

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 thoracoscopic talc poudrage performed without intubation, under local anaesthesia with moderate sedation.<sup>5</sup>

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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.

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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 bronchiocentric 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