

# APSR Respiratory Research Review

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## Welcome to APSR Respiratory Research Review.

APSR Respiratory Research Review is a unique publication providing topical, relevant and accessible information for healthcare professionals working in the area. In each edition our independent reviewers hand-pick some of the most important studies from key international and local journals. The Review summarises each study in an easy to read format, and our local experts provide commentary on the importance of the work and implications for clinical practice in the Asia Pacific region. Web links to the abstract or fully published papers are also provided where possible so you can make your own judgements.

We hope you enjoy the latest edition and welcome your feedback.

## Pulmonary function testing in New Zealand

**Authors:** Marsh S et al

**Summary:** This survey of lung function testing facilities examined the use of reference equations which generate predictive values for the interpretation of pulmonary function tests. The authors sought to determine the suitability of the reference equations in local use and compare them to those derived from the Wellington Respiratory Survey. The equations currently used were found to significantly under predict, by up to 20%, values measured for FEV1, PEF, TLC and RV. The choice of reference equation was also found to substantially alter the classification of the severity of COPD and asthma based on per cent predicted FEV1. The authors conclude that many of the reference equations currently used in New Zealand are no longer suitable and recommend that up-to-date equations are derived and implemented where required. Further investigation in to equations used in the greater Asia Pacific region is also suggested.

**Comment:** A reminder of the importance of locally derived up-to-date reference range equations for pulmonary function testing. This is particularly relevant to the Asia Pacific region due to the well recognised ethnic differences in lung function. It is recommended that all lung function labs in the region check which reference equations are used, whether they are applicable to the population being tested and if not, that locally derived reference equations are implemented.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2007.01071.x?journalCode=res>

**Reference:** *Respirol.* 2007; 12: 367-74



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## Prophylaxis for thromboembolism

**Authors:** Francis C

**Summary:** The reader is asked to consider whether thromboprophylaxis should be provided in the case of a 62-year old male who had been admitted with fever, cough and dyspnea. The patient was weak, had purulent sputum and appeared to be dehydrated. Assessment revealed respirations of 22, temperature of 39.2°C, blood pressure of 128/69 mm Hg, crackles over the left lower lung field and chest radiography showed a density in the left lower lobe consistent with pneumonia. The author then discusses key issues including assessment of risk, treatments strategies and guidelines.

**Comment:** A reminder of the importance of VTE prophylaxis in high risk medical inpatients. There is extensive literature indicating that VTE prophylaxis is seldom prescribed to high risk medical in-patients; innovative strategies ranging from evidence-based education programmes to pharmacist or computerised reminder systems are required. It is recommended that all hospital-based physicians should review the status of VTE prophylaxis in their hospitals and implement a strategy if required.

<http://content.nejm.org/cgi/content/short/356/14/1438>

**Reference:** *N Engl J Med.* 2007; **356:** 1438-44

*Independent commentary  
by Professor Richard Beasley*

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publications are intended for  
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## Early detection of chronic pulmonary allograft dysfunction by exhaled biomarkers

**Authors:** Van Muylem A et al

**Summary:** This study monitored recipients of lung grafts in order to compare the performance of exhaled NO and CO (which reflect airway inflammation) and the slope of the alveolar plateau for helium (which reflects heterogeneity of ventilation distribution) for the detection of bronchiolitis obliterans syndrome (BOS) stages 0-p and 1. Of the 65 patients observed 9 were in stage 0-p and 16 patients were in BOS stage 1 or higher. Whilst all biomarkers increased in BOS stage 0-p, the helium slope had superior sensitivity and was the only marker which increased in BOS stage 1. Considering exhaled NO and CO together improved their sensitivity however the three markers in combination provided the best sensitivity overall. The exhaled biomarkers had high negative predictive values, but low specificity and positive predictive values.

**Comment:** Intriguing study of the utility of exhaled biomarkers to detect BOS. Their role at this stage relates to their high negative predictive value, i.e. BOS is an unlikely cause of a progressive decline in FEV1 if exhaled biomarkers are not raised.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/7/731>

**Reference:** *Am J Respir Crit Care Med.* 2007; **175:** 731-6

## Prediction of oral appliance treatment outcome in obstructive sleep apnea

**Authors:** Zeng B et al

**Summary:** This study (n = 54) considered patients with obstructive sleep apnea (OSA) undergoing mandibular advancement splint (MAS) treatment to determine whether flow-volume curves might provide clinical utility in prediction of treatment outcome. Both expiratory and inspiratory flow-volume curves were measured in the erect and supine positions to determine mid-inspiratory flow (MIF<sub>50</sub>) and the ratio of expiratory to inspiratory flow at 50% of vital capacity (MEF<sub>50</sub>:MIF<sub>50</sub>). Patients who responded to MAS treatment were found to have lower MIF<sub>50</sub> (6.04 ± 1.80 vs 6.88 ± 1.08 L/second; p = 0.035) and higher MEF<sub>50</sub>:MIF<sub>50</sub> ratio (0.82 ± 0.23 vs 0.61 ± 0.15; p = 0.001). The most important predictive factor for treatment outcome was found to be the MEF<sub>50</sub>:MIF<sub>50</sub> but body mass index, age, and baseline apnea-hypopnea index (AHI) were also contributory. The authors conclude that flow-volume curves in combination with body mass index, age, and baseline AHI may be useful in predicting treatment outcome with MAS.

**Comment:** Identification of simple and reliable clinical predictors of treatment outcome with mandibular advancement splints for OSA represents a priority if this form of therapy is to be more widely used. These findings suggest that flow-volume curves may represent a simple inexpensive and clinically useful tool to assist in identifying patients who are suitable for this treatment modality.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/7/726>

**Reference:** *Am J Respir Crit Care Med.* 2007; **175:** 726-30

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## Transplantation update 2006

**Authors:** Corris PA et al

**Summary:** This update summarises transplantation research published in 2006. Included is an important review of consensus guidelines for referral and listing for lung transplantation and the 23rd official report from the International Society for Heart and Lung Transplantation. The latter reported the main worldwide indication for lung transplantation continues to be COPD which comprised 38% of all transplants in 2005. Survival figures included in this report were 78%, 49% and 25% at 1, 5 and 10 years respectively, with half-life survival being approximately 5 years. The update covers recent research regarding recipient selection as well as donor evaluation and management. Ischemia reperfusion injury and primary graft dysfunction are discussed with respect to epidemiology, clinical risk factors, pathogenesis and experimental therapies. New experimental approaches in both animal models and humans for Bronchiolitis Obliterans Syndrome are considered and the authors conclude with a discussion of other relevant medical problems.

**Comment:** An informative update on lung transplantation. Clear clinical guidelines are provided for recipient selection, donor evaluation and the management of complications. Worth a read, even for those not involved in transplantation programmes.

<http://ajrccm.atsjournals.org/cgi/content/short/175/5/432>

**Reference:** *Am J Respir Crit Care Med.* 2007; 175: 432-5

## Update in sleep and control of ventilation 2006

**Authors:** Horner RL et al

**Summary:** This review article divides recent literature into the categories of upper airway motor control; upper airway anatomy; neuromodulation and advances in control of breathing; Central Congenital Hypoventilation Syndrome, and Sleep Disordered Breathing (SDB, which is considered both as it relates to driving risk and cardiovascular disease). When considering upper airway motor control the authors conclude discussion of recent findings regarding obstructive sleep apnoea (OSA) in children; the concept that tonic drive activates respiratory muscles in wakefulness but not in sleep; and pharmacological strategies to increase pharyngeal muscle activity. Upper airway anatomy includes consideration of imaging techniques, risk factors associated with OSA including genetic factors and obesity. SDB and cardiovascular disease includes discussion of the association between OSA and cardiac arrhythmias, left ventricular hypertrophy and heart failure and finishes with a comment on cardiac pacing for OSA.

**Comment:** A comprehensive review of recent studies in SDB. The section on the relationship of SDB and cardiovascular disease is of particular interest. We need to encourage cardiologists to be more aware of the potential role of SDB in cardiovascular disorders, and to refer high risk patients for assessment.

<http://ajrccm.atsjournals.org/cgi/reprint/175/5/426>

**Reference:** *Am J Respir Crit Care Med.* 2007; 175: 426-31

## Update in tuberculosis 2006

**Authors:** Yew WW et al

**Summary:** This update regarding TB includes discussion of recent literature in the fields of epidemiology, genetics and immunology, diagnosis and treatment. Epidemiology contains studies of the effectiveness of screening, treatment prevention, reasons for treatment non-completion and the impact of HIV on TB control in sub-Saharan Africa. Recent literature on the genetics and immunology associated with TB covers IFN- $\gamma$  polymorphisms, the roles of iron acquisition and T cells. Diagnosis of latent TB infection and TB include effectiveness of skin testing, IFN- $\gamma$  assays and differing performance of two commercially available IFNGRAs. Treatment of TB and other mycobacterial disease includes research regarding patients who are underweight or HIV; a review of pulmonary TB treated with rifamycin-containing regimens; trials investigating other treatments including moxifloxacin and rifapentine; and treatment of Mycobacterium avium complex.

**Comment:** An interesting review of advances that have been made in the field of tuberculosis. In particular, significant progress has been made in the detection of LTBI through a number of in vitro assays which are now available for clinical use.

<http://ajrccm.atsjournals.org/cgi/content/full/175/6/541>

**Reference:** *Am J Respir Crit Care Med.* 2007; 175: 541-6

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## Atypical pathogens in community-acquired pneumonia

**Authors:** Arnold FW et al

**Summary:** This world-wide study sought to correlate the incidence of and clinical outcomes from community-acquired pneumonia (CAP) due to atypical pathogens with the proportion of patients treated with an atypical antibiotic regimen. For North America, Europe, Latin America and Asia/Africa the incidence of CAP due to atypical pathogens was 22, 28, 21 and 20% respectively and the proportion of patients treated with atypical coverage was 91, 74, 53, and 10%. Those patients treated with atypical coverage had a reduced time to clinical stability (3.7 vs 3.2 days,  $p < 0.001$ ), decreased length of stay (7.1 vs 6.1 days,  $p < 0.01$ ), decreased total mortality (11.1 vs 7%,  $p < 0.01$ ), and decreased CAP-related mortality (6.4 vs 3.8%,  $p = 0.05$ ). The authors conclude that “the better outcomes associated with antimicrobial regimens with atypical coverage support empiric therapy for all hospitalized patients with CAP with a regimen that covers atypical pathogens”.

**Comment:** Unique global data reporting a one in five incidence of atypical pathogens in community-acquired pneumonia, and the benefits of initial empiric anti-biologic therapy that covers these organisms. A strong case is put forward that all hospitalised patients with CAP should receive empiric therapy with a regime that covers both typical and atypical pathogens.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/10/1086>

**Reference:** *Am J Respir Crit Care Med.* 2007; 175:1086-93

## Predictive rules for assessing severity of community acquired pneumonia

**Authors:** Man SY et al

**Summary:** This prospective observational study ( $n = 1,016$ ) compared three validated prediction rules for community acquired pneumonia (CAP) in order to predict mortality for inpatients in Hong Kong. The predictive tools included the 20 variable Pneumonia Severity Index (PSI), the 6-point CURB-65 scale and the simpler CRB-65. All three assessments performed similarly, with areas under the ROC curve (95% CI) being 0.736 (0.687-0.736), 0.733 (0.679-0.787) and 0.694 (0.634-0.753) for the PSI, CURB-65 and CRB-65 respectively. High negative predictive values and relatively low positive predictive values were also noted for all rules. However the CRB-65 identified fewer low risk patients than the PSI and CURB-65 (12.6% vs 47.2% and 43.3%). Whilst the performance of all three rules was found to be similar the authors recommend use of the CURB-65 for assessment of CAP in emergency departments due to its relative simplicity and ability to identify low risk patients.

**Comment:** Interesting study validating the use of prediction rules for assessing severity of community-acquired pneumonia. The CURB65 score was preferred as it is easier to apply than the PSI and had a greater ability to identify low risk patients for outpatient care than the CRB65.

<http://thorax.bmj.com/cgi/content/abstract/thx.2006.069740v1>

**Reference:** *Thorax.* 2007; 62: 348-53

## Is the prevalence of wheeze in children altered by neonatal BCG vaccination

**Authors:** Linehan MF et al

**Summary:** This historical cohort study ( $n = 2,414$ ) sought to determine the influence of neonatal BCG vaccination on the prevalence of wheeze in children, aged 6 -11 years. A large community population which included both vaccinated and non-vaccinated children, was assessed for presence of wheeze using a parent completed questionnaire. Neonatal BCG vaccination was associated with a significantly lower prevalence of wheeze when assessed using univariate analysis (odds ratio, 0.69; 95% CI, 0.55-0.86) and was still significant when adjustments were made for potential confounders (odds ratio, 0.68; 95% CI, 0.53-0.87). These findings may be of considerable public health importance as they demonstrate a 27% reduction in the prevalence of asthma following the neonatal BCG vaccine, however the authors recommend further investigation.

**Comment:** Evidence to suggest that neonatal BCG vaccination may reduce the risk of childhood asthma. Due to the conflicting results from epidemiological studies to date, a large RCT is now required, preferably in high risk infants.

<http://www.jacionline.org/article/PIIS0091674907003612/abstract>

**Reference:** *J Allergy Clin Immunol.* 2007; 119: 1079-85

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