APSR Respiratory Research Review

Summmarising Significant Global Medicine — Issue 1 – 2006

In this issue:

Welcome to the first edition of the Respiratory Research Review, a novel APSR publication bringing you some of the most important scientific research from around the world every month.

The Respiratory Research Review has been established to help make life easier for the respiratory medicine community in the Asia-Pacific region. Every month around 10,000 scientific publications are printed worldwide. Many contain a few papers on respiratory medicine and several others are devoted entirely to respiratory research. In short, keeping up is hard and requires significant devoted time to screening out what is irrelevant to your practice. In essence we want to save you time.

Each month the ten most important published studies in respiratory medicine are identified and a summary provided, together with a commentary on why the studies are important and how then can affect practice. The Review also provides website links to the abstract or fully published trials to let you make your own judgements.

The Review represents an initiative of the Education Committee of the APSR. We hope you find the first edition stimulating and look forward to your comments.

Kind regards,

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Worldwide time trends in the prevalence of symptoms of asthma, allergic rhino-conjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys

Authors: Asher MI et al

Summary: Results from phase 3 of The International Study of Asthma and Allergies in Children (ISAAC) have shown mixed trends in prevalence of asthma and associated conditions. Almost 500,000 children worldwide were studied between 2002-2003 to compare prevalence of asthma, allergic rhinoconjunctivitis and eczema with results obtained 7 years previously. Although the results varied there were more increases in prevalence reported than decreases, with younger children (6-7 years) showing a more noticeable increase in prevalence than older children (13-14 years). However, the study also indicated that asthma prevalence had declined amongst older children in areas with a high incidence of asthma since phase 1 of ISAAC.

Comment: Reassuring findings from ISAAC Phase Three that the prevalence of asthma appears to have peaked in high prevalence countries. However, for some countries within the Asia-Pacific region, substantial increases in asthma prevalence have occurred over the last decade, reinforcing the public health importance of asthma in the region.

http://www.thelancet.com/journals/lancet/article/PIIS0140673606692830/abstract

Reference: Lancet 2006; 368: 733-43

Comparison of fixed-dose weight-adjusted unfractionated heparin and low-molecular-weight heparin for acute treatment of venous thromboembolism

Authors: Kearon C et al

Summary: Subcutaneous unfractionated heparin was found to have a similar safety and efficacy profile as low-molecular-weight heparin, when given to patients with acute venous thromboembolism (AVT) in this randomised, open-label clinical study. Over 700 patients, aged 18 and over, with AVT received either s.c. unfractionated heparin (333 U/kg, followed by 250 U/kg bd) or s.c. low-molecular-weight heparin (dalteparin or enoxaparin, 100 IU/kg bd) in addition to 3 month's treatment with warfarin. 72% of patients receiving unfractionated heparin and 68% of patients receiving lmw heparin were treated on an out-patient basis. Venous thromboembolism recurred in 3.8% and 3.4% of patients receiving unfractionated and lmw heparin and a major bleed within 10 days of treatment onset was experienced in 1.1% and 1.4% of patients.

Comment: This study provides strong evidence that unfractionated heparin administered subcutaneously, at fixed dose without APTT monitoring is as effective and safe as LMWH for initial treatment of DVT and PE. These findings are particular important in the Asia-Pacific region due to the substantially reduced costs of unfractionated heparin compared with LMWH.

http://jama.ama-assn.org/cgi/content/abstract/296/8/935

Reference: JAMA 2006; 296; 935-42

Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study

Authors: Rabe KF et al

Summary: A combination of budesonide-formoterol, when given as-needed to poorly controlled asthmatics, was found to decrease the incidence of severe exacerbations compared with as-needed formoterol or terbutaline. Over 3300 patients were enrolled in this 12-month study and received prn terbutaline (0.4mg), prn formoterol (4.5mcg) or prn budesonide-formoterol (160mcg/4.5mcg) in addition to maintenance therapy with budesonide-formoterol (one inhalation bd). The rate of severe exacerbations, as defined by in-patient/emergency room treatment or oral steroid use, was 19/100 patients/year for the combination product compared to 29 and 37 for formoterol and terbutaline respectively. The time to onset of first severe exacerbation was also longer for the combination product. Days when asthma was well controlled and adverse events were similar between the treatment groups.

Comment: This landmark study provides support for the use of the budesonide/formoterol combination inhaler "as required for relief of symptoms" in addition to low dose maintenance use in poorly controlled asthma. As acknowledged by the authors the study did not exclude the possibility that an increase in the maintenance dose of combination therapy, as currently recommended by guidelines, could have further improved clinical outcomes. They recommend that this issue will need to be addressed before the "maintenance and reliever" combination therapy regime can be widely adopted. The commentary is worth reading. [Lancet 2006; 368: 707-8]

http://www.thelancet.com/journals/lancet/article/PIIS0140673606692842/abstract

Reference: Lancet 2006; 368: 744-53

Environmental tobacco smoke and mortality in Chinese women who have never smoked: prospective cohort study

Authors: Wen W et al

Summary: This Chinese prospective study involving approximately 70,000 women was designed to investigate the impact of environmental smoke exposure on mortality and smoking related diseases. Women who had never smoked provided information on their husband's smoking and their exposure to smoke in their work-place and during their early childhood. An increased risk of overall mortality (hazard ratio 1.15) and mortality attributable to CV disease (HR 1.37) was associated with spousal smoking, whereas an increased risk of death by cancer (HR 1.19) and lung cancer (HR 1.79) were associated with work-place exposure. Women who had been exposed to smoke in their homes as children had an increased risk (HR 1.26) of CV disease mortality.

Comment: This important study quantifies the risk of mortality from environmental tobacco smoked. Due to the high prevalence of exposure to environmental tobacco smoke, both in the home and work environment, its impact on mortality is substantial, with a population-attributable risk of around 10%.

http://bmj.bmjjournals.com/cgi/content/abstract/333/7564/376

Reference: BMJ 2006; 333: 376-80

Association between nonspecific airway hyperresponsiveness and Arg16Gly ß2-adrenergic receptor gene polymorphism in asymptomatic healthy Japanese subjects

Authors: Fukui Y et al

Summary: The association between airway hyperresponsiveness (AHR) and polymorphism of the ß2-adrenergic receptor (AR) gene (Arg16Gly and Gln27Glu) was investigated in this Japanese clinical study. 120 healthy asymptomatic people underwent inhalation challenge with methacholine to establish the presence of AHR. Volunteers were also genotyped using kinetic real-time quantitative polymerase chain reaction in conjuction with allele-specific amplification. The results indicated that respiratory conductance started to diminish at a lower concentration of methacholine in indiviuals with the Gly16Gly genotype compared with those with the Arg16 allele. The authors conclude that "a specific ß2-AR polymorphism at codon 16 might be a genetic determinant of AHR, as judged by methacholine-induced bronchoconstriction in asymptomatic healthy subjects."

Comment: The clinical importance of this study is that it indicates a role for specific ß2-AR polymorphisms in airway hyperresponsiveness, independent of beta agonist therapy. This suggests that ß2-AR polymorphisms may contribute to the development of asthma, as well as asthma severity and its response to beta agonist treatment.

http://www.chestjournal.org/cgi/content/abstract/130/2/449

Reference: Chest 2006; 130: 449-54

FEV_1 decline in occupational asthma

Authors: Anees W et al

Summary: The findings from this British study clearly demonstrated that the rate of decline in FEV1, associated with a specific causative agent, could be reduced if exposure to that agent was halted. 90 patients with occupational asthma for whom lung function data were available before exposure ceased were found to have a mean decline in FEV1 of 100ml/year. When that agent was removed mean FEV1 increased by 12ml in the first year. For the 86 patients for whom extended data were available, the mean rate of decline in FEV1, once exposure had ceased, was found to be approximately 27ml/year. The results did not appear to be affected to inhaled corticosteroid use or smoking habit.

Comment: The important message of this paper is that removing a worker from exposure is the most important therapeutic measure to take in the management of occupational asthma. If workers remain exposed to the offending agents, they are likely to experience a rapid loss of lung function, with the development of severe irreversible asthma

http://thorax.bmjjournals.com/cgi/content/abstract/61/9/751

Reference: Thorax 2006; 61: 751-51-5

A virtual broncho-scopic navigation system for pulmonary peripheral lesions

Authors: Asano F et al

Summary: A team of researchers in Japan have recently trialled a new diagnostic tool for investigating peripheral pulmonary lesions with promising results. 37 patients underwent ultra-thin bronchoscopy whereby virtual bronchoscopy images together with actual images were obtained, allowing for accurate navigation to the target bronchus (3rd to 9th order). After confirmation of the correct placement of the bronchoscope by thin section CT scan, a biopsy was performed using forceps. The results of this preliminary trial found that 95% of the lesions targeted were correctly located by bronchoscope, a biopsy by forceps was possible for 87% of the lesions and 82% of the biopsies provided a diagnosis. The whole procedure generally took less than 30 minutes to perform.

Comment: A novel approach to the investigation of peripheral pulmonary lesions utilising ultra-thin bronchoscopy. The diagnostic yield from this method is considerably higher than other techniques. Due to the increasing use of low dose helical CT scanning to screen for lung cancer, further research and experience with this technique is urgently required.

http://www.chestjournal.org/cgi/content/abstract/130/2/559

Reference: Chest 2006; 130: 559-66

Independent commentary by Professor Richard Beasley

Research Review publications are intended for Medical Professionals

Impaired performance in commercial drivers role of sleep apnea and short sleep duration

Authors: Pack AI et al

Summary: A recent study of commercial drivers suggested that sleep duration may have more of an impact on driver performance than sleep apnoea. 406 drivers, of whom 247 were considered to be at high risk for sleep apnoea, underwent a series of tests including subjective sleepiness, objective sleepiness, and performance assessments. A reduction in sleep time was associated with increased subjective and objective sleepiness, and decreased performance. No clear links between sleep apnoea and sleepiness or performance were established with the exception of sleep latency, whereby the time taken to fall asleep was linked to the degree of sleep apnoea. Objective sleepiness was found to be similarly affected by severe apnoea (more than 30 episodes/night) or nightly sleeps of less than 5 hours.

Comment: An important clinical caution: do not simply focus on obstructive sleep apnoea (OSA) in the investigation of high risk patients with hypersomnolence. This study has shown in a group of "high risk" commercial drivers, that increases in objective sleepiness and poor driving performance were more strongly associated with shorter sleep durations than sleep apnoea severity. Insufficient sleep represents an important cause of hypersomnolence and disability in patients with OSA.

http://ajrccm.atsjournals.org/cgi/content/abstract/174/4/446

Reference: Am J Respir Crit Care Med 2006; 174: 446-54

Prognostic factors for surgical resection in patients with multidrug-resistant tuberculosis

Authors: Kim HJ et al

Summary: The purpose of this Korean study was to try to identify suitable candidates for lung resection in patients with multidrug-resistant tuberculosis. 79 patients who had undergone lung resection during an approximate 12 year period were included and their outcomes investigated. The results indicated that treatment failed in 28% of the patients, as defined by presence of positive cultures during a specified time period or the patient dying during treatment. The investigators reported that: "A body mass index <18.5 kg·m2, primary resistance, resistance to ofloxacin and the presence of a cavitary lesion beyond the range of the surgical resection were associated with treatment failure".

Comment: The therapeutic dilemma of the preferred approach to multidrug-resistant tuberculosis refractory to medical treatment – this study provides guidance on how to identify patients who are likely to do poorly from surgical resection

http://erj.ersjournals.com/cgi/content/abstract/28/3/576

Reference: Eur Respir J 2006; 28: 576-80

In a randomized, double-blind, parallel-group, placebo positive benefits of theophylline-controlled study of low-dose, slow-release theophylline in the treatment of COPD for 1 year

Authors: Zhou Y et al

Summary: Slow-release oral theophylline was found to improve symptoms in patients with chronic obstructive pulmonary disease (COPD) in this randomised, double-blind, placebo-controlled clinical study. 85 patients completed the one year study during which 42 patients received sr theophylline and 43 patients received placebo. The results indicated that, compared with placebo, sr theophylline resulted in increased pre-bronchodilator FEV1, lower incidence of exacerbations, longer time to first exacerbation and lower attendance at medical facilities. Patients taking sr theophylline reported an improved quality of life and were generally satisfied with their treatment, although some typical adverse events were noted.

Comment: This study provides further evidence for the efficacy of low dose theophylline in the long term treatment of stable COPD. As in the treatment of asthma, oral theophylline represents an alternative to inhaled long acting beta agonist therapy in COPD, particularly in developing countries where cost is an important determinant of the availability of medications.

http://www.blackwell-synergy.com/doi/abs/10.1111/j.1440-1843.2006.00897.x

Reference: Respirology 2006; 11: 603-10

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