

APSR Respiratory Research Review

Summarising Significant Global Medicine

Issue 2 - 2006

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Welcome to the second edition of the **Respiratory Research Review**, an APSR publication summarising some of the most important scientific research from around the world.

We were delighted to receive feedback and comments on the first edition from many members. I hope it continues to be a useful resource and helps the APSR membership save time and stay up to date with the latest developments. Any comments or requests should be emailed to rbeasley@asiapacificresearchreview.com, a change from the previous contact address and one established solely for this review.

The APSR has set up a separate section of the APSR website to host the new and past editions of the publication if you ever need to refer to them. Also, each Review provides live website links to the abstract or fully published study to allow you to fully explore those of most interest.

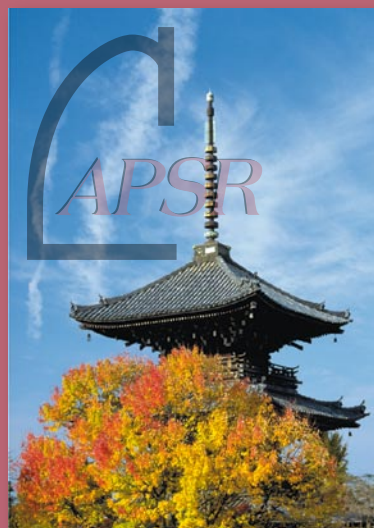
The Review is an initiative of the Education Committee of the APSR. We hope you find the latest edition helpful and stimulating.

Kind regards,

Richard Beasley

Chair, Education Committee, APSR

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11th Congress of the Asian Pacific Society of Respirology (APSR)

New Horizons in Respirology – Harmonization beyond Diversity

VENUE: Kyoto International Conference Hall

DATE: 19 -22 November 2006

PRESIDENT: Yoshinosuke Fukuchi, MD

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Safety and immunogenicity of an inactivated adjuvanted whole-virion influenza A (H5N1) vaccine: a phase I randomised controlled trial

Authors: Lin J et al

Summary: An inactivated adjuvanted whole-virion H5N1 vaccine met all European regulatory requirements for annual licensing of a seasonal influenza vaccine when given as two doses containing 10 μ g haemagglutinin. The safety and immunogenicity of four formulations of the vaccine were investigated in 120 volunteers aged 18-60 years in a phase 1, double-blind, placebo-controlled clinical trial. Volunteers were randomised to receive a two-dose regimen of placebo or vaccine containing 1.25 μ g, 2.5 μ g, 5 μ g, or 10 μ g haemagglutinin per dose with adjuvant aluminium hydroxide. The first dose was given on day 0 and the second on day 28. Antibody responses were evident for all vaccine formulations after the first dose, with the 10 μ g formulation inducing the highest immune response of 78% seropositivity after the second vaccine dose. The vaccine was well tolerated at all doses and there were no serious adverse events. Local and systemic reactions were generally mild and transient. The authors suggested that lower doses of the whole-virion H5N1 vaccine could induce equivalent immune responses to adjuvanted or non-adjuvanted split-virion vaccines and "use of a whole virion vaccine could be more adaptable to the antigen-sparing strategy recommended by WHO for protection against an influenza pandemic."

Comment: The latest progress report of the development of an H5N1 influenza vaccine. The key feature of this vaccine is the incorporation of the whole virion at a relatively low dose with an aluminium adjuvant.

<http://www.thelancet.com/journals/lancet/article/PIIS0140673606692945/abstract>

Lancet. 2006 Sep 16;368(9540): 991-7

Using local microbiologic data to develop institution-specific guidelines for the treatment of hospital-acquired pneumonia

Authors: Beardsley JR et al

Summary: The importance of using local microbiological data to develop institution-specific guidelines for the treatment of hospital-acquired pneumonia was demonstrated in a retrospective analysis of bacterial pathogens from 111 patients with hospital-acquired pneumonia in a North Carolina hospital. Staphylococcus aureus was the most commonly identified bacteria which was associated with 38% of pneumonias, followed by Acinetobacter baumannii (25%) and Pseudomonas aeruginosa (19%). The analysis showed that adding the fluoroquinolone ciprofloxacin to β -lactam therapy as per current guidelines would not enhance initial antibiotic coverage as it was active against less than 10% of the Gram-negative isolates resistant to β -lactam therapy. The aminoglycoside amikacin was active against more than 80% of the resistant isolates. About 80% of Gram-negative bacteria were susceptible to β -Lactam therapy or cefepime, with resistant organisms occurring significantly more frequently in patients who had been hospitalised for 10 days or more. The institution-specific guidelines therefore divided patients into those who acquired pneumonia within 10 days of hospitalisation and those acquiring pneumonia after 10 days or more and recommended treatment accordingly. The authors predicted that these guidelines would provide adequate initial therapy for more than 90% of late-onset pneumonias at their hospital.

Comment: This study reinforces the importance of basing local guidelines for antibiotic treatment in hospital acquired pneumonia on local microbiological data. The systemic analysis undertaken in this study provides a sound prototype for such an approach.

<http://www.chestjournal.org/cgi/content/abstract/130/3/787>

Reference: Chest. 2006;130:787-793

The effects of body mass index on lung volumes

Authors: Jones RL et al

Summary: Increased body mass index (BMI) was associated with significantly decreased lung volumes in a prospective study of 373 patients of varying BMI with normal airway function. Functional residual capacity (FRC) and expiratory reserve volume (ERV) decreased exponentially with increasing BMI with the greatest rates of change occurring in patients who were overweight or mildly obese. Morbidly obese patients were breathing near their residual volume. The FRC and ERV for a patient with a BMI of 30 kg/m² were 75% and 47% of those for a patient with a BMI of 20 kg/m². Mean values for vital capacity and total lung capacity remained within normal ranges even for morbidly obese patients.

Comment: An important study that will assist in the interpretation of lung function tests in obese subjects. Obesity causes a marked reduction in residual lung volumes but has relatively little effect on vital capacity and total lung capacity.

<http://www.chestjournal.org/cgi/content/abstract/130/3/827>

Reference: Chest. 2006; 130:827-833

Independent commentary by Professor Richard Beasley

Research Review publications are intended for Medical Professionals

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.



Abnormalities on chest radiograph reported in subjects in a cancer screening trial

Authors: Pinsky PF et al

Summary: A review of chest radiographs from more than 70,000 men and women who were enrolled in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial found nodules/masses that were suspicious for lung cancer in 8% of examinations and abnormalities that were not suspicious for lung cancer in 35% of examinations. These non-cancer abnormalities included granuloma, scarring/pulmonary fibrosis, bone/soft tissue lesions, cardiac abnormalities, pleural fibrosis, and COPD/emphysema. Non-cancer abnormalities tended to be more prevalent in men, older subjects, and smokers. Scarring/pulmonary fibrosis was significantly associated with an increased risk of lung cancer and increased overall mortality. Cardiac abnormalities, COPD and pleural fluid were significantly associated with increased overall mortality.

Comment: A word of caution regarding chest x-ray screening for lung cancer – this will identify a high incidence of specific and non-specific abnormalities that require further investigation. The frequency of such abnormalities are considerably greater with screening utilising CT scanning, limiting the usefulness of this approach.

<http://www.chestjournal.org/cgi/content/abstract/130/3/688>

Reference: *Chest*. 2006;130:688-693

Inhaled corticosteroids and mortality in COPD

Authors: Macie C et al

Summary: Treatment with inhaled corticosteroids after hospitalisation was associated with a 25% reduction in mortality in patients with COPD aged >65 years. An even larger mortality reduction was evident in COPD patients aged 35 to 64 years. The reduction in mortality was largely attributable to a reduction in cardiovascular deaths and was unaffected by the exclusion of patients with a diagnosis of asthma or previous inhaled corticosteroid use. Mortality increased with bronchodilator use, age, comorbidities and physician visits before and after hospital discharge. Mortality was higher in COPD patients who were treated with bronchodilators without inhaled corticosteroids than in patients who received no bronchodilators or both bronchodilators and inhaled corticosteroids. The analysis included patients from a population-wide research database for the Canadian Province of Manitoba who were hospitalised for COPD and followed for 90 to 365 days after hospital discharge.

Comment: Further evidence that inhaled corticosteroid therapy reduces the risk of mortality in COPD. Intriguingly, this effect appears to occur through a decrease in cardiovascular but not respiratory deaths. Understanding the mechanism of this effect is now a research priority.

<http://www.chestjournal.org/cgi/content/abstract/130/3/640>

Reference: *Chest*. 2006 Sep;130(3):640-6

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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.

Comparison of endobronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer

Authors: Yasufuku K et al

Summary: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) had high sensitivity and specificity for mediastinal and hilar lymph node staging in patients with lung cancer compared with positron emission tomography (PET) and thoracic CT. The three diagnostic techniques were prospectively studied in 102 patients with lung cancer who were being considered for surgical resection. Malignancy was identified in 37 lymph node stations using EBUS-TBNA, 92 lymph nodes using CT and 89 lymph nodes using PET. Using surgical histology to confirm lymph node metastases, the sensitivity of EBUS-TBNA for the correct diagnosis of mediastinal and hilar lymph node staging was 92.3% compared with 76.9% for CT and 80.0% for PET. EBUS-TBNA had 100% specificity compared with 55.3% and 70.1% for CT and PET, respectively. The diagnostic accuracy of EBUS-TBNA was 98.0% compared with 60.8% and 72.5% for CT and PET, respectively. EBUS-TBNA was successfully performed in all patients with no complications. The authors concluded that evaluation of the mediastinum using EBUS-TBNA should be considered early in the staging process of lung cancer.

Comment: Further pioneering research from Japan on the use of direct real time endobronchial ultrasound with guided transbronchial needle aspiration in the investigation of the extent of lymph node involvement in lung cancer. The findings of greater diagnostic accuracy with this technique, compared with CT and PET, suggest that further research and clinical experience into this technique are now urgently required prior to its implementation into clinical practice.

<http://www.chestjournal.org/cgi/content/abstract/130/3/710>

Reference: *Chest*. 2006; 130:710-7186

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Characteristics of COPD phenotypes classified according to the findings of HRCT

Authors: Kitaguchi Y et al

Summary: Chest high-resolution computed tomography (HRCT) was used to evaluate the dominance of emphysema and presence of bronchial wall thickening to classify 85 patients with stable COPD into three phenotypes. Patients with absence of emphysema or slight emphysema with or without bronchial wall thickening were classified as A phenotype. Patients with emphysema without bronchial wall thickening were classified as E phenotype and those with emphysema with bronchial wall thickening were M phenotype. The presence of bronchial wall thickening in A- and M- phenotypes was significantly associated with reversibility responsive to inhaled corticosteroids. A-phenotype patients were also more responsive to bronchodilators. The degree of emphysema was significantly associated with smoking history, lower body mass index (BMI), decreased lung diffusion and decreased FEV1/FVC. Characteristics such as never smoking, wheezing, higher BMI, higher lung diffusion and milder lung hyperinflation were more prevalent in A-phenotype patients.

Comment: An important conceptual study in which COPD phenotypes are classified according to HRCT findings. The challenge will be to develop simple clinical criteria for COPD phenotypes that are predictive of response to treatment and the natural history of the disease.

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

Reference: *Respir Med.* 2006 Oct;100(10):1742-52. Epub 2006 Mar 23

An ecological study of the association of metal air pollutants with lung cancer incidence in Texas

Authors: Coyle YM et al

Summary: Inhalation exposure to zinc, chromium and copper was positively associated with lung cancer rates in the US state of Texas. Chromium and copper were significantly associated with the incidence of non-small cell lung cancer following univariate analysis. Zinc was significantly associated with primary and non-small cell lung cancer rates in all analyses including those adjusted for sex, race, ethnicity, urbanisation and interaction with other metal air pollutants. This ecological study examined the association of 81,132 lung cancer cases reported in Texas during the period 1995 to 2000 with metal air releases reported by the Environmental Protection Agency from 1988 through 2000. Eight metals present in airborne particulate matter, tobacco smoke or known human lung carcinogens were examined.

Comment: This study is highly relevant to industrialised countries in the Asia Pacific region, with high rates of lung cancer and high levels of air pollutants. It underscores the importance of air pollution monitoring and regulatory enforcement to ensure that levels of pollutants, including metals, are below established levels.

<http://www.jto.org/pt/re/jto/abstract.01243894-200609000-00009.htm;jsessionid=FgXJgyLPwJcplZ2hzyvp3ZJ4yy6vjhyG7wzqL8xDxTzx5n8pBCc0!10963392651-949856144!8091!-1>

Reference: *Journal of Thoracic Oncology.* 1(7): 654-661, September 2006

Asthma insights and reality in Turkey (AIRET) study

Authors: Sekerel BE et al

Summary: A survey of 345 adults and 55 children with asthma in Turkey showed a low level of asthma control with only 1.3% of those surveyed achieving asthma control according to the Global Initiative for Asthma guidelines. Patients overestimated their level of disease control and underestimated their disease severity, but most reported that asthma impacted unfavourably on their social life. Daytime symptoms were experienced by more than 90% of adults and 75% of children. Lung function testing had been performed in only half of the patients and use of preventative medicine was low in patients with persistent disease. Smoking rates were high with 31.3% of adults being current cigarette smokers and 10.7% being former smokers. The authors concluded that improvements in guideline implementation and patient education are warranted.

Comment: An extension of the AIRIAP study to Turkey with similar findings, that there was a huge gap between the current level of asthma control and that which can be achieved with modern management. Many of the management initiatives developed in the Asia Pacific region may well be applicable to implementation in Turkey.

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

Reference: *Respir Med.* 2006 Oct; 100(10):1850-4. Epub 2006 Mar 27

Formoterol as needed with or without budesonide in patients with intermittent asthma and raised NO levels in exhaled air: a SOMA study

Authors: Haahtela T et al

Summary: Use of an inhaled corticosteroid/ β_2 -agonist combination as needed may be more beneficial than using a β_2 -agonist alone as needed in patients with intermittent asthma and signs of airway inflammation. In this double-blind study, 92 patients with intermittent asthma were randomised to receive formoterol 4.5 μ g as needed or combined budesonide/formoterol 160/4.5 μ g as needed for 24 weeks. Study medication was used more intensively in the formoterol group than the budesonide/formoterol group, with ≥ 4 inhalations per day required on 74 days compared with 21 days. The budesonide/formoterol combination had a greater effect on fractional exhaled nitric oxide (FeNO) than formoterol alone (18.2 ppb vs 2.8 ppb; 95% CI 7.5–23.5 ppb). The reduction in the combination group occurred during the first 4 weeks of treatment and remained low throughout the study.

Comment: The novel concept with this study was the use of raised FENO levels to identify patients with intermittent asthma symptoms who might respond to inhaled corticosteroid therapy. It is likely that monitoring of FENO levels will provide a useful guide to the titration of ICS therapy in asthma, as outlined in the recent review by Robin Taylor and colleagues [Thorax 2006;61(9):817-27].

<http://erj.ersjournals.com/cgi/content/abstract/28/4/748>

Reference: *Eur Respir J.* 2006 Oct; 28(4):748-55