

APSR Respiratory Research Review

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Issue 20 – 2008

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Welcome to the Respiratory Research Review. Many thanks for your interest and feedback.

The focus of this month's review is on pneumonia, air travel and asthma control. Hopefully you will enjoy the articles on reducing the time of first antibiotic dose, the audit on the efficacy of pneumococcal vaccine and thoughts on air travel in children and adults with lung disease.

Kind regards,

Dr Lutz Beckert

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Accuracy of pneumonia diagnoses with reduced time to first antibiotic dose

Authors: Welker JA et al

Summary: This retrospective review of 548 patients admitted with community-acquired pneumonia (CAP) investigated the impact on diagnostic accuracy of shortening the core quality measure of time to first antibiotic dose (TFAD) from <8 hours (group 1) to <4 hours (group 2). Patients in group 2 were 39.0% less likely to meet predefined diagnostic CAP criteria at admission than patients from group 1 (OR 0.61; 95% CI 0.42, 0.86; $p = 0.004$). There was agreement between the ED physician's diagnosis and predefined criteria for CAP in 62.0% and 53.9% of patients from groups 1 and 2, respectively ($p=0.06$), while agreement between the admitting and discharging physicians' diagnoses was greater for group 1 than group 2 (74.5% versus 66.9%; $p=0.05$). Moreover, mean TFAD was only about 10 minutes shorter in group 2 than it was in group 1.

Comment: One of the markers of quality care for pneumonia is not only the severity assessment but also the TFAD. This paper reports on the influence that these new quality standards of achieving TFAD within 4 hours had on the performance of emergency physicians. With this increased pressure placed upon the emergency team, the TFAD did not improve and the diagnostic accuracy of emergency physicians decreased from 60% to 54%. The authors discussed the effect of 'well-meaning' 'gold standards' on real-life performance and cast doubt on the validity of this core quality measurement.

<http://archinte.ama-assn.org/cgi/content/abstract/168/4/351?etoc>

Reference: *Arch Intern Med* 2008; 168(4):351-6



*Independent commentary by Dr Lutz Beckert,
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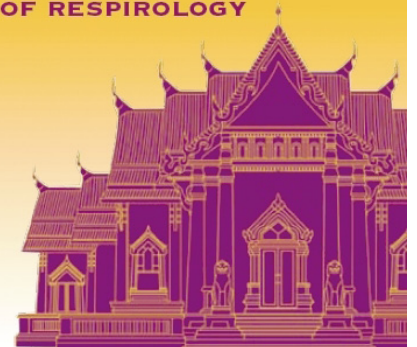
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Effect of an automated chest x-ray protocol on time to antibiotics in pneumonia

Authors: Cooper JJ et al

Summary: This study investigated the effect on time to antibiotics of an automated chest x-ray order system at triage for patients who presented at an ED with signs and symptoms of pneumonia. The protocol, which was derived using retrospective data from adults admitted with pneumonia, included an automatic chest x-ray order for patients presenting with dyspnoea, URTI, haemoptysis, fever or cough who were aged ≥ 50 years with any abnormal vital sign or aged < 50 years with a comorbidity of cancer, chronic alcoholism, diabetes, immunocompromise or transplantation. While the sensitivity of the protocol for identifying patients with pneumonia was only 35% (95% CI 28, 43), there were significant improvements in time to antibiotics (3.4 versus 4.2 hours; $p=0.01$) and time to chest x-ray (3.0 versus 2.0 hours; $p=0.01$).

Comment: This study aimed to achieve antibiotic administration for patients with community-acquired pneumonia within 4 hours by using an automated chest x-ray ordering protocol. When a triage nurse recorded dyspnoea as the presenting complaint, the computer would automatically request a chest x-ray if the patient was aged > 50 years with a fever, tachycardia or increased respiratory disease. This trial reduced the time to chest x-ray from 3.0 to 2.0 hours and the time to antibiotics from 4.2 to 3.4 hours. Unfortunately this protocol was only 35% sensitive for detecting patients with pneumonia and the positive predictive value was poor at only 7%.

<http://www.ncbi.nlm.nih.gov/pubmed/18358934>

Reference: *Am J Emerg Med* 2008; 26(3):264-9

Effect of PPV on outcomes in patients with CAP

Authors: Johnstone J et al

Summary: This prospective study investigated the effect of 23-valent polysaccharide pneumococcal vaccine (PPV) on outcomes among a cohort of 3415 patients (median age 75 years) hospitalised with community-acquired pneumonia (CAP) in Canada, of whom 22% had received PPV. Patients who had received PPV were less likely to die or be admitted to an ICU compared with those who had not received PPV (10% versus 21%; $p<0.001$); the propensity-adjusted odds of death or ICU admission associated with PPV was 0.62 (95% CI 0.42, 0.92; $p=0.02$). The investigators also noted that among patients eligible for PPV at discharge, only 9% were vaccinated.

Comment: This Canadian group used their database of 3415 patients who had been admitted with CAP to comment on the effectiveness of PPV. They found that 760 (22%) patients had received the vaccine some time prior to admission. In their cohort, 73 of 760 (10%) vaccinated patients versus 551 of 2655 (21%) unvaccinated patients died or were admitted to ICU. The authors concluded that prior PPV reduced the death rate or ICU admission by 40%. This paper adds weight to the idea that PPV may not prevent CAP, but leads to better outcome in those who eventually develop pneumonia.

<http://archinte.ama-assn.org/cgi/content/abstract/167/18/1938>

Reference: *Arch Intern Med* 2007; 167(18):1938-43.

Prognostic value of thin-section CT scans in lung adenocarcinoma

Authors: Hashizume T et al

Summary: The prognostic importance of thin-section CT (TSCT) scans in small-sized lung adenocarcinomas was investigated in 359 consecutive patients who had undergone surgical resection of peripheral lung adenocarcinomas measuring < 20 cm in diameter. Patients in whom TSCT scans identified air-containing tumours did not have any pathological invasive findings or disease recurrence, whereas 10–30% of those with solid-density type tumours had invasive pathology or disease recurrence. Air-containing type tumours were identified as a significant predictor of good prognosis ($p<0.001$).

Comment: This study from Japan reports on the prognostic value of TSCT scanning. If the TSCT showed an air-containing tumour, then none of the patients were found to have lymph node metastasis, pleural involvement, vascular invasion or recurrence. The 3-year survival after surgical resection in this group was 100%. The authors argued that these patients could be treated with limited resection, which would need to be confirmed in a prospective study.

<http://www.chestjournal.org/cgi/content/abstract/133/2/441>

Reference: *Chest* 2008; 133:441-7

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.



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Cut-off values for hypoxia tests in children with neonatal chronic lung disease

Authors: Martin AC et al

Summary: The effectiveness of the cut-off values of 85% and 90% in hypoxia inhalation tests for discriminating between young children with neonatal chronic lung disease (nCLD) and healthy children was investigated in this study of 35 children with nCLD and 34 healthy controls. Among children aged <2 years, there was no significant difference in the hypoxia test fail rates between the groups for the 90% cut-off ($p=0.56$). In contrast, the 85% cut-off resulted in 6 of 23 children with nCLD failing the hypoxia test, whereas only 1 of 24 controls failed ($p=0.048$).

Comment: This Perth group compared the outcomes of hypoxia inhalation tests between children with nCLD and healthy children. Reassuringly, they found that no children aged >24 months failed the test. Six children with nCLD failed the test when a cut-off of <85% was used. The only predictor of failing the hypoxia inhalation test was the length of oxygen treatment needed after birth. Hypoxia inhalation testing did not discriminate between healthy and nCLD children when using a 90% cut off, which led the authors to believe that a cut-off of 85% may be more appropriate in this study group. One child in the healthy control group had saturations <85%. Interestingly, this child fell asleep during hypoxia inhalation testing.

<http://www.chestjournal.org/cgi/content/abstract/133/4/914>

Reference: *Chest* 2008; 133:914-9

Hypoxia inhalation test to predict hypoxaemia in airline passengers with COPD

Authors: Kelly PT et al

Summary: In-flight oxygenation was compared with postflight hypoxia inhalation test and preflight respiratory function measures in 13 airline passengers with COPD. There was a significant reduction in oxygen saturation during the flight compared with preflight values (86% versus 95%), and this was worse with activity (78%), but no in-flight adverse events were recorded. The desaturation that resulted from the hypoxia inhalation test was comparable (84%) to that of in-flight oxygenation, although the mean in-flight PI_{O_2} was significantly greater than the hypoxia inhalation test PI_{O_2} (113mm Hg versus 107mm Hg; $p<0.001$), and there was a strong correlation between the in-flight and hypoxia inhalation test SpO_2 measurements ($r=0.84$; $p<0.001$).

Comment: This New Zealand group published data in patients with COPD, comparing the results of hypoxia inhalation test to oximetry data obtained during commercial flights. Although significant desaturations were recorded during the flight, with the nadir occurring during activity, no adverse events were observed. Desaturation during flights correlated best with preflight hypoxia inhalation test data rather than the severity of lung disease, DLCO or 6-minute walk test. Two articles on this topic are published in the same volume of *Chest* and are accompanied by a review article on the hypoxia inhalation test and an editorial.

<http://www.chestjournal.org/cgi/content/abstract/133/4/920>

Reference: *Chest* 2008; 133:920-6

Predictive value of hypoxia test for in-flight hypoxia in ex-preterm neonates

Authors: Resnick SM et al

Summary: The value of preflight hypoxia challenge testing (HCT) in infants who had been born at ≤ 35 weeks' gestation was investigated in this study. A pretransfer HCT consisting of 14% oxygen for 20 minutes was administered to 46 ex-preterm infants (median corrected age 35.8 weeks, median gestation 32.2 weeks; median birthweight 1667g). Of the 16 infants who required in-flight oxygen, 75% had passed the HCT test, and only 36% of those who failed the HCT test required in-flight oxygen. These findings equated to a failure of HCT to predict in-flight oxygen requirements in 42% of the infants.

Comment: The authors of this study compared results of HCT with oximetry readings in ex-preterm neonates on their return to the provincial hospital. Using a cut-off of saturations <85%, 11 infants failed the HCT but only 4 of those met oxygen criteria during flight. What is of great concern is that of the 16 infants needing oxygen during the flight, 12 had passed the HCT. No better measurement in predicting hypoxia during flight was found. Bottom line: HCT does not predict hypoxia in ex-preterm neonates and the authors have abandoned the test in this group in favour of monitoring in-flight response.

<http://www.chestjournal.org/cgi/content/abstract/133/5/1161>

Reference: *Chest* 2008; 133:1161-6

Extrapulmonary effects of COPD on physical activity

Authors: Watz H et al

Summary: The association between reduced physical activity and extrapulmonary effects of COPD and its comorbidities was investigated in this study of 170 outpatients with COPD. A multivariate linear regression analysis with either steps per day or physical activity level as a dependent variable showed that N-terminal pro-B-type natriuretic peptide levels, left ventricular diastolic function and systemic inflammation were associated with reduced physical activity, independent of BODE (Body mass index, airway Obstruction, Dyspnoea and Exercise capacity) score or GOLD (Global initiative for chronic Obstructive Lung Disease) stage.

Comment: This German study found reduced activity in two-thirds of COPD patients. Higher values of systemic inflammation and left cardiac dysfunction were associated with reduced physical activity in patients with COPD. According to GOLD or BODE index, this is independent of the clinical stages. The presence of nutritional depletion, depression, anaemia, peripheral arterial disease, pulmonary hypertension, and/or peripheral muscle strength did not contribute significantly to the inactivity observed in these patients. The accompanying editorial asks whether this group has identified a new form of 'cardiac dysfunction' that is similar to the skeletal muscle dysfunction known to occur in those with COPD. If confirmed, this may enable the domains of COPD amenable to therapeutic intervention to be identified.

<http://ajrccm.atsjournals.org/cgi/content/abstract/177/7/743>

Reference: *Am J Respir Crit Care Med* 2008; 177:743-51

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Controlling house dust mites in asthmatics' homes

Authors: Gøtzsche PC et al

Summary: The effect of minimising house dust mite antigen in the homes of asthmatic individuals sensitive to this allergen was investigated in this Cochrane review of randomised trials comparing house dust mite reduction methods with placebo or no intervention. The study consisted of 54 trials (involving 3002 patients), including 36 trials employing physical methods, 10 using chemical methods and 8 using a combination of physical and chemical methods for house dust mite reduction. House dust reduction methods did not significantly affect the number of patients with improved asthma (relative risk 1.01; 95% CI 0.80, 1.27), medication usage (standardised mean difference [SDM] -0.06; -0.18, 0.07), asthma symptom scores (SDM -0.04; -0.15, 0.07) or peak flow in the morning (assessed in 1565 patients; SDM 0.00; -0.10, 0.10).

Comment: It seems reasonable to try and control the level of environmental allergens when treating patients with asthma. These authors came to the conclusion that a reduction in house dust mite levels does not correlate with an improvement of asthma symptoms. This has been picked up in a *Lancet* editorial (*Lancet* 2008; 371:1390). The Cochrane review has a balanced discussion well worth reading. In the context of this topic, readers should consider studying the learned debate on evidence-based medicine published in *Chest*. The former editor of the *American Journal of Respiratory and Critical Care Medicine*, Martin Tobin, takes the stand that "evidence-based medicine lacks a sound scientific base" (*Chest* 2008; 133:1067-77).

<http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001187/frame.html>

Reference: *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No. CD001187

Chronic beryllium disease in residents near a beryllium facility

Authors: Maier LA et al

Summary: Medical records from individuals surrounding a beryllium manufacturing facility in the US city of Reading, Pennsylvania were reviewed in this paper to increase awareness of recently diagnosed cases of community-acquired chronic beryllium disease (CBD). Among 16 cases of potential community-acquired CBD, five definite cases and three probable cases were identified. The initial years of residence for the cases ranged from 1943 to 1953, and continued until 1956-2001, and most cases were diagnosed years after beryllium exposure. Among the eight cases, six required medical treatment, and the patient has died since diagnosis in three of the cases. The authors commented that there are likely to be other misdiagnosed cases in the community, and that it can be expected that more cases will be diagnosed.

Comment: The authors of this American study report eight cases of community-acquired CBD in people residing near a beryllium manufacturing facility. Three of these cases had been misdiagnosed as sarcoidosis or silicosis and three of these cases succumbed to their illness. This paper and accompanying editorial call for vigilance in the consideration of CBD when making a diagnosis, as it can cause significant morbidity and mortality. Beryllium is used in a wide range of industries including aerospace, automotive manufacturing, telecommunications, scrap recovery and recycling. The number of workers exposed to beryllium in the US is considered to be >130,000.

<http://ajrccm.atsjournals.org/cgi/content/abstract/177/9/1012>

Reference: *Am J Respir Crit Care Med* 2008; 177:1012-17

Predictive value of lymphocytic bronchiolitis on lung transplant outcomes

Authors: Glanville AR et al

Summary: This retrospective analysis evaluated the role of lymphocytic bronchiolitis (LB) as a risk factor for bronchiolitis obliterans syndrome (BOS) among 341 lung transplant recipients with 90-day survival. Transbronchial biopsy specimens were grouped according to highest LB B grade (BO [normal; n=501], B1 [minimal; 762], B2 [mild; 176], B3 [moderate; 70], B4 [severe; 4] or Bx [no bronchiolar tissue; 75]) prior to BOS diagnosis. A multivariate analysis identified highest B grade (relative risk [RR] 1.62; 95% CI 1.31, 2.00; p<0.001); longer ischaemic time (1.00; 1.00, 1.00; p<0.05); and recent transplant year (0.93; 0.87, 1.00; p<0.05) as significant risk factors for BOS. Risk factors for death were BOS (as a time-dependent covariable; RR 19.10; 95% CI 11.07, 32.96; p<0.001) and highest B grade (1.36; 1.07, 1.72; p<0.05).

Comment: These researchers from Sydney used their database of 341, 90-day lung transplant survivors, who underwent 1770 transbronchial lung biopsies, to investigate the role of LB as a predictor of BOS, morbidity and mortality after lung transplantation. Despite the limitations of a single-centre study, the authors showed that patients who developed LB post-transplantation were at increased risk of an adverse outcome. The authors called for the consideration of using LB as a marker of long-term outcome and a surrogate target for therapeutic trials.

<http://ajrccm.atsjournals.org/cgi/content/abstract/177/9/1033>

Reference: *Am J Respir Crit Care Med* 2008; 177:1033-40

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