known to be HIV positive and were excluded from further analysis. Of the remaining 236, 131 (56%) were offered an HIV test. 109 (83%) of those offered took this up and 18 (17% of sample tested, 8% of all TB patients) were found to be HIV positive.

When subjects were divided on the basis of where the diagnosis of TB was made, striking differences in HIV rates were noted (table 1). Inpatients were much more likely to be offered, to accept, and to test positive on HIV testing. There was no difference in the demographic parameters between inpatients and outpatients, although inpatients tended to have more symptoms and to be smear positive (data not shown). Where no HIV test was offered, we found common themes in patient care. The most important of these was a lack of TB nurses to offer testing, and patients being diagnosed outside the focused TB service. A problem specific to the outpatient setting was the lack of appropriate TB service. A problem specific to the out-patient setting was the lack of appropriate clinic space in which to discuss HIV testing.

The most common reason given by patients who declined to undergo testing was a perceived inability to cope with the dual diagnosis (46% of cases), especially if the initial diagnosis of TB itself had been difficult to deal with. Such individuals would rarely agree to further discussion on HIV testing at a later date. Other reasons—such as patients regarding themselves to be at low risk of HIV infection—were much less frequently reported (10%).

The overall high rate of HIV co-infection is in line with other metropolitan studies. Our data, as well as that of others, may appear to suggest that we should predominantly target inpatients (in whom the rates of HIV were 20 times greater than in outpatients). However, given the increasing HIV/TB rates in the UK, we feel that this is a short sighted approach as we would expect that more individuals will present with TB as their first HIV related illness in an outpatient setting.

HIV testing was unacceptable to some patients. There is need for in-depth qualitative analysis to explore issues such as the timing of the discussion on HIV testing and the belief systems and coping mechanisms of individuals.

Despite attempts to provide a focused HIV testing service within our TB clinics, we find low rates of uptake. Much of this stems from an apparent failure to offer testing to almost half our patients. This may be an overestimate as it is conceivable that other healthcare workers might have discussed testing but not documented it in the patient’s notes. Data systems need to be implemented which can accurately capture this information.

Achieving HIV testing targets will require dedicated resources as well as improvements in both staff and patient education. This would argue for a greater interaction between local TB and HIV services.

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### Table 1

<table>
<thead>
<tr>
<th>Outpatients</th>
<th>Inpatients</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offered HIV test</td>
<td>88 (49%)</td>
<td>43 (74%)</td>
</tr>
<tr>
<td>Accepted HIV test</td>
<td>61/88 (69%)</td>
<td>42/43 (98%)</td>
</tr>
<tr>
<td>HIV positive</td>
<td>1/61 (2%)</td>
<td>17/42 (40%)</td>
</tr>
</tbody>
</table>

* χ² test; † Fisher’s exact test.
disorders and ischaemic heart disease, the ITT is a safe test when performed in experienced centres. Indeed, a review of >6500 ITTs reported that only seven patients (0.1%) experienced an adverse event, all of which reversed following intravenous glucose. To our knowledge, only two studies have used the ITT to investigate the HPA axis in asthmatic children treated with inhaled fluticasone. The first reported an inadequate response to insulin-induced hypoglycaemia in three children taking 1000–2250 μg/day. In the second study, nine of 18 subjects treated with 250–750 μg/day fluticasone for up to 16 weeks exhibited evidence of adrenal suppression which recovered following cessation of treatment.

Finally, as hypopituitary of probable autoimmune aetiology has been reported in patients with sarcoid disease, the possibility that autoimmune hypophysitis contributed to the patients’ symptoms and pituitary deficiency cannot be definitely excluded.

In summary, this report suggests that inhaled (together with intranasal) fluticasone may suppress the HPA axis in adults and that symptomatic adrenal insufficiency may develop, particularly if dosing is variable and intermittent. These cases illustrate that clinical and subclinical signs may alert the physician to the possibility of adrenal suppression which can then be confirmed using basal and/or stimulated tests of HPA function in selected patients. Further investigation to determine the prevalence of these effects in adult patients is warranted.

### Table 1: Baseline biochemistry and peak cortisol levels following insulin induced hypoglycaemia in two female adult patients taking inhaled/intranasal corticosteroids

| Patient | Baseline cortisol (200–600 nmol/l) | 08:00 cortisol (200–600 nmol/l) | 08:00 ACTH (<12 pmol/l) | Free thyroxine (10–21 pmol/l) | Thyroid stimulating hormone (0.3–4 μU/l) | Prolactin (50–370 μU/l) | Luteinising hormone (IU/l) | Folic acid stimulating hormone (IU/l) | α-subunit (IU/l) | Anti-microsomal antibodies | Results of insulin tolerance test | Minimum blood glucose (<2.2 mmol/l) | 30 minute cortisol (nmol/l) | 60 minute cortisol (nmol/l) | 90 minute cortisol (nmol/l) | 120 minute cortisol (nmol/l) | Peak growth hormone (<13 μU/ml) |
|---------|----------------------------------|---------------------------------|------------------------|--------------------------------|--------------------------------------|----------------------|--------------------------|-----------------------------|-----------------|--------------------------|-----------------------------|--------------------------------|---------------------|-----------------|-----------------|-----------------|--------------------------|----------------------|
| Patient 1 | 169/198                          | 116/198                         | 4.5                    | 0.54                           | 0.57                                | 224                 | 11/3                     | 1.3                         | 0.41             | Negative       | <1.0                        | 1.9                          | 327                 | 430             | 450             | 227             | 40.3                      |
| Patient 2 | 113/198                          | 4.5                             | 2.8                    | 0.79                           | 1.77/1.95                           | 224                 | 11/3                     | 26/18.4                     | 0.41             | Positive        | 1.0                         | 1.9                          | 327                 | 430             | 450             | 227             | 40.3                      |

Normal ranges and units are in brackets. "Normal" peak cortisol level following hypoglycaemia >550 nmol/l. When more than one value is quoted, the tests were performed on different days.

### References


### BTNL2 gene variant and sarcoidosis

Sarcoidosis is an inflammatory granulomatous disorder that primarily affects the lungs and lymph nodes. Other organs such as the brain, eyes, heart, and skin can also be affected. The disease is characterised by non-casing granulomas and an exaggerated cellular immune response caused by increased interleukin-12 activity. The course of the disease is acute and mild in approximately 20% of all patients. In most patients a chronic stage develops which can lead to lung fibrosis. Although the exact pathogenesis of sarcoidosis remains unclear, familial clustering of the disease and the increased risk of relatives to develop sarcoidosis suggest that there might be a genetic predisposition to develop the disease.

A significant association was recently reported in Germany between sarcoidosis and a frequent single nucleotide polymorphism (SNP) in the BTNL2 gene, rs2076530. BTNL2 is a member of the immunoglobulin gene family and is related to CD89 and CD86 co-stimulatory receptors, although its exact function is unknown. BTNL2 is located on chromosome 6p21.3 in close proximity to the HLA gene cluster. rs2076530 is located at position 1 of the donor splice site in intron 5 and the associated A allele causes the usage of an alternative donor site leading to a 4 bp deletion at the mRNA level, frameshift, and premature truncation at the protein level. The rs2076530 SNP alone was also associated with sarcoidosis in a case-control study of white American subjects. No replication of the BTNL2 rs2076530 susceptibility to sarcoidosis has yet been studied in an independent German case-control study. We therefore performed a case-control association study in 210 patients with sarcoidosis and 202 controls. Written informed consent was given by each participant and the study was approved by the ethics committee of Bonn University School of Medicine.

The diagnosis of sarcoidosis was based on evidence of non-caseating epithelioid cell granuloma in biopsy specimens and chest radiographic abnormalities. Different stages were defined as previously described. A chronic course was defined as disease over at least 2 years or at least two episodes in a lifetime. Acute sarcoidosis was defined as one episode of acute sarcoidosis which had totally resolved at the date of the examination. None of the individuals in the control group (healthy white German subjects of mean age 38.32 (15.53) years) had a history of lung disease or showed any symptoms of lung or other disease by chest radiography or laboratory blood tests. Genotyping of rs2076530 was performed using the Taqman technique with a commercially available assay (Applied Biosystems, Germany). SPSS version 12 was used for data entry and analysis. The genotype distributions in the cohort were in accordance with the Hardy-Weinberg equilibrium.

The A allele frequency of rs2076530 was significantly increased in sarcoidosis patients compared with controls (A = 0.6929, G = 0.3071 in cases; A = 0.6188, G = 0.3812 in controls). It was significantly associated with an increased risk of sarcoidosis in the dominant and recessive models (OR 3.46, 95% CI 1.27 to 9.36; p = 0.006, table 1), but not in a recessive model (p = 0.276). The calculated population attributable risk (PAR) for AA homozygotes and AG heterozygotes was 34.6%. Our results were in accordance with the reported association between BTNL2 and sarcoidosis and replicated the finding that A allele carriers of rs2076530 have a more than twofold increased risk of developing sarcoidosis compared to AA homozygotes in the German population.

We also examined whether this increased risk is present in both chronic and acute forms of sarcoidosis. Interestingly, we found that the chronic form— but not the acute form— was significantly associated with the A allele in the dominant and dominant models (OR 2.87...