

the reduction in the efficacy of IL-5 at 1 ng/ml reflects the capacity of this higher concentration to induce eosinophil adhesion (figure 1C). IL-5 preincubation before the addition of each GC caused a concentration-dependent inhibition of the proapoptotic effects of these compounds (figure 1D–F). This occurred without any significant shift in the GC concentration–response curves, suggesting non-competitive antagonism.

This is the first demonstration of the proapoptotic capacity of FF in eosinophils and confirms the high potency of this compound compared with DEX. Despite this higher potency, IL-5 could still over-ride the proapoptotic effects of FF, suggesting that the IL-5 transduction pathway has GC-resistant elements.⁵ Whether this can be modulated by strategies to overcome resistance such as phosphatidylinositol 3-kinase and mitogen-activated protein kinase inhibitors is as yet unclear.¹ In conclusion, this study suggests a mechanism underlying poor responsiveness of eosinophils to GCs and may help define therapeutic approaches to overcome GC resistance.

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Vigilance is also required for pulmonary tuberculosis in UK-born subjects

Over and above the recommendation that 'Clinicians should have a higher index of clinical suspicion of extrapulmonary tuberculosis in non-UK born cases',¹ due to an increasing proportion of non-UK-born cases during 1999–2006,¹ we also need to be vigilant for the possibility that UK-born individuals who have escaped early detection of pulmonary tuberculosis might subsequently present with advanced pulmonary tuberculosis (APT), as was the case in the USA during the period 1993–2006. During that period 160 661 notified cases of pulmonary tuberculosis were subdivided into those with APT (35 584 cases), characterised by cavitation on chest radiograph and acid-fast bacilli smear-positive sputum, and those without advanced disease, the latter amounting to 125 077 cases. Further analysis revealed that, during that period, the proportion of patients with APT 'increased greatest among whites (65.4%), the employed (63.3%), and US born (59.2%)'.² Accordingly, a recommendation, which also has relevance to the UK, was made that 'Additional efforts should concentrate on reducing time to treatment initiation in low-incidence areas and among groups traditionally seen as being at low risk for tuberculosis disease'.² Cautionary tales already abound in the tabloid press^{3–4} of white UK-born young (age range 25–41) professionals (and, in one instance, a law student) in whom the diagnosis of pulmonary tuberculosis was delayed because of under-recognition of the significance of presenting symptoms in primary care and, in one instance, also in secondary care. What also needs to be recognised is that extrapulmonary tuberculosis itself poses a threat of transmission of the disease to other people, given the fact that, in the event of positive sputum culture results despite normal chest x-ray findings,⁵ 'transmission of tuberculosis from smear-negative, culture-positive patients has been well documented in other settings'.⁵

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Authors' reply

Our study examined trends in extrapulmonary tuberculosis in the UK and investigated the factors associated with recent changes highlighting this to clinicians.¹ Jolobe summarises reports from the USA and anecdotal media coverage of patients in whom the diagnosis of pulmonary tuberculosis was delayed due to the perception of low risk in native-born patients who subsequently presented with advanced pulmonary disease. We have previously reported delayed diagnosis in these groups in the UK.² As pulmonary tuberculosis is the infectious form of the disease with significant consequences of delayed diagnosis on the control effort and possible adverse clinical outcomes, we agree that the index of suspicion in patients with signs and symptoms suggestive of pulmonary tuberculosis should remain high.

This, however, raises an important clinical conundrum about uncommon illnesses. Among UK-born white adults aged 15–45 years, only 299 of 375 cases were reported with pulmonary tuberculosis. The number of cases in this subgroup of the population has remained relatively stable. A significant proportion of these will be individuals with other risk factors for tuberculosis such as homelessness and drug use or identified as contacts of a case of infectious tuberculosis. If every person with, for example, a cough lasting 3 weeks is investigated for tuberculosis, this will result in significant unnecessary investigation, especially in primary care. With <9000 cases in a population of 60 million, the majority of whom are resident in urban areas,³ the average general practitioner in a rural area in

the UK may not see a single case of tuberculosis in several years.

Nevertheless, given the consequence of pulmonary tuberculosis to the individual and society, it is appropriate for clinicians and general practitioners to ensure that tuberculosis is among the differential diagnoses in patients with relevant symptoms and signs and to investigate for tuberculosis fairly promptly. Every attempt should be made to obtain a microbiological diagnosis. As Jolobe points out, it is also true that patients with smear-negative culture-positive tuberculosis can transmit infection, although less so than those who have a positive smear from direct sputum examination.⁴ Exclusive extrapulmonary tuberculosis is, however, not infectious and the suggestion to the contrary is erroneous.

In view of the current rise in the incidence of tuberculosis, without high case detection and the adequate treatment of cases, tuberculosis may not remain an uncommon illness in the UK. Vigilance for both

pulmonary and extrapulmonary tuberculosis is required.

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CORRECTION

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The paper entitled “Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis” by G J Rodrigo and J A Castro-Rodriguez (*Thorax* 2005;**60**:740–746. doi:10.1136/thx.2005.047803) was published twice online first, on one of those occasions with an incorrect DOI (doi:10.1136/thx.2005.040444).