

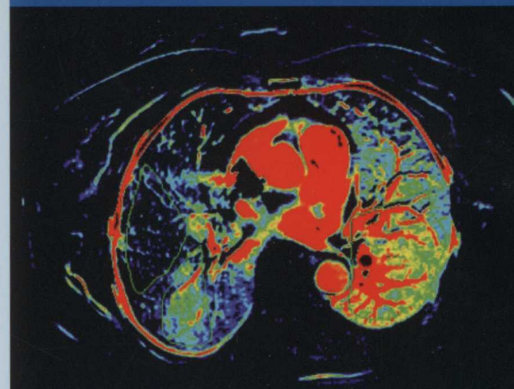


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EDITORIAL

Bronchodilator reversibility in COPD: the roguish but harmless little brother of airway hyperresponsiveness?

ORIGINALS

Operational definitions of asthma in studies on its aetiology

The protease inhibitor PI*S allele and COPD: a meta-analysis

Characterisation of natural killer cells and CD56+ T-cells in sarcoidosis patients

Quality control of equipment in home mechanical ventilation: a European survey

Pulmonary manifestations of multicentric Castleman's disease in HIV infection: a clinical, biological and radiological study

REVIEW

Computed tomographic imaging of the airways: relationship to structure and function

SERIES

ATS/ERS Task Force: standardisation of lung function testing

General considerations for lung function testing

64502/ 55

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EDITORIALS

Volume 26, Number 1 July 2005

- 1** Coming together: the ATS/ERS consensus on clinical pulmonary function testing
V. Brusasco, R. Crapo and G. Viegi
- 3** Identifying asthma in population studies: from single entity to a multi-component approach
G.B. Marks
- 6** Bronchodilator reversibility in COPD: the roguish but harmless little brother of airway hyperresponsiveness?
E.F. Hansen and J. Vestbo

ORIGINAL ARTICLES

- Clinical forum: bronchiectasis**
- 8** Non-CF bronchiectasis: does knowing the aetiology lead to changes in management?
A.M. Li, S. Sonnappa, C. Lex, E. Wong, A. Zacharasiewicz, A. Bush and A. Jaffe
- Respiratory cell biology**
- 15** Nerve growth factor is released by IL-1 β and induces hyperresponsiveness of the human isolated bronchus
N. Frossard, E. Naline, C. Olgart Höglund, O. Georges and C. Advenier
- 21** Modulation of airway inflammation and resistance in mice by a nicotinic receptor agonist
M-R. Blanchet, E. Israël-Assayag and Y. Cormier
- Asthma**
- 28** Operational definitions of asthma in studies on its aetiology
J. Pekkanen, J. Sunyer, J.M. Anto and P. Burney, on behalf of the European Community Respiratory Health Study (ECRHS)
- 36** Traditional and patient-centred outcomes with three classes of asthma medication
C.R. Jenkins, F.C.K. Thien, J.R. Wheatley and H.K. Reddel
- COPD**
- 45** Bronchodilator response in the lung health study over 11 yrs
N.R. Anthonisen, P.G. Lindgren, D.P. Tashkin, R.E. Kanner, P.D. Scanlon and J.E. Connett for the Lung Health Study Research Group
- 52** Exhaled nitric oxide from lung periphery is increased in COPD
C. Brindicci, K. Ito, O. Resta, N.B. Pride, P.J. Barnes and S.A. Kharitonov
- 60** Decreased macrophage release of TGF- β and TIMP-1 in chronic obstructive pulmonary disease
A.R. Pons, J. Saulea, A. Noguera, J. Pons, B. Barceló, A. Fuster and A.G.N. Agusti

ORIGINAL ARTICLES (CONT.)

Genetics in COPD

- 67** The protease inhibitor PI*S allele and COPD: a meta-analysis
M. Dahl, C.P. Hersh, N.P. Ly, C.S. Berkey, E.K. Silverman and B.G. Nordestgaard

Interstitial lung disease

- 77** Characterisation of natural killer cells and CD56+ T-cells in sarcoidosis patients
K. Katchar, K. Söderström, J. Wahlstrom, A. Eklund and J. Grunewald

Mechanical ventilation

- 86** Quality control of equipment in home mechanical ventilation: a European survey
R. Farre, S.J. Lloyd-Owen, N. Ambrosino, G. Donaldson, J. Escarabill, B. Fauroux, D. Robert, B. Schoenhofer, A. Simonds and J.A. Wedzicha

Cheyne-Stokes respiration

- 95** Improvement in Cheyne-Stokes respiration following cardiac resynchronisation therapy
J.Y. Gabor, D.A. Newman, V. Barnard-Roberts, V. Korley, I. Mangat, P. Dorian and P.J. Hanly

ARDS

- 101** VEGF levels in the alveolar compartment do not distinguish between ARDS and hydrostatic pulmonary oedema
L.B. Ware, R.J. Kaner, R.G. Crystal, R. Schane, N.N. Trivedi, D. McAuley and M.A. Matthay

Ventilator-associated pneumonia

- 106** Early gastrostomy reduces the rate of ventilator-associated pneumonia in stroke or head injury patients
E. Kostadima, A.G. Kaditis, E.I. Alexopoulos, E. Zakyntinos and D. Sfyas
- 112** Effect of ventilation strategy and surfactant on inflammation in experimental pneumonia
A.H.L.C. van Kaam, R. Lutter, R.A. Lachmann, J.J. Haitsma, E. Herting, M. Snoek, A. De Jaegere, J.H. Kok and B. Lachmann

HIV and the lung

- 118** Pulmonary manifestations of multicentric Castleman's disease in HIV infection: a clinical, biological and radiological study
A. Guihot, L.-J. Couderc, F. Agbalika, L. Galicier, P. Bossi, E. Rivaud, A. Scherrer, D. Zucman, C. Katlama and E. Oksenhendler

Paediatric tuberculosis

- 126** Tuberculosis infection in children who are contacts of immigrant tuberculosis patients
S. Verver, J.H. van Loenhout-Rooyackers, R. Bwire, J.A.C.M. Annee-van Bavel, H.J.M. de Lange, P.J.H.J. van Gerven and M.W. Borgdorff

Occupational lung disease

- 133** Airflow limitation and changes in pulmonary function among bleachery workers
A.J. Mehta, P.K. Henneberger, K. Torén and A.-C. Olin

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AIMS & SCOPE

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Front cover picture: Quantitative map of tissue perfusion
measured by multidetector row computed tomography at the
level of the main pulmonary artery in a patient with chronic
thromboembolic pulmonary hypertension. The colour
indicates perfusion rate in $\text{mL} \cdot \text{min}^{-1} \cdot 100 \text{ mL}^{-1}$ tissue; red is
the high end of the scale, blue the low end.

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REVIEW

- 140 Computed tomographic imaging of the airways:
relationship to structure and function
P.A. de Jong, N.L. Müller, P.D. Paré, H.O. Coxson

SERIES

SERIES "ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING"

Edited by V. Brusasco, R. Crapo and G. Viegi
Number 1 in this Series

- 153 General considerations for lung function testing
M.R. Miller, R. Crapo, J. Hankinson, V. Brusasco,
F. Burgos, R. Casaburi, A. Coates, P. Enright,
C.P.M. van der Grinten, P. Gustafsson, R. Jensen,
D.C. Johnson, N. MacIntyre, R. McKay, D. Navajas,
O.F. Pedersen, R. Pellegrino, G. Viegi and
J. Wanger

SERIES "CONTROVERSIAL ISSUES IN TUBERCULOSIS"

Edited by A. Torres and J. Caminero
Number 8 in this Series

- 162 The dream of a vaccine against tuberculosis;
new vaccines improving or replacing BCG?
C. Martin

CASE STUDY

- 168 The use of iloprost in early pregnancy in
patients with pulmonary arterial hypertension
C.A. Elliott, P. Stewart, V.J. Webster, G.H. Mills,
S.P. Hutchinson, E.S. Howarth, F.A. Bu'Lock,
R.A. Lawson, I.J. Armstrong and D.G. Kiely

CASE FOR DIAGNOSIS

- 174 Hoarseness, cough and cervical
lymphadenopathy
A.J. Turk, T. Brack, C. Alfaré, A. Gaspert and
E.W. Russi

CORRESPONDENCE

- 178 Early noninvasive ventilation failure in COPD
with acute on chronic respiratory failure
A. Cuvelier, L.C. Molano and J-F. Muir
- 178 Antibody deficiency in bronchiectasis
M. Miravittles, M. Vendrell and J. de Gracia
- 180 Combination therapy with bosentan and
phosphodiesterase-5 inhibitor in pulmonary
arterial hypertension
A.H. Morice, S. Mulrennan and A. Clark;
M.M. Hooper
- 181 Efficacy of fluticasone on cough
F. Hargreave and K. Parameswaran; B.P. Ponsioen,
P.N.R. Dekhuijzen, A.M. Bohnen and N.A. Vermue
- 182 EUS: confusion about terminology and its
consequences
C.T. Bolliger; J.T. Annema and K.F. Rabe

185 BOOK REVIEW

d,f,h,i,p MEETING CALENDAR

- 3 de Gracia J, Vendrell M, Álvarez A, *et al.* Immunoglobulin therapy to control lung damage in patients with common variable immunodeficiency. *Int Immunopharmacol* 2004; 6: 745–753.
- 4 de Gracia J, Morell F, Bofill JM, Rodrigo MJ, Coscolluela C. Impaired lung function in patients with IgA deficiency and low levels of IgG2 or IgG3. *N Engl J Med* 1986; 314: 925–926.
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Combination therapy with bosentan and phosphodiesterase-5 inhibitor in pulmonary arterial hypertension

To the Editors:

HOEPER *et al.* [1] have produced an interesting report of their clinical experience of combined therapy with bosentan and sildenafil in patients with idiopathic pulmonary arterial hypertension. Whilst it is true that the relatively scant literature supporting the use of phosphodiesterase-5 inhibitors is centred around sildenafil, its relatively short duration of action requires the use of a thrice-daily regime. This has significant implications for compliance and, since treatment is continual, has large implications in the cost of treatment. It would be more logical to use a long-acting phosphodiesterase-5 inhibitor, and, with the advent of tadalafil, once-daily treatment becomes possible.

Here, we report our experience with a combination of bosentan and tadalafil in a 42-yr-old male with idiopathic pulmonary hypertension who had documented poor compliance with nebulised iloprost. Sildenafil 25 mg *t.d.s.* was added to bosentan, following a clinical deterioration and the finding of an estimated pulmonary artery systolic pressure of 130 mmHg, and this caused a fall in pulmonary artery pressure to 50 mmHg. Treatment with sildenafil was stopped 1 month later at another centre, and the pulmonary artery systolic pressure increased to 100 mmHg. Subsequently, sildenafil was restarted in combination with bosentan, and exercise tolerance doubled. After 3 months of combination treatment, the issue of compliance was raised by the patient and it was decided to

substitute tadalafil 20 mg once daily for the sildenafil. The patient has continued on tadalafil for 9 months with an excellent symptomatic response. The last estimated pulmonary artery pressure was 61 mmHg.

A.H. Morice, S. Mulrennan and A. Clark

Division of Academic Medicine, University of Hull, Castle Hill Hospital, Hull, UK.

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From the authors:

I am grateful for the comments by A.H. Morice and coworkers, although their case report leaves several questions unanswered. More information than just the systolic pulmonary artery pressure is needed to appraise the haemodynamic response to tadalafil. One wonders whether this patient ever underwent pulmonary vasoreactivity testing. With such a

dramatic fall in pulmonary artery pressure, the patient might fulfil the responder criteria (fall in mean pulmonary artery pressure by >10 mmHg to <40 mmHg in the presence of a cardiac output), and may, therefore, be a candidate for treatment with calcium channel blockers [1].

I agree with A.H. Morice and coworkers that the relatively short half-life of sildenafil (3–4 h) may be a drawback of this drug. Patients' compliance may rarely be an issue. However, the fluctuations in sildenafil plasma concentrations are poorly tolerated by some patients. A drug with a much longer half-life, such as tadalafil (~18 h), might be advantageous, but caution is necessary. GHOFrani *et al.* [2] have demonstrated substantial variability in the haemodynamic effects of several phosphodiesterase-5 inhibitors. For the time being, there is a strong body of evidence for the safety and efficacy of sildenafil in pulmonary arterial hypertension, but there is a lack of comparable data for other phosphodiesterase-5 inhibitors, such as tadalafil.

M.M. Hoepfer

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Efficacy of fluticasone on cough

To the Editors:

In the original article by PONSIOEN *et al.* [1], there is no mention of the predictive value of the type of airway inflammation that is associated with cough, or whether there was any benefit from inhaled corticosteroid treatment.

There is increasing evidence that eosinophilic airway inflammation, *i.e.* an eosinophilic bronchitis, which can be identified from spontaneous or induced sputum cell counts, predicts the benefit from corticosteroid treatment in chronic cough, asthma and chronic obstructive pulmonary disease and that a lack of eosinophilia indicates an absence of any benefit [2–6].

An eosinophilic bronchitis occurs in only 10–30% of patients referred to a specialist with an isolated chronic cough [7–9]. Hence, in an unselected population of patients with cough, the majority of whom will not have eosinophilic bronchitis, the benefit from inhaled steroid treatment is likely to be small, as indicated in the study by PONSIOEN *et al.* [1], or absent. Measurement of airway inflammation is necessary to interpret the results of treatment with anti-inflammatory medications.

F. Hargreave and K. Parameswaran

Firestone Institute for Respiratory Health, McMaster University and St. Joseph's HealthCare, Hamilton, ON, Canada.

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DOI: 10.1183/09031936.05.00023205

From the authors:

We would like to thank F. Hargreave and K. Parameswaran for their suggestion that sputum eosinophils and the provocative dose causing a 20% fall in forced expiratory volume in one