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Authors' response

We would like to thank Dr Parisinos for his letter and interest in our study on the role of Th17 cells in sarcoidosis.¹ His recent report on the development of sarcoidosis in two patients affected by Crohn's disease and treated with natalizumab² further highlights the indubitable link existing between the immune pathogenesis of the two disorders. In fact, sarcoidosis and Crohn's disease are both characterised by an abnormal cell-mediated immune response to still unknown factor(s) that ultimately leads to granuloma formation and tissue damage. Furthermore, in both diseases Th1 and Th17 cytokines play a crucial role in the development of immune reactions taking place in the involved organs. Interestingly, the presence of IL-17-producing T cells marks out other immune-mediated and chronic inflammatory diseases that have been described to be associated with sarcoidosis, such as systemic lupus erythematosus, autoimmune chronic hepatitis, multiple sclerosis, coeliac disease and ulcerative colitis.

In the cases described by Parisinos *et al*, the use of natalizumab might represent an intriguing therapeutic option for its direct function (ie, the inhibition of the $\alpha 4$ -mediated adhesion of leucocytes to their counter-receptors) and even for its effects on T cells, particularly on regulatory T cells (FoxP3 + Tregs), that are expanded by the treatment with natalizumab.³ This issue raises a number of questions that should be addressed. First, considering that sarcoidosis is characterised by an abnormal expression of Tregs that, from a functional point of view, are unable to totally suppress TNF α and IFN γ secretion and granuloma formation,⁴ it remains to be established whether the induction of a strong Treg response may really favour the recovery of the disease. Furthermore, keeping in mind that cytokines that are released during both Crohn's and sarcoid inflammatory processes, such as IL-6, TGF- β and IL-1 β , are able to convert naive T cells and/or Tregs into Th17 lymphocytes via STAT3 expression,⁵ the effect of

natalizumab on Th17 and Treg plasticity has to be tested in both diseases.

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GWAS in lung disease

We read with interest the recent article 'Genome-wide association studies in lung disease' by Artigas *et al*.¹ While we agree that a greater understanding of the biological pathways underlying disease development and progression (susceptibility) will be a major outcome from these genetic epidemiological studies, we suggest other benefits may also stem from this research.

The genetics of chronic obstructive pulmonary disease (COPD) and lung cancer represent unique models for the genetics of lung disease because they result in the main from a 'single' measurable and preventable environmental exposure (cigarette smoking). That we can stratify for smoking exposure in these genetic association studies is critical to disease gene discovery and study design, as many of the underlying 'susceptibility genes' only become clinically evident (ie, expressed as disease) after several decades of daily smoking exposure. In studies of lung cancer, where cases and controls are carefully stratified by smoking exposure it appears the genes

relevant in smokers are distinct to those in non-smokers.^{2,3} When smokers are stratified by smoking exposure and lung function, it appears that genes implicated in lung cancer overlap with those implicated in COPD.³ This might explain why COPD predates lung cancer in up to 80% of cases, conferring a two- to sixfold greater risk compared with smokers with normal lung function. By stratifying for COPD (lung function), this approach has also identified genes conferring a 'protective' effect in lung cancer (ie, found in healthy or resistant smokers).³ Until cigarette smoking is eradicated, understanding the biology of resistance to smoking may be of greater clinical relevance than that of susceptibility. Specifically, if the pathogenetic processes that protect smokers from COPD also protect them from lung cancer,^{3,4} then chemo-preventive approaches might target these pathways. Of more immediate clinical utility is the use of genetic data (from a cheek swab) to help identify smokers at the greatest risk of COPD and/or lung cancer.³ To this end, we and others have combined genetic data with known clinical variables (eg, COPD) to develop risk models for lung cancer.³ Preliminary studies suggest such gene-based risk assessment might help motivate some smokers to quit smoking^{3,5} and may help target those most in need of CT screening.³ We conclude that COPD and lung cancer GWAS studies have much to contribute to respiratory medicine notably the possible basis of differential responsiveness of smokers to smoking exposure, the link between COPD and lung cancer, and the potential to develop new strategies in prevention and early diagnosis.

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Chest drain insertion— training is the key, Seldinger or otherwise

We welcome Maskell *et al*'s timely editorial highlighting the shortfalls of safe chest drain insertion.¹ Modernising Medical Careers states that competence in chest drain insertion should be achieved as a part of core medical training but does not set out how this might be practically achieved. The authors suggest that chest drain insertion should not be a generic skill but be confined to respiratory teams. Where there is a large presence of chest physicians, this may be possible. Few hospitals can achieve this. Where all chest drains cannot be inserted by the chest team, all registrars who take part in

unselected acute medical take service should be trained.

Our trust, with seven chest physicians, has over the past 3 years addressed training by developing and validating a training module for chest drain insertion using a Porcine–Resin model. The module focuses on decision making and simulation training using the model with assessment using a direct observation of procedural skills; a session takes 4 h. Before proceeding to perform independently on patients, close supervision with feedback is provided until the trainee is deemed competent and confident. The West Midlands Deanery recognising the importance of training has funded a Teaching Fellow to train all Core Medical Trainees in the region using the module. We also run a training day for newly appointed Respiratory Registrars (ST3) as they lack experience and feel vulnerable.

The National Patient Safety Agency (NPSA) report² in May 2008 highlighted the risks associated with chest drain insertion. We conducted a postal survey of Lead Chest Physicians in all acute hospitals in England and Wales in August 2009, which showed training sessions and competency assessment were established in only 58 of the 110 hospitals that responded to the survey. There was no register of competent trainees in 76% of the departments. The NPSA's recommen-

dation on pleural procedures audits has only been implemented by 55% of the hospitals, 1 year on.

As we uphold the mantra 'It is not the gun that is dangerous, it's the person holding it', regular training courses need to be a formal part of the training curriculum and respiratory consultants' time should be recognised in their job plans.

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