

APSR Respiratory Research Review

Making Education Easy

Issue 10 - 2007

In this issue:

- *Outcomes for patients with HIV and TB*
- *Treatment of mild persistent asthma*
- *Treatment reduction in mild persistent asthma*
- *Predicting response to omalizumab*
- *Telephone consultations in secondary care*
- *Bone mineral density in children with CF*
- *Infliximab in moderate to severe COPD*
- *Unsuspected PE with MDCT scanning*
- *Cryptogenic haemoptysis*
- *Diagnostic agreement in parenchymal lung diseases*

Welcome to APSR Respiratory Research Review

APSR Respiratory Research Review is a unique publication providing topical, relevant and accessible information for healthcare professionals working in the area. In each edition our independent reviewers hand-pick some of the most important studies from key international and local journals. The Review summarises each study in an easy to read format, and our experts provide commentary on the importance of the work and implications for clinical practice in the Asia Pacific region. Web links to the abstract or fully published papers are also provided where possible so you can make your own judgements.

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

Treatment outcomes in patients with HIV and tuberculosis

Authors: Nahid P et al

Summary: In this retrospective study, patient records were used to evaluate outcomes for HIV-infected patients who received rifamycin-based treatment for tuberculosis (TB). 700 patients with TB were identified, of which 38% were infected with HIV. Mean treatment duration was significantly longer for HIV-infected patients, 10.2 vs 8.4 months ($p < 0.001$). Relapse rates were higher in HIV-infected individuals, 9.3 per 100 person-years versus 1.0 ($p < 0.001$). Increased relapse rates were also seen in HIV-infected individuals who were treated with a standard 6-month rifamycin-based regimen compared to those who were treated for longer (HR 4.33; $p = 0.02$) and those who received intermittent versus daily therapy (HR 4.12; $p = 0.04$). Highly active anti-retroviral therapy was associated with faster culture negativity and improved survival. The authors concluded that "standard 6-month therapy may be insufficient to prevent relapse in patients with HIV."

Comment: This study challenges current recommendations regarding the preferred length of TB treatment in patients co-infected with HIV. Regrettably neither a standard six month rifamycin based course or intermittent therapeutic regimes were adequate, with higher relapse rates noted than in those patients who received longer durations of therapy or daily dosing. This suggests that the current recommendation for a six month rifamycin-based regime is inadequate for HIV infected patients with TB. The other important finding of this study was that the use of highly active anti-retroviral therapy was associated with faster culture negativity and improved survival.

<http://ajrcm.atsjournals.org/cgi/content/abstract/175/11/1199>

Reference: *Am J Respir Crit Care Med* 2007; 175:1199-1206



12th CONGRESS OF THE APSR/
2nd JOINT CONGRESS OF THE APSR/ACCP
30 November - 4 December 2007

Gold Coast Convention Centre
& Exhibition Centre
Queensland, Australia

www.apsresp.org

apsr
2007
ASIAN PACIFIC SOCIETY OF RESPIROLOGY

Treatment of mild persistent asthma: case vignette

Authors: Kraft M et al

Summary: A case vignette is used to illustrate issues around the treatment of mild persistent asthma. The subject, a 30 year-old woman had a lifelong history of asthma. Although she had visited her hospital for acute treatment during childhood, she had not been admitted. In her late teens her asthma had become quiescent, reappearing at age 25 following the birth of her first child. No emergency care was required but she experienced night wakening approximately once per month and became short of breath following exercise. With inhaled beclomethasone (160 µg twice daily), and as-needed albuterol she has remained stable for the past 4 years. She has no nocturnal symptoms and uses albuterol 2-3 times per week, usually prior to exercise. The patient would like to know if she could use less medication in order to mitigate long-term side effects. She is prepared to tolerate some additional symptoms. Three alternative treatment options are outlined and readers are asked to consider which will best meet the patient's needs.

Comment: The different options for the treatment of mild persistent asthma are discussed in this Clinical Decisions article in the NEJM. The treatment options discussed illustrate the evidence base that now exists for the management of this group of patients.

<http://content.nejm.org/cgi/content/extract/356/20/2096>

Reference: *New Engl J Med* 2007; 356: 2096

*Independent commentary
by Professor Richard Beasley*

Strategies for reducing treatment in mild persistent asthma

Authors: The American Lung Association Asthma Clinical Research Centre

Summary: The authors sought to investigate the effect of "stepping down" treatment in patients with well controlled asthma. 500 well controlled asthma patients receiving inhaled fluticasone (100 µg twice daily) were randomised to 16 weeks of double-blind treatment with either continued fluticasone (100 µg twice daily), montelukast (5 or 10 mg once daily), or fluticasone (100 µg) plus salmeterol (50 µg) once daily. Treatment failure occurred in significantly fewer patients in both fluticasone groups; approximately 20% versus 30.3% with montelukast (hazard ratio for both comparisons 1.6, 95% CI 1.1-2.6; p = 0.03). However the percentage of symptom free days was similar in all 3 groups (range 78.7 to 85.5%).

Comment: This study addresses the important issue of stepping down therapy in patients whose asthma is well controlled. It suggests that, in addition to the option of reducing the ICS dose, changing to a once daily dose of combination ICS/LABA therapy is a worthy option to consider.

<http://content.nejm.org/cgi/content/full/356/20/2027>

Reference: *New Engl J Med* 2007; 356: 2027-39

Predicting and evaluating response to omalizumab in patients with severe allergic asthma

Authors: Bousquet J et al

Summary: The authors analysed 7 randomised, controlled trials of omalizumab in severe, persistent allergic asthma in order to identify baseline patient characteristics which could predict both responders and those with a superior response to omalizumab. Pooled efficacy data from the 7 studies was examined using univariate and multivariate analysis. The only factor which predicted omalizumab efficacy was baseline total immunoglobulin E (IgE). However, patients in the pooled analysis benefited from treatment regardless of baseline IgE level. The best method of identifying responders following a course of treatment was the physicians overall assessment at 16 weeks which found 61% of subjects were responders. In conclusion, the authors find that treatment benefit with omalizumab cannot be predicted reliably from baseline characteristics and note that the most meaningful measure of response to therapy is the physicians overall assessment.

Comment: One of the priorities in the use of omalizumab therapy is knowing how to predict which patients with severe asthma are likely to respond best, thereby allowing targeted therapy. Regrettably, this meta-analysis of RCTs indicated that there were no baseline measures that reliably predicted benefit. Intriguingly, the physician's overall assessment after 16 weeks of treatment was the most helpful measure of response. These findings provide some support for the strategy of prescribing an initial 16 week course of omalizumab therapy in patients with severe persistent asthma uncontrolled with optimal therapy, and then the physician assessing response to determine whether treatment should be continued beyond this period.

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

Reference: *Respir Med* 2007; 101:1483-92

Privacy Policy: APSR will record your email details on a secure database and will not release it to anyone without your prior approval. APSR and you have the right to inspect, update or delete your details at any time.

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.

Research Review is an online medical publication company.

*Research Review electronic journals are independent, free to recipients and delivered by email.
To enrol a colleague or to unsubscribe please contact :*

*Secretariat, Asian Pacific Society of Respiratory, Yoshikawa Bldg. No. 2,
2-9-8 Hongo, Bunkyo-ku, Tokyo, Japan 113-0033
email: kyu00671@nifty.com*

Research Review acknowledges the kind support of



Telephone consultations in secondary care

Authors: Roberts NJ et al

Summary: This observational study was designed to assess the role of telephone consultations in respiratory medicine. Participants were 500 sequential respiratory outpatients attending three different outpatient respiratory clinics, whose next planned appointment was replaced with a telephone consultation. Outcome measures included the proportion of patients for whom telephone consultation was suitable and their satisfaction with the service. Practical issues including availability of the patient and length of the phone call were also addressed. The authors found that for one third of this patient group, telephone consultations were an effective alternative to a traditional face-to-face consultation. Benefits of using the telephone included being able to receive the phone call at a more convenient location than the hospital. 23.9% of participants chose to receive the consultation at their place of work.

Comment: It is now time that the strategy of offering telephone consultations for selected patients attending respiratory outpatient clinics is seriously considered. This study indicates that up to a third of patients may be suitable, and outlines the potential advantages and disadvantages. Practical recommendations are made on how to set up and conduct the telephone service. It is significant that the authors have now implemented telephone consultations as normal practice in their busy central London teaching hospital clinic.

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

Reference: *Respir Med* 2007; 101:1665-9

Low bone mineral density in young children with cystic fibrosis

Authors: Sermet-Gaudelus I et al

Summary: The authors aimed to evaluate bone mineral density (BMD) in children with cystic fibrosis (CF). The impact of factors including nutritional status, body composition, pulmonary disease severity, corticosteroid usage, dietary calcium, caloric intake, and vitamin D status on BMD were also assessed. The cohort comprised 25 children under the age of 6, 53 aged 6 to 10 years, and 36 adolescents aged 11 to 18 years. In the youngest group of children, mean LS z score was significantly lower than normal (-0.96; SEM, 0.3), but was not different to that in children aged 6 to 10 years (-0.91; SEM, 0.2) or adolescents (-1.4; SEM, 0.2). Multiple-regression analysis found a positive correlation between LS z score and fat-free mass. In patients with mild pulmonary disease and normal nutritional status, 34% had an LS z score of less than -1. The authors conclude that "the origin of CF bone disease in early childhood may be independent of nutritional status or disease severity."

Comment: A reminder of the likely presence of low bone mineral density in young children with cystic fibrosis. Interestingly the presence of low BMD appeared to be independent of either nutritional status or disease activity. The authors recommend that all children with CF undergo an assessment of BMD and body composition early in life to make it possible to target those who need preventive treatment.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/9/951>

Reference: *Am J Crit Care Med* 2007;175: 951-7

Research Review publications are intended for Medical Professionals

APSR Respiratory Research Review is an initiative of the APSR education committee

The safety and efficacy of infliximab in moderate to severe COPD

Authors: Rennard SI et al

Summary: This multi-centre, randomised, double-blind, placebo-controlled, parallel-group study assessed the effects of infliximab in 77 patients with moderate-to-severe COPD. Patients received infliximab (3 or 5 mg/kg) or placebo at weeks 0, 2, 6, 12, 18, and 24 with follow-up to week 44. No treatment benefits were observed with infliximab on measures including the Chronic Respiratory Questionnaire, pre-bronchodilator FEV₁, 6-minute walking distance, SF-36 physical score, transition dyspnea index, or rate of moderate-to-severe COPD exacerbations. Young or cachectic patients improved on the 6-minute walking distance in a post-hoc analysis. Infliximab was generally well tolerated although rates of discontinuation due to adverse events were higher with infliximab (20-27%) than with placebo (7%). Rates of infection requiring antibiotics were not different to placebo although numerically rates of pneumonia were higher. No opportunistic infections occurred and there were no infection-related deaths. There was a non-significantly higher rate of malignancies diagnosed in infliximab-treated patients (5.7%) compared to placebo (1.3%) during the study.

Comment: A negative study of infliximab (anti-TNF- α antibody) therapy in patients with moderate to severe COPD. Not only was there no evidence of clinical efficacy, but there was a worse safety/side effect profile. The high rate of cancer with infliximab therapy was of particular concern in regard to its use in rheumatoid arthritis and Crohn's disease. The associated editorial is worth reading – *AJRCCM* 2007; 175:866-7.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/9/926>

Reference: *Am J Crit Care Med* 2007; 175:926-34

Coming Educational Seminar of the APSR – ESAP

Avian/emerging flu – Basic biology to public health and disaster management
30 November 2007 – Gold Coast, Australia – Just prior to the 12th APSR Congress
For more information see: <http://www.apsresp.org/education/esap.html#esap004>

Cryptogenic haemoptysis

Authors: Savale L et al

Summary: The authors sought to examine the clinical spectrum, pathological findings and course of patients with cryptogenic haemoptysis. Data were obtained from a cohort of 81 patients with cryptogenic haemoptysis referred to a respiratory intermediate and intensive care unit following clinical evaluation, chest radiography, fibre-optic bronchoscopy, and CT scan. Mean follow-up was 47 months. On admission, mean cumulative volume of haemoptysis was 190 ml. In 90% of patients, haemoptysis was controlled with conservative measures and bronchial artery embolisation. 7% received emergency surgery following failure of embolisation. 4 patients experienced a recurrence of haemoptysis within 1 year, and recurrence was observed in 6 others between 1 and 8 years of follow-up. 2 patients required surgery for recurrence. Dieulafoy disease, unsuspected after routine imaging, was identified in 5 of the 9 patients who required surgery. There were no cases of lung cancer.

Comment: An informative case-series describing the clinical spectrum, management and outcomes of a large cohort of patients with cryptogenic haemoptysis. Patients were defined as cryptogenic haemoptysis after history, physical examination, chest x-ray, bronchoscopy and CT scan excluded any specific lesion that could have been identified as the source of the bleeding. In most patients, bleeding was controlled using conservative measures and bronchial artery embolisation – surgery was seldom required. A helpful management algorithm is presented. Incidentally, in those with marked haemoptysis who underwent surgery, the most common abnormality was a specific bronchial vascular abnormality – Dieulafoy disease.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/11/1181>

Reference: *Am J Respir Crit Care Med* 2007; 175:1181-5

Evaluation of unsuspected PE on contrast enhanced multi-detector CT (MDCT) scanning

Authors: Ritchie G et al

Summary: The authors sought to quantify the incidence of unsuspected pulmonary emboli (PE) in patients undergoing thoracic contrast enhanced multi-detector CT (MDCT) scanning. All inpatients, excluding those with previous or suspected current PE, who received thoracic MDCT scanning over a 10 month period were included in the analysis. Of 487 identified patients, 5.7% had unidentified PE, and 32.1% of these had not been identified by the original reporting radiologist. Older patients were more likely to have unidentified PE; rates were 9.2% in those over 70, and 16.7% in those older than 80 ($p < 0.001$). The majority of positive scans (64.3%) were at the segmental or sub-segmental level. No other factors increasing the incidence of unidentified PE were observed, and there was no significant difference between 4 and 16-slice MDCT. In conclusion, PE should be routinely sought in all contrast enhanced MDCT scans of the chest.

Comment: The message from this paper is clear – PE should be routinely sought in all contrast enhanced MDCT scans of the chest regardless of the indication of the CT scan.

<http://thorax.bmj.com/cgi/content/abstract/62/6/536>

Reference: *Thorax* 2007; 62:536-40

Diagnostic agreement in parenchymal lung diseases

Authors: Flaherty KR et al

Summary: This paper examined differences between academic and community-based physicians with regard to the diagnosis of parenchymal lung diseases (DPLDs). The cases of 39 patients with DPLD were retrospectively reviewed by 19 participants at 2 community and 1 academic location. Inter-observer agreement in diagnosis was improved when there were interactions between clinicians, radiologists, and pathologists. Diagnostic agreement was greater within the academic centre than within the community centres. Diagnostic differences between academic and community physicians were clinically significant. A final diagnosis of idiopathic pulmonary fibrosis was more commonly made by community physicians. The authors suggest that ideally patients be referred to centres with expertise in DPLDs in order to ensure correct diagnosis and treatment.

Comment: The key message from this study is that patients with suspected diffuse parenchymal lung disorders should be referred to centres with expertise in this area to help clarify the diagnosis and for suggestions regarding management. If the option of a tertiary referral centre does not exist, it may be preferable for one physician within a respiratory department to look after all cases of diffuse pulmonary lung disease to develop the expertise required.

<http://ajrccm.atsjournals.org/cgi/content/abstract/175/10/1054>

Reference: *Am J Crit Care Med* 2007; 175: 1054-60

> **advertise your conference,
job or service here**

Contact: office@researchreview.co.nz