Dear APSR Colleagues:

Since the last APSR Respiratory Update on Interstitial Lung Disease (February 2010), there have been significant advances in Interstitial Lung Diseases (ILD), including new guidelines and the results of large global trials. Among the important outstanding articles published in 2010 and 2011, I have selected ten papers. It was difficult to select 10 important publications for this issue as there were many more important articles published during the year. Please understand that pages are limited, and we could not list all of these articles. We hope the selected manuscripts will help your clinical practice and research on ILD.

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Idiopathic Interstitial Pneumonias (IIPs)

An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management

Authors: Raghu G et al.
URL: http://ajrccm.atsjournals.org/cgi/content/full/183/6/788

Comment: In 2000, the "Idiopathic pulmonary fibrosis: diagnosis and treatment: international consensus statement" was published by the American Thoracic Society (ATS) and the European Respiratory Society (ERS). This was an important epoch-defining statement, but the article was limited in its scope as it was a consensus statement, rather than guidelines, because there was little evidence. During the past 11 years, we have accumulated much more evidence about the diagnosis, treatment, and management of idiopathic pulmonary fibrosis (IPF). These guidelines provide an update on the current state of knowledge regarding IPF, and there are also sections on definition and epidemiology, risk factors, diagnosis, natural history, staging and prognosis, treatment, and monitoring the course of the disease. The ATS/ERS are also preparing to update the ATS/ERS International Multidisciplinary Consensus Classification of the IIPs (Am J Respir Crit Care Med 2002; 165: 277–304).

Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomized trials

Authors: Noble PW et al.
URL: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60405-4/fulltext

Comment: IPF is a progressive and fatal lung disease. Pirfenidone, an anti-fibrotic and anti-inflammatory drug that was recently approved in Japan for the treatment of IPF, was suspected to reduce deterioration in pulmonary function in patients with IPF. In two concurrent trials (004 and 006), patients with IPF were randomly assigned to oral pirfenidone or placebo for a minimum of 72 weeks. The primary endpoint was change in percentage predicted forced vital capacity at week 72. The data showed that pirfenidone has a favourable benefit risk profile and is an appropriate treatment option for patients with IPF. Based on these results, pirfenidone was not approved in the US, but will be approved in Europe.

A controlled trial of sildenafil in advanced idiopathic pulmonary fibrosis

Authors: IPF Clinical Research Network, Zisman DA et al.

Comment: Sildenafil is a phosphodiesterase-5 inhibitor, and is suspected to improve blood flow to well-ventilated regions of the lung in advanced IPF, leading to improved gas exchange. A double-blind, randomized, placebo-controlled trial of sildenafil over two periods was conducted. The first period consisted of a double-blind comparison between sildenafil and a placebo control over 12 weeks. The primary endpoint was the proportion of patients with an increase in 6-minute walk distance of 20% or more. Unfortunately, this study did not show a benefit of sildenafil for the primary endpoint.
BUILD-3: A randomized, controlled trial of bosentan in idiopathic pulmonary fibrosis

Authors: King TE Jr et al.
URL: http://ajrccm.atsjournals.org/cgi/reprint/201011-1874OCv1

Comment: A previous trial of bosentan in IPF showed a trend to delay of worsening and death, and improvements in some measures of dyspnoea and health-related quality of life. This paper reports the results of a prospective, randomized, double-blind, placebo-controlled, event-driven, parallel-group, morbidity–mortality trial of bosentan in IPF of <3 years duration, as confirmed by surgical lung biopsy, and without extensive honeycombing on high-resolution computed tomography. The primary objective was to determine whether bosentan delays time to worsening of IPF or death. The primary objective was not met, but bosentan was well tolerated.

A common MUC5B promoter polymorphism and pulmonary fibrosis

Authors: Seibold MA et al.

Comment: By genome-wide linkage scanning, the authors studied the linkage between IIPs and a 3.4-Mb region of chromosome 11p15 in 82 families. The authors evaluated genetic variation in gel-forming mucin genes expressed in the lung, among 83 subjects with familial interstitial pneumonia, 492 subjects with IPF, and 322 controls. MUC5B expression was assessed in lung tissue. A common polymorphism in the promoter of MUC5B was associated with familial interstitial pneumonia and IPF. Dysregulated MUC5B expression in the lung may be involved in the pathogenesis of pulmonary fibrosis. These results not only provide a new therapeutic target in IPF, but also provide insight into the particular clinical manifestations leading to earlier detection, predictable prognosis, and personalized strategies for specific treatment.
Other Interstitial Lung Diseases (ILDs)

European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis

Authors: Johnson SR et al.
URL: http://erj.ersjournals.com/content/35/1/14.long

Comment: These are the first international clinical guidelines for the diagnosis and management of lymphangioleiomyomatosis (LAM) published by the European Respiratory Society. The guidelines are well written, and will be useful for pulmonary physicians worldwide. However, in the last 2 or 3 years important manuscripts have been published on this topic.

Efficacy and safety of sirolimus in lymphangioleiomyomatosis

Authors: McCormack FX et al.

Comment: Lymphangioleiomyomatosis (LAM) is associated with abnormal activation of mammalian target of rapamycin (mTOR) signalling, and sirolimus (rapamycin) inhibits mTOR. The authors conducted a two-stage trial of sirolimus, involving 89 patients with LAM who had moderate lung impairment: a 12-month randomized, double-blind comparison of sirolimus with placebo, followed by a 12-month observation period. The primary end point was the difference between the groups in the rate of change in FEV₁. Sirolimus significantly stabilized lung function, reduced serum vascular endothelial growth factor D levels, and there was an association with reduction in symptoms and improvement in quality of life in patients with LAM. Sirolimus therapy may be useful in selected patients with LAM. This study was conducted with the support of the LAM patients support group, the LAM Foundation.

Inhaled granulocyte/macrophage-colony stimulating factor as therapy for pulmonary alveolar proteinosis

Authors: Tazawa R et al.
URL: http://ajrccm.atsjournals.org/cgi/content/full/181/12/1345

Comment: In a previous paper, the investigators reported the presence of anti-granulocyte/macrophage-colony stimulating factor (GM-CSF) auto-antibodies in the lungs and sera of patients with idiopathic (autoimmune) pulmonary alveolar proteinosis (PAP), which was somewhat of a breakthrough. To evaluate the safety and efficacy of inhaled GM-CSF in patients with autoimmune PAP, the investigators have now conducted a nationwide, multicentre, phase II trial at nine pulmonary centres. The patients received high-dose therapy (250 mg, days 1-8; x 6 cycles; 12 weeks), and low-dose therapy (125 mg, days 1-4; x 6 cycles; 12 weeks), and were followed up for 52 weeks. Inhaled GM-CSF therapy was safe, effective, and provided a sustained therapeutic effect in patients with autoimmune PAP.
Gene set analysis of lung samples provides insight into pathogenesis of progressive, fibrotic pulmonary sarcoidosis

Authors: Lockstone HE et al.
Reference: Am J Respir Crit Care Med 2010; 181: 1367-75.
URL: [http://ajrccm.atsjournals.org/cgi/content/full/181/12/1367](http://ajrccm.atsjournals.org/cgi/content/full/181/12/1367)
Comment: Thirty to forty percent of patients with pulmonary sarcoidosis have chronic disease courses with varying levels of progressive-fibrotic disease. The aim of this study was to assess the differential gene expression profile in lungs of patients with self-limiting sarcoidosis compared to patients with progressive-fibrotic disease. The findings suggest that patients with progressive or fibrotic pulmonary sarcoidosis show intense immune activity related to host defence in their lungs, with processes more similar to hypersensitivity pneumonitis than IPF. These results may provide biomarkers for prognosis or potential therapeutic targets.

Combined pulmonary fibrosis and emphysema syndrome in connective tissue disease

Authors: Cottin V et al.
Comment: The syndrome of combined pulmonary fibrosis and emphysema (CPFE) was recently introduced by the authors, as a spectrum of smoking-induced chronic lung diseases. In this paper, CPFE was evaluated in connective tissue diseases (CTD). Imaging and pulmonary function findings in patients with CPFE and CTD were similar to those of patients with idiopathic CPFE, and differed from those of patients with CTD-associated ILD without emphysema.