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 glucocorticoids. To our knowledge, only two studies have used the ITT to investigate the HPA axis in asthmatic children treated with inhaled flunisolide. 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 for up to 16 weeks exhibited evidence of adrenal suppression which recovered following cessation of treatment.

Finally, as hypopituitarism 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 definitively 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 symptoms 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.

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doi: 10.1136/thx.2005.049643

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

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>40</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>27.4</td>
</tr>
<tr>
<td>Time to hypoglycaemia (minutes)</td>
<td>60</td>
</tr>
<tr>
<td>Baseline cortisol (nmol/l)</td>
<td>227</td>
</tr>
<tr>
<td>30 minute cortisol (nmol/l)</td>
<td>327</td>
</tr>
<tr>
<td>60 minute cortisol (nmol/l)</td>
<td>450</td>
</tr>
<tr>
<td>90 minute cortisol (nmol/l)</td>
<td>313</td>
</tr>
<tr>
<td>120 minute cortisol (nmol/l)</td>
<td>227</td>
</tr>
<tr>
<td>Peak growth hormone (&lt;1 µU/ml)</td>
<td>40.3</td>
</tr>
</tbody>
</table>

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.

On thyroxine.

References

4. Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy: A systematic review and meta-analysis. Intern Med 1999; 159:941–53

BTNL2 gene variant and sarcoidosis

Sarcoidosis is an inflammatory granulomatous disorder that primarily affects the lungs and lymphoid nodes. Other organs such as the brain, eyes, heart, and skin can also be affected. The disease is characterised by non-casating granulomas and an exaggerated cellular immune response caused by increased inflammatory 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 BTN2L2 gene, rs207653. BTN2L2 is a member of the immunoglobulin gene family and is related to CD89 and CD86 co-stimulatory receptors, although its exact function is unknown. The BTN2L2 gene is located on chromosome 6p21.3 in close proximity to the HLA gene cluster. rs207653 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 rs207653 SNP was also associated with sarcoidosis in a case-control study of white American subjects. Replication of the BTN2L2 rs207653 SNP 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 (15.33) 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 rs207653 was performed using the Taqman technique with a commercially available assay (Applied Biosystems, Germany). SPSS Version 12 was used for statistical analysis.

The genotype distributions in the cohort were in accordance with the Hardy-Weinberg equilibrium.

The A allele frequency of rs207653 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 codominant and dominant models (OR 2.95 (CI 1.24 to 4.23); 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 BTN2L2 and sarcoidosis and replicated the finding that A allele carriers of rs207653 have a more than twofold increased risk of developing sarcoidosis compared with 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 codominant and dominant models (OR 2.87).
(95% CI 1.29 to 6.42), p<0.0069; table 1) with a PAR for AA homozygotes and AG heterozygotes of 50%.

This study underlines the importance of the association of the rs2076530 variant with the susceptibility to develop sarcoidosis in a German population. Furthermore, our data suggest that susceptibility is preferentially towards the chronic form of the disease.

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Competing interests: none.

References

Table 1 Statistical analysis of the case-control study

<table>
<thead>
<tr>
<th></th>
<th>Co-dominant</th>
<th></th>
<th></th>
<th></th>
<th>Dominant (AA/AG v GG)</th>
<th></th>
<th></th>
<th></th>
<th>Recessive (AA v AG/GG)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA</td>
<td>AG</td>
<td>GG</td>
<td>P value</td>
<td>AA</td>
<td>AG</td>
<td>GG</td>
<td>OR (95% CI)</td>
<td>P value</td>
<td>AA</td>
<td>GG</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Controls</td>
<td>84</td>
<td>41</td>
<td>4</td>
<td>82 (41%)</td>
<td>166</td>
<td>36</td>
<td></td>
<td>2.31 (1.27 to 4.23)</td>
<td>0.006</td>
<td>84</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>99</td>
<td>47</td>
<td>4</td>
<td>93 (44%)</td>
<td>192</td>
<td>18</td>
<td>2</td>
<td>1.29 (0.68 to 3.28)</td>
<td>0.576</td>
<td>99</td>
<td>111</td>
<td>1.25 (0.85 to 1.85)</td>
</tr>
<tr>
<td>Sarcoid</td>
<td>30</td>
<td>42</td>
<td>4</td>
<td>45 (22%)</td>
<td>32</td>
<td>9</td>
<td>1</td>
<td>1.49 (0.68 to 3.28)</td>
<td>0.358</td>
<td>30</td>
<td>41</td>
<td>0.99 (0.57 to 1.71)</td>
</tr>
<tr>
<td>Acute</td>
<td>59</td>
<td>52</td>
<td>4</td>
<td>47 (24%)</td>
<td>106</td>
<td>6</td>
<td>2</td>
<td>2.87 (1.29 to 6.42)</td>
<td>0.007</td>
<td>59</td>
<td>55</td>
<td>0.87 (0.43 to 1.71)</td>
</tr>
</tbody>
</table>

Significant associations are shown in bold.

Reference

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In the paper entitled “No increase in the prevalence of asthma, allergies, and atopic sensitisation among children in Germany: 1992–2001” by I K Zöllner et al which appeared in the July 2005 issue of Thorax (2005;60:545–8), the authors apologise for a mistake which occurred in the reference list. Reference number 18 should be number 21 and references 19–21 should be listed as 18–20.

doi: 10.1136/thx.2005.040444corr1

The paper entitled “Antihistamines 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 (10.1136/thx.2005.040444) has been published previously on 17 June 2005 as a Thorax Online First article but under the incorrect DOI (10.1136/thx.2005.047803). The publishers apologise for this error. The definitive version of the article can be found at the following citation: Thorax 2005;60:740–6.

doi: 10.1136/thx.2005.040881corr1

In the paper entitled “Hormone replacement therapy, body mass index and asthma in perimenopausal women: a cross sectional survey” by F Gómez Real et al published in the January 2006 issue of Thorax (2006;61:34–40), the fourth author should be K A Franklin, not K Franklin.

In asthma and allergies in Germany

We read the study by Zöllner and colleagues published recently in Thorax about the leveling off of asthma and allergies among children in Germany between 1992 and 2001.1 We have published a study looking at the lifetime prevalence of asthma and hay fever, except in one subgroup. The effect found in 13–14 year old girls could also be due to a former underdiagnosis of asthma in girls, as discussed in their paper.

Since our results are based on six cross sectional surveys, we consider the title and the conclusion—that we did not see an increase in asthma and allergies from 1992 to 2001—to be appropriate.

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In their investigation Maziak et al did not find a significant increase in the lifetime prevalence of asthma and hay fever, except in one subgroup. The effect found in 13–14 year old girls could also be due to a former underdiagnosis of asthma in girls, as discussed in their paper.

Since our results are based on six cross sectional surveys, we consider the title and the conclusion—that we did not see an increase in asthma and allergies from 1992 to 2001—to be appropriate.

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BTNl2 gene variant and sarcoidosis

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