

# APSR Respiratory Research Review

Making Education Easy

Issue 3 - 2006

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**Welcome** to APSR Respiratory Research Review's third edition. It was a pleasure to meet so many APSR members at the recent congress and to receive such positive feedback to the publication.

With the end of the year fast approaching, we hope the review is helping to give you the extra time you need during this busy period and keeping you up to date with as little effort as possible.

This month provides some interesting research on the potential role of spirometry in primary care and some key studies on the use of testing and assessment methods to determine diagnoses and optimum treatment regimes.

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

Kind regards,

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## D-Dimer testing to determine the duration of anti-coagulation therapy

**Authors:** Palareti G et al

**Summary:** Approximately 600 patients with a recent idiopathic DVT or pulmonary embolism took part in this clinical study to evaluate the role of D-dimer in defining the duration of anticoagulant therapy. All patients had received a Vitamin K antagonist for at least 3 months and had ceased anticoagulant treatment one month prior to entry into the study. At enrolment 37% of patients were found to have an abnormal D-dimer level; these patients were randomly assigned to either resume anticoagulant therapy or cease treatment. Patients with normal D-dimer levels did not recommence treatment. Recurrence of DVT or major bleed during the study follow up occurred in 6.2% of patients with normal D-dimer, 2.9% of patient with abnormal D-dimer who resumed anticoagulant therapy and 15% of patients with abnormal D-dimer who discontinued treatment.

**Comment:** These findings reinforce the importance of assessing future risk to determine the length of anti-coagulant therapy for idiopathic VTE, rather than using a predetermined course of 6 or 9 months. In addition to a positive D-dimer after an initial therapeutic course of warfarin, other markers of increased risk include older age, underlying thrombophilia state and incomplete DVT resolution.

<http://content.nejm.org/cgi/content/abstract/355/17/1780>

**Reference: NEJM 2006; 355:1780-1789**

## Microscopic-observation drug-susceptibility assay for the diagnosis of TB

**Authors:** Moore DAJ

**Summary:** The Microscopic-Observation Drug-Susceptibility (MODS) assay, which involves microscopic examination of broth cultures, was shown to be an effective method of diagnosing tuberculosis and multi-drug resistant tuberculosis in this Peruvian study. Analysis of 3760 sputum samples indicated that MODS was 97.8% sensitive at detecting positive cultures, with a median time of 7 days being required for both culture positivity and susceptibility tests. This compared favourably with an automated mycobacterial culture which was 89% sensitive and required 13-22 days to provide results and the Löwenstein-Jensen culture which was 84% sensitive and required 26-68 days. MODS showed a 92%-100% correlation with the reference standard for susceptibility for key therapeutic agents including rifampin, isoniazid and streptomycin.

**Comment:** One of the attractive features of the MODS assay is that it can be established in any lab with basic equipment and training, and does not require a commercial product or kit. The superior performance of this assay compared with gold standard methods would suggest that the MODS assay may become the preferred microbiological method to detect TB and identify multi-drug resistant TB.

<http://content.nejm.org/cgi/content/abstract/355/15/1539>

**Reference: NEJM 2006; 355:1539-1550**

## Survival of patients with Stage I lung cancer detected on CT screening

**Authors:** International Early Lung Cancer Action Program Investigators

**Summary:** The potential value of CT screening for lung cancer in high-risk populations was demonstrated in this large international clinical study. Of the 31567 asymptomatic people screened during a 12 year period 484 were found to have lung cancer, of whom 85% were diagnosed with stage 1 disease. 73% of patients diagnosed with stage 1 lung cancer subsequently underwent surgery within one month. The predicted 10-year survival rate of patients with stage 1 disease was 88%; this figure increased to 92% for patients who underwent surgery. Eight patients who were diagnosed with stage 1 disease and underwent no treatment died within 5 years of initial screening.

**Comment:** Encouraging results regarding CT screening for lung cancer in high risk populations – with evidence presented that in terms of outcome (i.e. survival), this approach may compare favourably to mammography screening and resection for early stage breast cancer. The accompanying editorial provides a valuable public health and clinical perspective to the findings. [See editorial – Unger M. NEJM 2006; 355: 1822-4]

<http://content.nejm.org/cgi/content/abstract/355/17/1763>

**Reference: NEJM 2006; 355:1763-1771**

Asthma.can.be.frustrating. Repeated.asthma.attacks.keep.interrupting.patients'.lives. Almost.like.a.sentence.with.too.many.full.stops.

Seretide helps them overcome stops in life and leave asthma behind.



By aiming for total control ... leave asthma behind.



## Inhaled fluticasone propionate and adrenal effects in adult asthma: systematic review and meta-analysis

**Authors:** Masoli M et al

**Summary:** A meta-analysis of placebo-controlled, randomised dose-response clinical studies was performed to investigate the effect of inhaled FP on adrenal function in adults. Five studies of greater than 4 weeks' duration, involving 732 asthmatic patients, in which adrenal function was assessed by cosyntropin stimulation test were included. 3.9% of patients receiving placebo were found to have adrenal function below the lower limit of normal. The odds ratio of having an abnormal adrenal function was found to be increased by 1.38 for each increase of 500mcg FP /day. The authors conclude that administration of FP within the recommended dose range has minimal effects on adrenal function. However, they also highlight the fact that the study included only limited data on doses >1000mcg/day or administration of FP for an extended duration.

**Comment:** A novel approach for assessing the degree of adrenal suppression with inhaled corticosteroid therapy – the risk of an abnormal result. Reassuring findings that there is minimal risk of adrenal suppression with fluticasone when prescribed to adults within the recommended therapeutic dose-response range of 50 to 500µg per day.

<http://erj.ersjournals.com/cgi/content/abstract/28/5/960>

**Reference:** *Eur Respir J* 2006; 28:960-967

## Effect of primary-care spirometry on the diagnosis and management of COPD

**Authors:** Walker PP et al

**Summary:** The use of spirometry in a primary care setting was found to increase the rate of diagnosis of COPD and improve medical management according to the authors of this British clinical study. 1508 patients from local primary care providers were referred for spirometric evaluation over an approximate 4 year period. 235 of these patients were found to have COPD, of whom 130 were newly diagnosed. As a result of the spirometric evaluations the use of pharmacotherapy increased by 19% for anticholinergics and inhaled steroids and by 17% for long acting beta2-agonists compared with pre-evaluation usage. The majority of patients also received advice on smoking cessation.

**Comment:** Encouraging findings for the use of spirometry in primary care practice – its use both increased pick-up rate for COPD and led to improvements in its management. The introduction of spirometry in primary care within the Asia Pacific region would be a worthwhile initiative for APSR members to support within their communities.

<http://erj.ersjournals.com/cgi/content/abstract/28/5/945>

**Reference:** *Eur Respir J* 2006; 28:945-952

## Spirometry and smoking cessation advice in general practice: A randomised clinical trial

**Authors:** Buffels J et al

**Summary:** The role of GPs in motivating patients to stop smoking was investigated in this Belgian clinical study. 16 GPs who were trained to provide support for smoking cessation identified 1206 smokers, of whom 221 agreed to attempt to stop smoking. Approximately half were prescribed either nicotine replacement therapy or bupropion and the GPs maintained a minimal intervention strategy throughout the study. After 6 months 29% of the patients who had attempted to stop smoking had succeeded, with this figure decreasing to 19% of patients after one year and 15% after 2 years. Being informed of their lung function was found to have no real impact on patients' ability to stop smoking. The author concludes that GPs can, with minimal intervention, play a significant role in reducing smoking amongst patients.

**Comment:** The important message from this study is that training primary care doctors in smoking cessation advice is highly cost-effective. Training programmes for smoking cessation advice for GPs would represent an important initiative for members of the APSR to establish within their region. It would also be important to ensure that such training is provided as part of the standard medical school undergraduate curriculum.

<http://www.sciencedirect.com/science>

**Reference:** *Respiratory Medicine* 2006; 100:2012-2017

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## Sleep-disordered breathing and continuous positive airway pressure compliance in a group of commercial bus drivers in Hong Kong

**Authors:** Hui DSC et al

**Summary:** Continuous positive air pressure (CPAP) was found to be beneficial in improving sleepiness in bus drivers but had a relatively low uptake according to the findings of this clinical study. Just over 1000 Hong Kong bus drivers were interviewed and provided the following results: 61% were sleepy at work, 24% snored at least 3 times a week, 4% experienced sleep apnoea and 24% reported having fallen asleep whilst driving. Approximately 200 of those interviewed subsequently took part in a home-sleep study: 40% had 5 or more respiratory disturbances/hour (RDI), 26% had an RDI of  $\geq 10$ /hour and 17.5% had an RDI of  $\geq 15$ /hour. Nine drivers commenced CPAP therapy which improved sleep related factors within three months. Neck circumference, increased BMI and intensity of snoring were all associated with increased RDI.

**Comment:** This study can be used as a model for an occupational health programme to detect and treat obstructive sleep apnoea in "high risk" workforces. Implementation of similar programmes is warranted in transport and other industries where the consequences of undiagnosed and untreated obstructive sleep apnoea are major for both the worker and the public.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2006.00932.x>

**Reference: Respirol 2006; 11:723-730**

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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.

## Effectiveness of early budesonide intervention in Caucasian versus Asian patients with asthma: 3-year results of the START study

**Authors:** Tan WC et al

**Summary:** Over 6600 patients with mild persistent asthma, including 1995 Asian patients, took part in this randomised, double-blind clinical trial to investigate the effects of early intervention with inhaled budesonide. Patients aged 5-66 randomly received either 400mcg budesonide once daily via Tubuhaler (200mcg for patients under 11 years) or placebo in addition to their usual asthma medication for 3 years. Compared with placebo patients receiving budesonide reported improved asthma symptoms, a reduction in the number of sleep disturbances and increased pre- and post-bronchodilator FEV1. The need for additional asthma therapy was also decreased in this group. The risk of having a first severe asthma exacerbation was also reduced by 45.5% following treatment with budesonide (42% for Caucasians and 49% for Asians) and the incidence of adverse events was similar between racial groups. The author concludes that the effects of early budesonide treatment in this patient population are equally beneficial in people of both Caucasian and Asian ethnicity.

**Comment:** Important findings for the Asia Pacific region – that the initiation of ICS therapy in asthma achieves similar benefits in Asian as with Caucasian patients with asthma. The greater use of low dose ICS in patients with persistent asthma in the Asia Pacific represents a priority – it is arguably the most important initiative that can be undertaken to reduce the burden of asthma within the Asia Pacific region.

<http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2006.00945.x>

**Reference: Respirol 2006; 11:767-775**

## Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study

**Authors:** Whitney CG et al

**Summary:** A recent U.S. clinical study was performed to assess the effectiveness of the seven-valent pneumococcal conjugate vaccine in the protection against invasive pneumococcal disease. Over 3200 children aged 3-59 months, of whom over 780 had invasive disease and the remainder were matched controls, were enrolled. The results showed that in healthy children the vaccine was 96% effective at preventing pneumococcal disease; this effectiveness decreased to 81% in children with additional health complications. The investigators also established that vaccination, regardless of the immunisation schedule employed, was better at preventing disease than no vaccination, and specifically that inclusion of a booster dose following 3 infant doses conferred improved protection than the 3 infant doses alone.

**Comment:** Further evidence of the efficacy of pneumococcal vaccination in young children. A reminder to familiarise ourselves with the recommended indications and high priority uses of the pneumococcal vaccine in children under 5 years in our respective countries.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673606696372/abstract>

**Reference: The Lancet 2006; 368:1495-1502**

**Independent commentary by Professor Richard Beasley**

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