Prediction of obeche wood-induced asthma by specific skin prick testing

T. Hannu, I. Lindström, P. Palmroos, O. Kuuliala and R. Sauni
Finnish Institute of Occupational Health, Finland.

Background
It has previously been shown that a positive skin prick test (SPT) result is a good predictor of a positive specific inhalation challenge (SIC) in patients with occupational asthma (OA) related to wheat or rye flours. This association has not been previously studied in OA attributable to obeche wood.

Aims
To describe a clinical series of patients with OA induced by obeche wood. To investigate if the SPT result can be used as a predictor for the outcome of SIC tests.

Methods
OA was diagnosed according to patient history, lung function examinations and SIC tests, as well as the determination of obeche SPTs. We analysed sensitivity, specificity and positive (PPV) and negative predictive values (NPV) at different wheal sizes of the SPTs and drew receiver-operating characteristic plots using the SIC test result as the gold standard.

Results
Obeche wood SIC tests were performed on 34 symptomatic workers. Of these, 27 workers had a positive test result and were diagnosed as having OA. The minimal cut-off value with a PPV of 100% was an SPT wheal of 3.5 mm from obeche wood. This means that all workers with a wheal size of ≥3.5 mm from obeche wood had a positive SIC.

Conclusions
Positive SPT results in symptomatic workers were good predictors of a positive SIC. SIC with obeche wood may be unnecessary in strongly sensitized workers.

Key words
Inhalation challenge test; occupational asthma; skin prick test; wood dust.

Introduction
For some wood types, including obeche (*Triplochiton scleroxylon*) wood dust, immunoglobulin E sensitization has been demonstrated on patients diagnosed with occupational asthma (OA) [1]. In Finland, obeche wood has been used as a moisture and heat resistant wood material in saunas and also in furniture, plywood and framing production. The literature contains several case reports of OA induced by obeche wood [2–5], but no analysis exists of large patient series from clinics of occupational medicine.

The specific inhalation challenge (SIC) of a suspected occupational agent is considered the gold standard for diagnosis of OA [6]. However, the SIC can be a time-consuming and expensive method because it is often carried out on inpatient wards. Moreover, SIC can provoke severe reactions and exacerbate asthma. This has led clinicians to find other methods for confirming the diagnosis of OA, such as prediction of SIC results by measurements of skin prick tests (SPT) [7].

We describe a clinical series of symptomatic workers exposed to obeche wood dust, in whom OA was confirmed with a SIC. We investigated also if SPT results could predict the outcome of the SIC.

Methods
The patient register of the Finnish Institute of Occupational Health (FIOH) from 1980–2008 was used to identify all the patients who had undergone obeche wood SICs due to a clinical suspicion of OA. FIOH's Ethical Committee approved the study.

SPTs for common environmental allergens (ALK-Abello A/S, Copenhagen, Denmark) as well as obeche wood were performed as reported previously [8]. Histamine hydrochloride (10 mg/ml) was used as the positive control. A positive reaction was defined as a wheal diameter of ≥ 3 mm in the absence of a reaction to the diluent and in the presence of a positive reaction to histamine hydrochloride.
OA was diagnosed according to European guidelines [9]. SICs were performed in a 6 m³ challenge chamber on the consecutive days, each with a 24 hour follow-up [10]. In the control challenge the patient was exposed to lactose powder for 30 min. The challenge with obeche dust was done as such or diluted with lactose 1:10–1:2 (depending on the level of sensitization) and lasted until a positive reaction occurred, or for 30 min at most. The SIC was considered positive for OA when forced expiratory volume in 1 second or peak expiratory flow fell substantially by ≥20% of the pre-challenge value in the obeche challenge without significant changes in the control challenge.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with 95% confidence interval (CI) values were calculated for wheal size in the obeche dust SPT. The golden standard was the obeche dust SIC results. Receiver operating characteristic (ROC) plot was drawn and the area under the curve (AUC) value was calculated. Wheal sizes in workers with a positive or negative challenge test result were compared with the Mann–Whitney U-test. The analyses were performed using the SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA). A P-value of <0.05 was considered significant.

Results

From FIOH’s patient register, we identified 34 eligible patients. They were mostly carpenters, construction workers, painters and sawmill workers. Of these patients, 27 (79%) had a positive SIC with obeche and were diagnosed with OA, and seven (21%) had a negative SIC (Table 1).

All patients with OA suffered from work-related lower respiratory symptoms. Twenty-three also had symptoms of rhinitis and 11 had conjunctival symptoms. During the SIC, the asthmatic reaction was immediate (occurred during the first post-challenge hour) in all patients and 21 patients (78%) had a positive SIC with obeche dust, have verified asthma, and the association of lower respiratory tract symptoms related to exposure to obeche dust, have verified asthma, and the association of workplace exposure and asthma should be established. However, in instances where only low-grade sensitization exists or when there is no evidence of sensitization at all, SIC tests should be considered necessary.

In workers challenged with obeche wood (n = 34), wheal sizes from obeche wood ranged from 0 to 10 mm (median 5 mm). The AUC of the ROC plot for SPT was 0.89 for obeche wood. Sensitivity, specificity, PPV and NPV were calculated for a cut-off value of ≥ 3 mm (Table 2). Using obeche wood SPT, sensitivity was 74% (95% CI: 59–89), specificity 86% (95% CI: 74–98), PPV 95% (95% CI: 88–102) and NPV was 54% (95% CI: 37–71). Wheal sizes were significantly greater in workers with positive challenge test (n = 27) (median 5 mm, range 0–10 mm), than in those with negative challenge test (n = 7) (median 0 mm, range 0–3 mm, P = 0.002). The optimal cut off value that maximized the sum of sensitivity and specificity was 3.5 mm for obeche wood according to ROC analysis. This was also the minimal cut-off value for a PPV of 100% (Table 2). This finding means that all workers with a wheal size of ≥3.5 mm from obeche wood (n = 18) had a positive SIC.

Discussion

Our patients were mainly middle-aged men, which is in accordance with previous studies [2–4]. Over 60% of them were atotics, whereas the corresponding figure was 100% in a series comprising seven patients [10]. The mean duration of exposure to obeche dust prior to onset of respiratory symptoms was 5 years. This was somewhat longer (7.5 years) in a series of eight patients [2]. Most of our patients had nasal symptoms and ~40% of them also had conjunctival symptoms, which is in line with prior studies [3–5]. Overall, our clinical findings based on nearly 30 patients confirm the results obtained from previous case studies.

According to our findings, if the obeche SPT reaction was ≥3.5 mm, all patients had a positive SIC. Clinically, the present results indicate that SIC tests may be unnecessary in strongly sensitized workers in OA examinations. The patient should naturally also have lower respiratory tract symptoms related to exposure to obeche dust, have verified asthma, and the association of workplace exposure and asthma should be established. However, in instances where only low-grade sensitization exists or when there is no evidence of sensitization at all, SIC tests should be considered necessary.

Of note, our results are only applicable to a selected population (symptomatic workers exposed to obeche

| Table 1. General characteristics and allergologic examinations of study patients |
|---------------------------------|----------------|----------------|
| Age, mean (min-max), years      | 40.4 (21–59)  | 40.1 (29–58)  |
| Male, n (%)                     | 25 (93%)      | 5 (70%)       |
| Smoking status, current/ex/never, n | 8/8/11       | 3/1/3         |
| Duration of exposure at work prior to onset of respiratory symptoms, mean (range), years | 5.4 (1–20) | 3.3 (1–7) |
| Atopy*, n (%)                   | 17 (63%)      | 4 (57%)       |
| Positive SPT to obeche wood, n (%) | 20 (74%)     | 1 (14%)       |
| Wheal size of SPT from obeche wood, median (range), mm | 5 (0–10) | 0 (0–3) |

*One or more positive reactions in SPTs to environmental allergens.
wood dust in the clinical examinations for OA) and cannot be applied to the general population.

The relationship between SPT and the outcome of the SIC has rarely been investigated with occupational allergens [7]. In a study by van Kampen et al., all the patients had a positive SIC with wheat flour, if the wheat SPT was ≥5.0 mm [7]. Similarly, if the rye SPT was ≥4.5 mm, the SIC with rye flour was positive in all patients.

### Key points
- A positive obeche skin prick test result was a good predictor of positive specific inhalation challenge in symptomatic workers exposed to obeche wood dust.
- Specific inhalation challenge with obeche wood may be unnecessary in strongly sensitized workers.
- Where only low-grade sensitization exists, specific inhalation challenge should be considered necessary.

### Conflicts of interest
None declared.

### References

### Table 2. Sensitivity, specificity and PPV and NPV of SPT for obeche using an obeche dust-based SIC as a golden standard

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>Positive SPT</th>
<th>Negative challenge</th>
<th>Negative SPT</th>
<th>Positive challenge</th>
<th>Negative challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive SPT</td>
<td>Negative SPT</td>
<td>Positive challenge</td>
<td>Negative challenge</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive SPT</td>
<td>Negative SPT</td>
<td>Positive challenge</td>
<td>Negative challenge</td>
<td></td>
</tr>
<tr>
<td>≥3 mm</td>
<td>20</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>≥3.5 mm</td>
<td>18</td>
<td>0</td>
<td>9</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Evaluation was performed using minimal cut-off and cut-off for which 100% PPV was obtained.