

remains improved since the addition of omalizumab. Both patients have also been on long-acting  $\beta_2$  agonists and inhaled corticosteroids in standard doses throughout the time to control mild asthma symptoms (GINA I). In addition, they have required low dose prednisolone (5–10 mg) over the course of time to control blood eosinophilia, a hallmark of CSS exacerbation. We agree with Giavina-Bianchi *et al* that the long-term control of CSS requires immunosuppressant therapy and consider omalizumab as an effective add-on therapeutic agent. Because of the variability in the symptoms presented and the subspecialty of the referral centres who see these patients, a registry of patients with CSS is needed, based on clinical symptoms, regional background and therapeutic strategies. The underlying mechanisms as to how eosinophilia and cytokine signalling affects the course of the disease remains elusive and requires standardised treatment options and clarification of the molecular pathways to improve patient care.

**C Grohé, S Pabst**

University of Bonn, Bonn, Germany

**Correspondence to:** Dr C Grohé, University of Bonn, Sigmund Freud Strasse 25, Bonn 53105, Germany; Christian.grohe@ukb.uni-bonn.de

**Competing interests:** None.

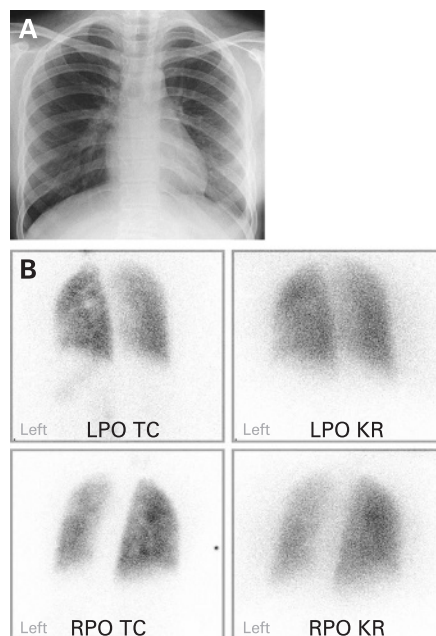
Accepted 13 November 2008

## Ventilation-perfusion scans in children treated for empyema

Empyema is a frequent complication in children hospitalised with pneumonia. Parenchymal changes have been demonstrated on chest radiographs and chest CT scans in empyema,<sup>1</sup> and it is plausible that functional outcome may be affected. Studies that have used spirometry in children of school age to assess function following empyema have largely demonstrated normal lung function.<sup>2</sup> The ventilation-perfusion (V/Q) scan has been used occasionally in follow-up,<sup>3</sup> but evidence is lacking as to its value in this context.

We retrospectively reviewed V/Q scans of eight children originally recruited as part of a published study comparing video-assisted thoracoscopic drainage (VATS) with percutaneous chest drain insertion and urokinase for empyema.<sup>4</sup> Our aim was to assess whether empyema causes functional abnormalities following clinical resolution.

All subjects in the original study consented to have a V/Q scan at follow-up. Ethical approval was obtained. Of the total 60 children recruited (median age 3.7 years, range 0.5–15.8), only 8 (median age 7 years, range 1.1–14.4) agreed to have a V/Q scan. Seven of these had VATS and one had percutaneous drain insertion with urokinase.



**Figure 1** (A) Chest radiograph showing residual left pleural shadowing and blunting at the left costophrenic angle. (B) Ventilation/perfusion (V/Q) scan (posterior oblique views) showing borderline reduction in ventilation and perfusion of the left lung compatible with minimal left-sided pleural thickening seen on the chest radiograph. V/Q scan images were acquired with a single head gamma camera equipped with a parallel hole collimator. Tc<sup>99m</sup>-Marco aggregates of albumin and 81m-krypton were used for perfusion and ventilation, respectively.

The median time from hospital discharge to V/Q scan and contemporaneous chest radiography was 6.5 months (range 4.5–13). All children had made a complete clinical recovery at assessment. All follow-up chest radiographs showed minor changes such as pleural shadowing. No major focal parenchymal defects were found on the V/Q scan in any of the children. Six of the V/Q scans showed normally distributed ventilation and perfusion. One scan, following a left empyema treated with VATS, showed global borderline reduction in the function of the left lung (fig 1B), which correlated well with the chest radiograph (fig 1A). Another V/Q scan showed a small focal abnormality in part of the right lower lobe on both ventilation and perfusion studies.

We found that V/Q scans in children with empyema at a median interval of 6.5 months following discharge did not demonstrate major focal defects.

The main limitation of our observation is the small number of children studied. All the children in our study were previously healthy and were reluctant to take part in a potentially unpleasant investigation (intravenous cannulation for injecting radioisotope) once the acute illness had resolved. The only paediatric study evaluating lung

perfusion following empyema found that more than 50% of the children had diminished perfusion on the side of the empyema.<sup>3</sup> However, the time to the perfusion scan spanned >10 years following empyema, with no details of patients' ages, management, morbidity and interval infections.

The prognosis in children with empyema is excellent, with most making a complete clinical and radiological recovery.<sup>5</sup> British Thoracic Society guidelines recommend that children should be followed up after discharge until complete clinical and near normal radiological resolution.<sup>5</sup> However, there is a dearth of studies evaluating long-term functional outcome in children with empyema which needs to be addressed.

We conclude that medium-term lung function as assessed by V/Q scans in a small series of children with resolved empyema is normal or near normal. V/Q scans do not add additional information to functional assessment in a clinically well child following empyema.

**R C Mew,<sup>1</sup> A Jaffe,<sup>1,2,3</sup> L Bissioni,<sup>4</sup> S Sonnappa<sup>1,2</sup>**

<sup>1</sup> Department of Respiratory Medicine, Great Ormond Street Hospital for Children NHS Trust, London, UK; <sup>2</sup> Portex Anaesthesia, Intensive Therapy and Respiratory Unit, UCL, Institute of Child Health, London, UK; <sup>3</sup> Sydney Children's Hospital, Randwick and University of New South Wales, Sydney, Australia; <sup>4</sup> Department of Radiology, Great Ormond Street Hospital for Children NHS Trust, London, UK

**Correspondence to:** Dr S Sonnappa, Portex Anaesthesia, Intensive Therapy and Respiratory Unit, UCL, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK; s.sonnappa@ich.ucl.ac.uk

**Competing interests:** None.

Accepted 6 November 2008

*Thorax* 2009;64:273. doi:10.1136/thx.2008.107516

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## Pleurodesis by talc poudrage under simple medical thoracoscopy: an international opinion

We read with interest the editorial by Davies *et al*<sup>1</sup> and were pleased to learn that talc is preferred by most respiratory physicians worldwide as an effective pleurodesing agent. Based on scientific data, the authors

recognise that the talc currently used in the UK and USA has serious side effects because of systemic dissemination of small particles. They omitted, however, an important experimental study which used larger talc particles (ie, the talc currently used in Europe for >70 years) and clearly showed that this talc does not disseminate in organs,<sup>2</sup> unlike previous studies using American or Brazilian talc. This explains why many European respiratory physicians have used talc as a pleurodesing agent for >50 years without experiencing serious side effects.<sup>3</sup>

We thank the authors for referring to our European prospective study showing that talc poudrage under medical thoracoscopy is safe.<sup>4</sup> There is, however, some misunderstanding of our results. In our paper we reported that we did not find any significant difference in oxygen saturation after the procedure. Physicians had a free choice of patient follow-up after thoracoscopy. There was, indeed, an increase in supplemental oxygen saturation, but we should not forget that routine use of oxygen by nasal prongs is often performed after thoracoscopy, as is done after many interventional procedures such as bronchoscopy. We agree that 7/558 patients developed radiographic pulmonary infiltrates after talc poudrage. However, this does not prove that talc was responsible for this rare infiltrate, which might have been the result of lung re-expansion after pleurodesis.

On the other hand, we are not sure that control of the calibre of talc particles will increase the cost of graded talc. The current graded talc used in Europe since 1930 is safe, but has a unique drawback. It is very cheap and does not interest pharmaceutical companies because of the lack of potential for financial benefit.

We agree that more research needs to be done into the mechanism of pleurodesis. However, in the meantime, the talc debate should be clarified; many patients suffering from lasting and severe dyspnoea related to malignant pleural effusion are relieved by thorascopic talc poudrage performed without intubation, under local anaesthesia with moderate sedation.<sup>5</sup>

**J M Tschopp,<sup>1</sup> J M Schnyder,<sup>1</sup> P Astoul,<sup>2</sup> M Noppen,<sup>3</sup> M Froudarakis,<sup>4</sup> C T Bolliger,<sup>5</sup> S Gasparini,<sup>6</sup> G F Tassi,<sup>7</sup> F Rodriguez-Panadero,<sup>8</sup> R Loddenkemper,<sup>9</sup> Y Aelony,<sup>10</sup> J P Janssen<sup>11</sup>**

<sup>1</sup> Centre Valaisan de Pneumologie, Montana, Switzerland; <sup>2</sup> Hôpital Sainte-Marguerite, Marseille, France; <sup>3</sup> University Hospital UZ Brussels, Brussels, Belgium; <sup>4</sup> University Hospital Alexandroupolis, Alexandroupolis, Greece; <sup>5</sup> Tygerberg Academic Hospital, Cape Town, South Africa; <sup>6</sup> Azienda Ospedali Riuniti, Ancona, Italy; <sup>7</sup> Spedali Civili, Brescia, Italy; <sup>8</sup> Hospital Universitario Virgen del Rocío Sevilla, Seville, Spain; <sup>9</sup> Lungenklinik Heckeshorn, Berlin, Germany; <sup>10</sup> Harbor-UCLA Medical Center, Torrance, California, USA; <sup>11</sup> Canisius Wilhemina Hospital, Departement of Pulmonary Diseases B01, Nijmegen The Netherlands

**Correspondence to:** Professor J M Tschopp, Centre Valaisan de Pneumologie, CH 3962 Montana, Switzerland; jean-marie.tschopp@rsv-gnw.ch

**Competing interests:** None.

Accepted 6 November 2008

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## Authors' reply

We agree that the European cohort study by Janssen *et al* is a high quality study providing strong evidence for greater safety with large particle talc,<sup>1</sup> as stated clearly in our editorial.<sup>2</sup> However, to assume that these results prove complete safety is an extrapolation beyond the data, and risks overlooking milder or rarer (but important) adverse events.

We agree with the authors' paper that "the small increases in temperature and oxygen use after talc pleurodesis ... might be due to mild systemic and lung inflammation caused by talc". In their European cohort, 60.7% of the patients were using oxygen on day 1 and 56.8% still required supplementation 48 h after pleurodesis. A rise in the volume of supplemental oxygen of 0.25 l/min ( $p=0.001$ ) on day 1 and 0.21 l/min ( $p=0.025$ ) on day 2 was noted. We recognise that oxygen therapy was not included in the protocol for this study, so it is difficult to know if supplementation was "needed" or just "given". However, this means the dataset is uninformative about talc-induced hypoxaemia; it does not exclude it. In a randomised comparison of talc types (in which oxygen therapy was included in the protocol), 12/21 patients (57%) had an increase in their alveolar-arterial oxygen gradient after large talc (in 4/21 (19%) this was by >2 kPa), and 17% had an arterial oxygen tension of <8 kPa.<sup>3</sup>

We believe that carefully executed studies of pleurodesis, such as the European cohort study, have begun to cast light on the details of what happens to patients receiving talc pleurodesis, to the great benefit of clinical care. This growing evidence base is identifying yet more questions (such as whether and how large particle talc may produce hypoxaemia), and further large studies will help clarify these questions.

**H E Davies, Y C G Lee, R J O Davies**

Centre for Respiratory Research, Rayne Institute, University College London, London, UK

**Correspondence to:** Professor R J O Davies, Oxford Centre for Respiratory Medicine, Churchill Hospital, Oxford OX3 7LJ, UK; robert.davies@ndm.ox.ac.uk

**Competing interests:** None.

Accepted 13 November 2008

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## Progressive diffuse pulmonary Langerhans cell histiocytosis improved by cladribine chemotherapy

Langerhans cell histiocytosis (LCH) is a group of disorders characterised by monoclonal proliferation of histiocytic cells (Langerhans cells) producing tumour-like masses in multiple organs including the bone, skin, lymph nodes and central nervous system. In contrast to multiorgan LCH, pulmonary LCH (PLCH) usually involves only a single organ and presents as an infiltrative lung disease. PLCH is strongly correlated with smoking and presumably reflects reactive Langerhans cell proliferation triggered by some inhaled agent.<sup>1</sup> In early cellular PLCH, Langerhans cells aggregate in multiple small bronchiolocentric granulomas which may further cavitate to form inflammatory thick-walled cysts, usually predominating in the upper lobes. With disease progression, PLCH may evolve towards irreversible lung destruction by cicatricial fibrotic thin-walled cysts, respiratory insufficiency and death or lung transplantation.<sup>1</sup>

No treatment has hitherto proved effective in PLCH. Tumour-like LCH has been reported to respond to cladribine (2-chlorodeoxyadenosine),<sup>2–4</sup> a chemotherapeutic agent cytotoxic for lymphocyte and monocyte cells. Cladribine was also observed to have an effect in one case of tumour-like LCH involving the lung.<sup>5</sup> One patient with PLCH improved after multiple treatments including cladribine, but the effect of this agent could not be clearly established.<sup>6</sup> Whether cladribine as a single agent is effective in PLCH presenting as infiltrative lung disease is currently unknown. We report the effect of cladribine chemotherapy in one patient with PLCH presenting as infiltrative lung disease with progressive lung function impairment.

A 39-year-old woman presented with dry cough, dyspnoea class II NYHA, fatigue and weight loss. She had smoked 1.5 packs/day between the ages of 25 and 27 years, then reduced her consumption to 1 cigarette/day and had maintained it unchanged since then. Between the ages of 22 and 31 years she was exposed to passive smoking while working as a nurse in a psychiatric hospital. Clinical examination was unremarkable. There were no features of extrathoracic