

APSR Respiratory Research Review

Making Education Easy

Issue 26 – 2008

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Welcome to this edition of the APSR Research Review.

Returning invigorated and inspired from an excellent European Respiratory Society conference in Berlin, there have been plenty of offers for articles to be selected for this November Research Review. Actually, at times it feels as though the gaps are larger than the material covered. For example, this edition focuses on asthma and pneumonia, yet we do not have space to review the excellent updated practice parameter for diagnosis and management of rhinitis. Unfortunately we also won't be reviewing the new [British guidelines for emergency use of oxygen](#); however, these are freely available via the [BTS website](#).

We are reviewing data suggesting a relationship between childhood paracetamol [acetaminophen] and asthma, and also a further paper on housing heating reducing asthma morbidity. We have reviewed articles that found an association between the use of oxygen and the use of statins with a reduction in pneumonia mortality. Also, the intriguing effect of streptococcus pneumonia conjugate vaccine on unvaccinated household members sheds a new light on a pneumococcal vaccine. We hope you enjoy reading the Research Review and welcome any feedback.

Kind regards,

Dr Lutz Beckert

lutzbeckert@researchreview.co.nz

The relation between paracetamol use and asthma

Authors: Shaheen S et al

Summary: The impact of paracetamol use on asthma risk was investigated in 521 cases of patients diagnosed with asthma and reporting asthma symptoms within the previous 12 months and 507 matched controls (with no asthma diagnosis or asthma symptoms in the previous 12 months). There was a strong association between weekly paracetamol use and asthma independent of confounding factors. Use of other analgesics was not significantly associated with asthma.

Comment: This is a case-control study that found a positive association between weekly paracetamol use and asthma symptoms. The authors recruited adults in several European centres and investigated the use of paracetamol versus nonparacetamol medications such as aspirin or ibuprofen. As with the paediatric study (see p2), this study design does not allow for the exclusion of bias or confounders. However, the result is consistent with other findings and is biologically plausible via glutathione depletion and increased oxidative stress. The authors also call for an intervention study to determine whether or not this relationship is causal.

Reference: *Eur Respir J* 2008; 32(5): 1231-6

<http://erj.ersjournals.com/cgi/content/abstract/32/5/1231>



Educational Seminar of the Asian Pacific Society of Respirioly

Lung Cancer and Bronchology Symposium

19 - 20 February 2009



Tel: (65) 63214700/ 4685 Fax: (65)62271736 Email: pynglee16@gmail.com

Course description

A State of the Art Review on Imaging, Diagnosis, Staging and Treatment of Lung Cancer. New technologies aimed at imaging for early lung cancer detection, precision targeting of pulmonary nodules, endoscopic ultrasound for mediastinal staging as well as therapeutic bronchoscopic and pleuroscopic techniques for palliation will be discussed. The course features live demonstration by the experts and allows participants to have "hands-on" experience. In addition there are sessions on lung pathology and its precursors, new international classification for lung cancer as well as research into biomarkers for targeted therapy in the future.

Who should attend

Specialists, trainees in Pulmonary Medicine, Oncology, Thoracic Surgery, Pathology and researchers with interest in lung cancer. CME points will be awarded.

Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6–7 years

Authors: Beasley R et al

Summary: This analysis of data from children aged 6–7 years from phase III of the International Study of Asthma and Allergies in Childhood (ISAAC) programme investigated possible links between paracetamol use and symptoms of asthma, eczema and rhinoconjunctivitis. Paracetamol use for fever during the first year of life among these children was associated with an increased risk of asthma symptoms (OR 1.46; 95% CI 1.36, 1.56), and the ORs for asthma symptoms associated with current medium and high paracetamol use compared with no use were 1.61 (1.46, 1.77) and 3.23 (2.91, 3.60), respectively. The population-attributable risks for severe asthma symptoms associated with paracetamol use were 22–38%. There were also increased risks of rhinoconjunctivitis and eczema associated with paracetamol use during the first year of life.

Comment: The authors found a strong, dose-dependent association between paracetamol use and symptoms of asthma, rhinoconjunctivitis and eczema in more than 200,000 children in 31 countries. They argue that this relationship is probably clinically relevant because: 1) paracetamol use was associated with an increased risk of asthma; 2) a strong dose relationship was found; 3) the association was present across various lifestyles, medical practices and cultural boundaries; 4) it was also shown previously in an RCT; 5) exposure preceded the response; and 6) there is a temporal relationship between the paracetamol dose and increase of childhood asthma over the last 50 years. The mechanism for this relationship could be attributed to the depletion of glutathione stores. This article and accompanying editorial both argue for a population-based randomised trial with paracetamol compared with ibuprofen and a placebo.

Reference: *Lancet* 2008; 372(9643): 1039-48
<http://tinyurl.com/lancet-372-1039>

Effects of improved home heating on asthma in community dwelling children

Authors: Howden-Chapman P et al

Summary: This study explored the impact of installing nonpolluting, more effective home heating systems in the homes of 409 children with asthma. Compared with control households (heating system installed after the study period), children in the intervention group (heating system installed prior to the study period) had fewer days off school, fewer asthma-related doctor and pharmacy visits, less night-time dry cough, less sleep disturbance due to wheezing, fewer reports of poor health and reduced lower respiratory tract symptom scores. Lung function was not significantly improved in the intervention group. Household temperatures were higher and NO₂ levels were lower in both the child's bedroom and the living room in households in the intervention group.

Comment: This NZ study investigated the effect of improving home heating on controlling asthma. The authors randomised 409 households with children to receive replacement heaters (heat pump, wood pellet burner or flued gas) before or after winter. The authors found no significant differences in the objective spirometric lung function assessments, but they did find a reduction in cough and wheeze. In addition, the children had fewer doctor and pharmacy visits and fewer days off school. An improved well-being was also reported. The authors argue that the improvement in asthma symptoms is clinically relevant and that this environmental intervention is an effective adjunct to standard therapy.

Reference: *BMJ* 2008; 337: a1411

http://www.bmj.com/cgi/content/abstract/337/sep23_1/a1411

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Can lay people deliver asthma self-management education as effectively as primary care based practice nurses?

Authors: Partridge MR et al

Summary: The question of whether well-trained lay people can be as effective as primary-care nurses in delivering self-management education to patients with asthma was addressed in this paper. Of the 567 participants entered into the study, 146 and 171 attended their first session with a practice nurse or a lay educator, respectively. Management changes were made for 24.0% and 32.7% of these participants in the nurse and lay educator groups, respectively. Among the 418 patients in whom 1-year data on use of unscheduled healthcare were available, 29.8% and 30.5% of the nurse- and lay-led groups, respectively, required such care. The level of patient satisfaction was similar between the two groups.

Comment: These British authors found comparable outcomes of trained lay educators versus practice nurses delivering asthma self management education in unscheduled healthcare needs, patient satisfaction and courses of oral steroids. As encouraging as this was, unfortunately the researchers found a similar dropout rate of practice nurses (45.6%) and lay educators (60%). This contributed to the inability of the study to reach their target numbers of patients recruited. Another factor that was not anticipated was that 30% of patients needed unscheduled healthcare during 12 months' follow-up. Bottom line: asthma self management can be delivered by trained lay educators, but the problems of recruitment, retention and unscheduled healthcare visits remain the same.

Reference: *Thorax* 2008; 63(9): 778-83

<http://thorax.bmj.com/cgi/content/abstract/63/9/778>

Effect of hydrofluoroalkane-ethanol inhalers on estimated alcohol levels in asthmatic subjects

Authors: Bruce C et al

Summary: This paper aimed to answer the question 'Can ethanol/hydrofluoroalkane (HFA)-containing metered dose inhalers (MDIs) raise breath alcohol concentrations above the legal limit?'. Breath alcohol concentrations were measured in participants with asthma (n=16) and normal control participants (n=15) following use of each of three MDIs containing HFA/ethanol, chlorofluorocarbons (CFCs) or placebo administered in a random order. Baseline breath alcohol concentrations increased from 0.002 to 0.138 mg/100mL (p=0.001) and 0.001 to 0.016 mg/100mL (p=0.002) in asthmatic and normal subjects, respectively. However, breath alcohol concentrations were no longer significantly different from baseline concentrations 5 minutes postinhalation in asthmatic and control participants.

Comment: All asthma inhalers are not created equal and the same is true for the solvent used. Over the last few years CFC has been phased out and replaced with HFA with different levels of ethanol as a cosolvent. Unfortunately, ethanol solvent can be detected in breath alcohol testing. These Australian researchers plotted out the time curves in 16 asthmatic subjects and 15 controls. Ethanol-containing inhalers did indeed increase the detected breath alcohol concentrations above the legal limit for learners or provisional drivers. However, this effect was very transient and lasted in both asthmatic and control groups for only about 2 minutes. After 5 minutes, the breath ethanol concentration had returned to baseline.

Reference: *Respirology* 2008; Early view

<http://www3.interscience.wiley.com/journal/121389770/abstract>

What is the burden of chronic cough for families?

Authors: Marchant JM et al

Summary: This paper explored the impact of chronic cough on the families of 190 children newly referred with the condition by getting parents to complete questionnaires. A correlation between burden scores at presentation and parents' depression, anxiety and stress 21-item scale (DASS) scores was evident. Parental anxiety and depression scores were not abnormal, but stress was the main contributor to their emotional distress. Parents' DASS subscale scores all declined when their children stopped coughing.

Comment: Each year about 29.5 million patients seek medical help for cough and spend billions on over-the-counter medication. These Australian researchers examined the parental burden of chronic cough in 190 children. About 80% had >5 visits to a doctor and 53% had >10 visits to a doctor within 12 months. Patients had seen at least three different doctors and expressed that their greatest burden was feeling frustrated, upset, sleepless, sorry for the child and helpless. Interestingly, the parental anxiety and depression scores were low. Bottom line: this study highlights the need to improve the management of children with chronic cough, including the clinician being cognisant of the emotional distress of parents and addressing this early on in the consultation process.

Reference: *Chest* 2008; 134(2): 303-9

<http://www.chestjournal.org/cgi/content/abstract/134/2/303>

Improved oxygen systems for childhood pneumonia

Authors: Duke T et al

Summary: The impact of providing an improved oxygen system on mortality among children with pneumonia in five hospitals in Papua New Guinea was investigated by comparing death rates before and after the system was implemented. Prior to the new oxygen system (2001–2004) the case fatality rate was 4.97%, compared with 3.22% after the oxygen system was implemented (2005–2007), equating to a 35% lower risk of death associated with the new system (risk ratio 0.65; 95% CI 0.52, 0.78; p<0.0001).

Comment: Just at the time of publication of the new oxygen guidelines, this study from Papua New Guinea reminds us of the importance of this therapy. Pneumonia kills 2 million children younger than 5 years of age every year. The authors invested in oxygen concentrators and oximeters in five hospitals in Papua New Guinea. With these simple measures they demonstrated a 35% reduction in hospital mortality at a cost of US\$51 per patient treated and US\$1673 per life saved. The article and editorial are both well written and make sobering reading, but also remind us of the therapeutic benefit of oxygen therapy in hypoxic patients.

Reference: *Lancet* 2008; 372(9646): 1328-33

<http://tinyurl.com/lancet-9646-1328>



*Independent commentary
by Dr Lutz Beckert,
Respiratory Physician at
Christchurch Hospital,
New Zealand.*

Indirect effect of 7-valent pneumococcal conjugate vaccine on pneumococcal colonization among unvaccinated household members

Authors: Millar EV et al

Summary: This study explored the rate of invasive pneumococcal disease among nonvaccinated individuals living with vaccinated people in a group of south-western American Indian communities involved in a phase III efficacy trial of 7-valent pneumococcal conjugate vaccine (PCV7). Colonisation with vaccine-type pneumococci was significantly less likely among adults and children aged <5 years, but not children aged 5–17 years, who lived with a PCV7 recipient than those who lived with someone who had received meningococcal conjugate vaccine against serogroup C (control group). Increases in nonvaccine pneumococci type carriage countered decreased carriage of vaccine type. The likelihood of an adult having the same serotype as a cohabitant colonised with vaccine-type pneumococcus was lower if their cohabitant had received the PCV7 vaccine than it was if their cohabitant had received the control vaccine (OR 0.34; 95% CI 0.11, 0.99).

Comment: This research follows a group-randomised phase III efficacy trial of PCV7 conducted between 1997 and 2000. This study had been very successful and PCV7 is now recommended for children in the US. The authors investigated the indirect effect of the vaccination on unvaccinated adults and children living in the same household. They demonstrated a significant reduction in invasive pneumococcal disease in nonvaccinated adults aged >65 years in families where children were vaccinated. Most of the effect was seen in a reduction of the strains contained in the vaccine. This article has attracted an editorial and a review article on a “new paradigm for protecting elderly adults”. Bottom line: vaccinate children who are potential carriers for invasive streptococcus and you will also reduce the burden of disease in the elderly, vulnerable population.

Reference: *Clinical Infectious Diseases* 2008; 47(8): 989-96

<http://www.journals.uchicago.edu/doi/abs/10.1086/591966>

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.

Proton-pump inhibitor use and the risk for community-acquired pneumonia

Authors: Sarkar M et al

Summary: This nested case-control study investigated the risk of community-acquired pneumonia (CAP) associated with proton-pump inhibitor (PPI) use in 80,066 cases with an incident diagnosis of CAP and 799,881 matched controls. Current PPI use did not increase the risk of CAP (adjusted OR 1.02; 95% CI 0.97, 1.08) or hospitalisation for CAP (1.01; 0.91, 1.12). However, there were increased risks of CAP associated with current PPI use initiated within the previous 2 (adjusted OR 6.53; 95% CI 3.95, 10.80), 7 (3.79; 2.66, 5.42) and 14 days (3.21; 2.46, 4.18), but not with longer term current PPI use. The investigators commented that there is no obvious biological explanation for the risk of CAP increasing as the period since initiation of PPI therapy shortens, and that the observational nature of their study rules out establishing a causal relationship based on their data.

Comment: This group of American researchers used a general practice database to investigate whether current PPI use is a risk factor for developing CAP. Reassuringly, there was no relationship between PPI users and CAP. Recently started PPI therapy was associated with increased risk of a CAP diagnosis; however, the authors doubt that this is a causal effect. Bottom line: from the evidence available, long-term PPI use is not associated with increased risk for CAP.

Reference: *Ann Intern Med* 2008; 149(6): 391-8

<http://www.annals.org/cgi/content/abstract/149/6/391>

Preadmission use of statins and outcomes after hospitalization with pneumonia

Authors: Thomsen RW et al

Summary: The effect of preadmission administration of HMG-CoA reductase inhibitors (statins) on outcomes in patients hospitalised with pneumonia was investigated in this population-based cohort study. Current statin use was recorded in 1371 of 29,900 patients in the cohort. Statin users had a lower mortality rate than nonusers, with 30- and 90-day mortality rate ratios of 0.69 (95% CI 0.58, 0.82) and 0.75 (0.65, 0.86), respectively. Statin use was not a significant predictor of bacteraemia or pulmonary complications, and previous statin use and current use of other prophylactic cardiovascular agents did not have a significant impact on mortality.

Comment: These researchers used a Danish primary-care database to investigate whether preadmission statin use had any effect on 30- or 90-day pneumonia-related mortality. They identified 29,900 patients, with 4.7% of these patients receiving a statin at the time of admission to hospital. They documented a 90-day mortality rate of 16.8% in statin users versus 22.3% in nonusers. This relationship remained robust when corrected for confounders and in subanalyses. Unfortunately this study design can not exclude the fact that statin users may be younger, healthier, better educated and privileged than nonusers. Bottom line: consistent data have shown that statins may decrease pneumonia-related mortality, but randomised trials are needed prior to using them clinically for this purpose.

Reference: *Arch Intern Med* 2008; 168(19): 2081-7

<http://archinte.ama-assn.org/cgi/content/abstract/168/19/2081>

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