M. pneumoniae* infections occurred in school-age children. Significantly greater mortality was observed with typical bacterial infections (8.9%) versus *M. pneumoniae* (0.3%) and viral pneumonias (0%) ( $p < 0.001$ ). Resistance to aminopenicillins was documented in over 50% of *S. pneumoniae* and *H. influenzae* isolates, however these agents were often prescribed for these infections.

**Comment:** This study highlights the importance of obtaining current local, clinical and microbiological surveillance data including antimicrobial resistance patterns in CAP. Marked variations in CAP occur throughout the Asia/Pacific region and local up-to-date data provide a sound basis for local guidelines.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2006.01036.x>

**Reference:** *Respirology*. 2007; 12:254-61

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