

APSR Respiratory Research Review

Making Education Easy

Issue 13 - 2007

In this issue:

- *GOLD Executive Summary*
- *BOLD: international prevalence of COPD*
- *Passive smoking & COPD risk in China*
- *Viral aetiology of AECOPD in Hong Kong*
- *Infant and adult lung function*
- *Mannitol in asthmatics with mucus hypersecretion*
- *Asthma, asthma symptoms & CRP*
- *Early discharge of patients with PE*
- *VTE prophylaxis strategies*
- *CO poisoning: risk factors for cognitive sequelae*

Welcome to APSR Respiratory Research Review.

The focus of this month's edition is COPD. The GOLD Executive summary has recently been published in the AJRCCM and the Lancet has published a series on COPD. These studies highlight the major global burden of COPD and the importance of tobacco control measures. Members of the APSR are encouraged to take a strong advocacy role for tobacco control measures within their countries.

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

Global strategy for COPD: GOLD Executive Summary

Authors: Rabe KF et al

Summary: COPD currently ranks as the 4th leading cause of chronic morbidity and mortality in the United States, and is expected to be ranked 5th in the WHO burden of disease ratings by 2020. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was formed in 1998 with objectives which included to increase awareness of COPD, and to help those who suffer from the disease and its complications. In 2001, the consensus report "Global Strategy for the Diagnosis, Management, and Prevention of COPD" was published. The current report follows the same format as its predecessor, but has been updated to reflect recent changes in the knowledge base. The authors acknowledge the achievements of the previous 5 years but caution that considerable work lies ahead if this major public health problem is to be controlled. "The GOLD initiative will continue to bring COPD to the attention of governments, public health officials, health care workers, and the general public, but a concerted effort by all involved in health care will be necessary."

Comment: A beautifully written summary of the state of knowledge of COPD – worth reading.

<http://dx.doi.org/doi:10.1164/rccm.200703-456SO>

Reference: *Am J Respir Crit Care Med* 2007; 176:532-55

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International variation in the prevalence of COPD: the BOLD Study

Authors: Buist AS et al

Summary: This worldwide study aimed to measure the prevalence of COPD (by GOLD staging criteria) and its risk factors, using postbronchodilator spirometry testing plus questionnaires about respiratory symptoms, health status, and exposure to COPD risk factors. 9,425 participants across 12 sites were included. Overall prevalence of stage II or higher COPD was 10.1% (11.8% men, 8.5% women). The overall odds ratio for 10-year age increments was 1.94 (95% CI 1.80 to 2.10) and was similar for men and women. There was a variance in odds ratio for site-specific pack-years for women (OR 1.28, 95% CI 1.15 to 1.42, $p = 0.012$) but not men (1.16, 1.12 to 1.21, $p = 0.743$). The authors noted the prevalence of COPD was at higher levels and more advanced staging than had typically been reported and that the variance in prevalence was not fully explained by differences in age or smoking status of the populations studied.

Comment: Standardised international data on the prevalence of COPD reporting high rates worldwide including centres in the Asia Pacific region. One of the important observations was the fairly high prevalence of COPD in non-smokers, highlighting the importance of factors other than smoking in the causation of COPD (see editorial p 715-16).

[http://dx.doi.org/DOI:10.1016/S0140-6736\(07\)61377-4](http://dx.doi.org/DOI:10.1016/S0140-6736(07)61377-4)

Reference: *Lancet* 2007; 370:741-50

Passive smoking exposure and risk of COPD among adults in China

Authors: Yin P et al

Summary: The authors of this cross-sectional study examined the relationship between passive smoking and COPD using baseline data from the Guangzhou Biobank Cohort Study. 15,379 never smokers aged 50 and over from the original cohort of 20,430 were studied. Valid spirometry data were available for 6,497. Exposure to second hand smoke was measured by subject self-report, and diagnosis of COPD by spirometry and defined by the GOLD guidelines. Risk of COPD was associated with self-reported exposure to second hand smoke at home and work (OR 1.48, 95% CI 1.18 to 1.85 for high level exposure). Self-reported respiratory symptoms and increasing second hand smoke exposure were also positively correlated (OR 1.16, 1.07 to 1.25 for any symptom). The authors estimated that if exposure to second hand smoke was causal for COPD, passive smoking could be responsible for 1.9 million excess deaths from COPD in never smokers in China.

Comment: An indication of the major burden of COPD due to passive smoking can be obtained from this study. A staggering 1.9 million excess deaths from COPD amongst never smokers could be attributed to passive smoking in the current population in China. Tobacco control measures including legislation prohibiting smoking in public places and workplaces, remains a high public health priority in the Asia Pacific region. The APSR must assume a strong advocacy role in supporting such measures (see editorial p 716-7).

[http://dx.doi.org/DOI:10.1016/S0140-6736\(07\)61378-6](http://dx.doi.org/DOI:10.1016/S0140-6736(07)61378-6)

Reference: *Lancet* 2007; 370:751-7

Viral aetiology of acute exacerbations of COPD in Hong Kong

Authors: Ko FWS et al

Summary: The viral aetiology of acute exacerbations of COPD (AECOPD) in Hong Kong was assessed in this prospective study of 196 patients admitted to hospital with 262 episodes of AECOPD. Positive PCR results indicating viral infection were obtained from nasopharyngeal aspirates in 22.1% of episodes. The viruses identified were influenza A (7.3%), coronavirus OC43 (4.6%), rhinovirus (3.1%), influenza B (2.7%), and respiratory syncytial virus (2.3%). The likelihood of identifying a viral infection in patients with AECOPD was not affected by FEV1 and viral infection did not influence the rate of readmission or mortality over 1 year. The authors suggest that these findings be considered "in developing diagnostic and intervention strategies pertaining to AECOPD".

Comment: A key study from Hong Kong showing that viral infections are an important cause of exacerbations of COPD. After influenza, the "common cold" viruses, coronavirus and rhinovirus were the next most commonly identified. These findings compliment those in asthma in which the common cold viruses are the most common cause of severe exacerbations.

<http://dx.doi.org/doi:10.1378/chest.07-0530>

Reference: *Chest* 2007; 132:900-8



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Poor airway function in early infancy and lung function by age 22 years

Authors: Stern DA et al

Summary: In this non-selective longitudinal cohort study, the association between airway function at birth and in early adulthood was studied. 169 participants were enrolled at birth. First measurements of maximal expiratory flows at functional residual capacity ($V_{max}[FRC]$) were obtained using the chest compression method at a mean age of 2.3 months. Repeat lung function measurements including FEV₁, FVC, and FEF₂₅₋₇₅ were taken at ages 11, 16 and 22. In the adjusted analysis, subjects who were in the lowest quartile for infant $V_{max}(FRC)$ had significantly poorer lung function up to age 22, compared to those in the other 3 quartiles: FEV₁/FVC ratio (-5.2%, $p < 0.0001$), FEF₂₅₋₇₅ (-663 mL/s, $p < 0.0001$), and FEV₁ (-233 mL, $p = 0.001$). These results were unaffected after adjustment for wheeze, smoking, atopy, or parental asthma. In conclusion, poor lung function at birth appears to be a risk factor for airways obstruction in young adults.

Comment: Further evidence of the role of early lung development in the pathogenesis of airflow obstruction in adult life. It is time to look beyond smoking to better understand the causation of COPD (see editorial p 717-9).

[http://dx.doi.org/DOI:10.1016/S0140-6736\(07\)61379-8](http://dx.doi.org/DOI:10.1016/S0140-6736(07)61379-8)

Reference: *Lancet* 2007; 370:758-64

Association between asthma, asthma symptoms and C-reactive protein in US adults

Authors: Arif AA et al

Summary: The authors investigated the associations between C-reactive protein (CRP), a marker elevated in a number of inflammatory diseases, and the presence of asthma and asthma symptoms. Data for the 8,020 adult subjects aged > 20 years were obtained from the US National Health and Nutrition Examination Survey. Mean CRP levels were significantly greater in non-Hispanic blacks compared with non-Hispanic whites, and most women (69.5%) were in the highest (4th) quartile for CRP. For those in the 4th quartile of CRP the adjusted odds were 1.60 (95% CI 1.02 to 2.53) for current asthma and 1.43 (95% CI 1.07 to 1.91) for past asthma. For those in the 3rd or 4th quartile for CRP the adjusted odds for wheezing and nocturnal cough were 2.18 and 3.40 respectively. CRP levels are increased in adults with asthma and asthma symptoms.

Comment: An interesting study providing support for the concept that asthma is associated with systemic as well as local airways inflammation.

<http://dx.doi.org/doi:10.1111/j.1440-1843.2007.01122.x>

Reference: *Respirology* 2007; 12:675-82

Independent commentary by Professor Richard Beasley

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Inhaled mannitol changes the sputum properties in asthmatics with mucus hypersecretion

Authors: Daviskas E et al

Summary: This prospective, open-label study investigated the effect of mannitol on the physical properties of sputum in 12 asthmatics with chronic cough and sputum production. Sputum was collected at baseline and following eformoterol (24 µg). During each subsequent visit, subjects received eformoterol followed by inhaled mannitol at 635 mg (visit 1), 240 mg (visit 2), 360 mg (visit 3) and 360 mg plus montleukast (visit 4). Sputum properties were not different from baseline following eformoterol. Mannitol at all study doses significantly reduced sputum properties including elasticity ($p < 0.0001$), viscosity ($p < 0.0001$), surface tension ($p < 0.0001$), contact angle-glass ($p < 0.0001$), and percentage solids $p < 0.0001$). The addition of montleukast did not enhance reductions in any sputum property ($p > 0.4$). The effects of mannitol observed in this study were consistent with the osmotic effect of mannitol causing water efflux in the airway lumen.

Comment: Further encouraging data on the possible therapeutic role of inhaled mannitol in the management of respiratory disorders associated with mucus hypersecretion. Beneficial effects have also been observed with inhaled mannitol in bronchiectasis and cystic fibrosis. RCTs are now urgently required to determine whether the routine use of mannitol results in clinical benefits in these conditions and can be safely administered in the community.

<http://dx.doi.org/doi:10.1111/j.1440-1843.2007.01107.x>

Reference: *Respirology* 2007; 12:683-91

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Early discharge of patients with pulmonary embolism

Authors: Davies CWH et al

Summary: The authors examined the potential for outpatient management of low-risk patients with VTE (n = 225) using low molecular weight heparin. Indications for standard inpatient treatment included admission for another medical reason; need for additional monitoring or oxygen; bleeding disorders; previous PE/further PE while on warfarin; co-existing major DVT; likelihood of poor compliance; significant immobility; and pregnancy. 43.6% of patients were considered suitable for outpatient treatment and 157 received outpatient anticoagulation therapy. No deaths, bleeding or recurrent thromboembolic events occurred during acute outpatient therapy. Median length of hospital stay was 1 day in those receiving outpatient care, a mean saving of 5 bed-days per patient. 96.6% of patients said they would consider outpatient treatment for any subsequent PE. In conclusion, early discharge and outpatient management of selected low-risk patients with PE is safe and acceptable.

Comment: A really helpful study from which an early discharge policy for selected low risk patients with pulmonary embolism can be developed. This appears to be a suitable approach for around half of all patients presenting to hospital with PE.

<http://erj.ersjournals.com/cgi/content/abstract/30/4/708>

Reference: *Eur Respir J* 2007; 30:708-14

Venous thromboembolism prophylaxis in acutely ill hospitalised medical patients

Authors: Tapson VF et al

Summary: The authors used data from the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE), an ongoing multinational, observational study, in order to assess VTE prophylaxis practices. Of the 15,156 patients enrolled to September 2006, 50% received in-hospital VTE prophylaxis. According to guideline recommendations from the American College of Chest Physicians (ACCP), 52% of US patients and 43% of those from elsewhere should have received prophylaxis. However only around 60% of those meeting the ACCP criteria for prophylaxis did receive it. There were considerable variations in prophylaxis practices. In the US, patients were most likely to receive medical prophylaxis with intermittent pneumatic compression (22% of patients) or pharmacologic prophylaxis with unfractionated heparin (21%). Elsewhere, low-molecular-weight heparin was the most common approach (40%). On this evidence the authors suggest that "physicians' practices for providing VTE prophylaxis to acutely ill hospitalized medical patients are suboptimal".

Comment: Yet another international study showing that VTE prophylaxis to acutely ill hospitalised medical patients is inadequate. A timely reminder to review the status in your own hospital and implement evidence-based guidelines if necessary.

<http://dx.doi.org/doi:10.1378/chest.06-2993>

Reference: *Chest* 2007; 132:936-45

Carbon monoxide poisoning: risk factors for cognitive sequelae and the role of hyperbaric oxygen

Authors: Weaver LK et al

Summary: The authors aimed to examine the risk factors for cognitive sequelae from carbon monoxide (CO) poisoning. Subjects (n = 163) were aged 15 years and above with acute CO poisoning. Overall 42% of subjects who did not receive hyperbaric oxygen (HBO₂) developed sequelae. Univariate analysis found risk factors for sequelae were age of 36 years or more (OR 2.6; 95% CI 1.3 to 4.9; p = 0.005), and exposure intervals > 24 hours (OR 2.4; 95% CI 1.2 to 4.8; p = 0.019). By subgroup analysis, loss of consciousness and carboxyhemoglobin levels > 25% were also identified as risk factors. In patients who did receive HBO₂, a reduction in sequelae was observed in those aged over 36 years (OR 0.3; 95% CI 0.2 to 0.6; p < 0.001). Patients with acute CO poisoning should receive HBO₂ if they are aged 36 years or older, have exposure intervals > 24 hours, have loss of consciousness or carboxyhemoglobin levels > 25%.

Comment: Informative study of the factors which identify high risk patients for bad outcomes in carbon monoxide poisoning. As many patients presenting with carbon monoxide poisoning need transfer to a tertiary centre for hyperbaric oxygen therapy, this data is really helpful in terms of identifying high risk patients who require this treatment.

<http://dx.doi.org/doi:10.1164/rccm.200701-026OC>

Reference: *Am J Respir Crit Care Med* 2007; 176:491-7

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Research Review acknowledges the kind support of

