Sino-nasal cancer and exposure to leather dust

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**Background** In 1987, the International Agency for Research into Cancer classified shoemaking and cobbling as a definite human carcinogen. However, there are 10 times fewer articles published on Medline compared to wood dust which also induces sino-nasal cancer.

**Aim** To improve the medical, technical and social management of this type of cancer in the shoe trades.

**Methods** A literature review was conducted by two independent experts to identify articles describing epidemiological studies of this link (with no stipulated time frame).

**Results** The search resulted in 14 studies, including one meta-analysis of case–control studies: four out of five of the case–control studies found an excess risk associated with exposure to leather dust. Of five cohort mortality studies, excess risk was found in all studies conducted in the shoe trades but not in the tanning industry. The four studies of the incidence of sino-nasal cancer confirm the excess risk in shoemaking.

**Discussion** In the shoe trades, there is an excess risk of sino-nasal cancer, especially among those working in shining, finishing and shoe repair. Incidence levels among employees are estimated at 1–7/100 000 depending on the specific job. The risk fraction which can be attributed to this type of exposure for this cancer in France is estimated at 3%. In the light of these findings, all involved should be made aware of the link and motivated (as has already been done in the wood industries) to get this occupational disease recognized as such for the shoe trades.

**Key words** Dust; epidemiology; leather; paranasal sinus neoplasm; review.

**Introduction**

The leather trades in which workers are exposed to leather dust include shoemaking and the production of leather clothes and other leather goods. The workers who are most exposed are those involved in cutting, assembly, buffing, finishing and shining. Among the occupational causes of sino-nasal cancer, the International Agency for Research into Cancer (IARC) has classified wood dusts [1] as definitely carcinogenic (Group 1) although the exact carcinogenic factors have not been precisely identified [2,3]. They have also implicated work in the manufacture and repair of leather goods [4,5]. Although in the wood trades, the link with sino-nasal cancer has led to measures to reduce the level of dust and monitor workers’ health as well as recognition as an occupational disease, the same is not true in the leather trades. In this context, there is less scientific consensus and preventive measures have not been implemented to the same extent (by occupational health experts and others) so workers are not adequately protected against this risk. A brief consultation of Medline since 1987 [when the shoemaking trades were classified as definitely carcinogenic (Group 1) by the IARC] finds nearly 200 articles on ‘wood’ + ‘dust’ whereas ‘leather’ and ‘dust’ finds only 20.

The purpose of this study was to perform a systematic review of the literature on the excess risk of cancer of the nasal fossae linked to exposure to leather dust, to define the number of cases in France and to raise awareness in the profession of the need for improved management—technical, medical and social—of this risk in certain leather-related occupations.

**Methods**

This work involved a search for sino-nasal cancers in the National Occupational Disease Surveillance and Prevention Network (RNV3P, Réseau National de Vigilance
et prevention de Pathologie Professionnelle) to highlight the proportion of cancer cases that are potentially related to leather dust, and then a systematic review of the literature.

Since 1 January 2001, the RNV3P network has systematically registered in a standardized format all occupational health problems (OHPs) reported to 29 Occupational Disease Consultation centres based in University Hospitals. Patients are referred to these centres by various physicians (occupational health, general practitioners and hospital physicians) for the diagnosis of an occupational aetiology for their disease [6]. An OHP corresponds to an association between an occupational disease (possibly combined with one or two co-morbidities) and a certain occupational environment, i.e. the associated occupational hazard (one to five) as well as the relevant trade and type of activity. For each hazard, be it toxicological, physical or psychosocial, the experts attribute a degree of causality (strong, moderate or weak).

The literature search was performed by two readers of the Medline and INRS databases as well as the Google Scholar search engine, who selected articles independently on the basis of the criteria defined below. In the rare cases of disagreement (fewer than 5%), consensus was sought. The inclusion criteria were articles published in English and Italian since 1980 (last search performed on 30 November 2006) containing the following keywords: dust + leather, shoemaker, sino-nasal cancer, ethmoid cancer. Articles which did not present any epidemiological results were excluded.

### Results

A search in the RNV3P database >5 years revealed 14 malignant tumours of the facial sinuses, of which nine were specifically encoded as ethmoid cancer. Table 1 shows the corresponding hazards which were classified by the experts as strongly, moderately or possibly causal. Exposure to leather dust was not classified as a hazard in any case. In 11 cases, exposure to wood dust was classified by the experts as strongly causal. In one case welding fumes and in another exposure to crystalline silica were both deemed strongly causal, and in a third case, exposure to calcium hydroxide was judged weakly causal.

The literature review identified 24 papers with the keyword association; eight papers were excluded as they did not present data on leather dust exposure. After comparison and harmonization of the results of the two experts’ searches, 16 articles were identified corresponding to 15 different studies, namely, five case–control studies, five mortality cohorts, four cancer incidence cohorts and one meta-analysis.

Table 2, which includes the five case–control studies of sino-nasal cancer and leather dust exposure [7–10,11], shows an excess risk of sino-nasal cancer associated with exposure to leather dust as well as wood dust in four of the five studies in which such an association was investigated. The work by Comba et al. [7] shows that the link between sino-nasal cancer and shoemaking is stronger than that with exposure to wood dust; the study of Merler et al. [8] conducted in the shoe-making industry detected a dose–response correlation. No excess risk was detected in the tanning industry (in which the mode of exposure is different) in any of these studies.

A combined meta-analysis of seven European case–control studies of sino-nasal cancer [12] includes the two European studies shown in Table 1 [7,8] and five other studies carried out in sectors of industry other than shoemaking which included a total of 555 cases and 1705 controls. This meta-analysis revealed an overall estimate of risk associated with exposure to leather dust in men as follows: OR of 1.92 (1.10–3.35); this is of the same order as that associated with wood dust [OR = 2.36 (1.75–3.20)] and formaldehyde [OR = 1.66 (1.27–2.17)].

The results of the cohort studies (mortality and incidence) are presented in Table 3. The four mortality studies conducted in shoemakers [13–16] show an excess mortality from sino-nasal cancer with, in the study of Pippard and Acheson [14], a very high SMR among shining and finishing workers [SMR = 1408 (457–3280)]. In contrast, no such excess risk was detected among tanners [16].

Of the two studies addressing cancer of the nasal cavities (Table 3), only that of Andersen et al. [17] conducted in the shoe-making industry showed any excess risk [Standardized Incidence Ratio = 2.94 (1.47–2.56)]; the other, conducted in the tanning industry, was of insufficient power to justify any firm conclusions [18].

Three incidence studies could not be included in Table 3 because the published data were insufficiently precise. Acheson et al. [19], analysing nasal cancer incidence figures from Northamptonshire (1950–79), showed an excess incidence in workers in the shoe-making industry even though they were only handling leather tanned

### Table 1. Sino-nasal cancer figures from the RNV3P database

<table>
<thead>
<tr>
<th>Tumour</th>
<th>CIM10 code</th>
<th>Wood</th>
<th>Leather</th>
<th>Other industrial substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant tumour of the ethmoidal sinus</td>
<td>C31</td>
<td>8</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Malignant tumour of the facial sinuses</td>
<td>C319</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>
Table 2. Case–control studies of sino-nasal cancer and leather dust exposure

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Country</th>
<th>Sino-nasal cancer</th>
<th>Numbers</th>
<th>Prevalence of exposure</th>
<th>OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cases</td>
<td>Controls</td>
<td>Exposure</td>
</tr>
<tr>
<td>Comba et al. [7]a</td>
<td>1982–1987</td>
<td>Italy</td>
<td>Epithelial neoplasm</td>
<td>78</td>
<td>254</td>
<td>Leather industry 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Shoemakers –</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Leather tanners 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Woodworkers 14</td>
</tr>
<tr>
<td>Merler et al. [8]a</td>
<td>1968–1982</td>
<td>Italy</td>
<td>Adenocarcinoma</td>
<td>21</td>
<td>42</td>
<td>Heavy leather dust exposure 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Light leather dust exposure 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Heavy leather dust exposure 11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Light leather dust exposure 7</td>
</tr>
<tr>
<td>Bimbi et al. [10]</td>
<td>1982–1985</td>
<td>Italy</td>
<td>Epithelial neoplasm</td>
<td>53</td>
<td>217</td>
<td>Leather industry 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Woodworkers 3</td>
</tr>
<tr>
<td>Meta-analysis of seven European case-control studies of sino-nasal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t’Mannetje et al. [12]</td>
<td>1979–1990</td>
<td>Italy (3)</td>
<td>Women</td>
<td>4</td>
<td>9</td>
<td>Wood dust 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>15</td>
<td>41</td>
<td>Formaldehyde 15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>France</td>
<td></td>
<td>7</td>
<td>7</td>
<td>Leather dust 2.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Netherlands</td>
<td></td>
<td>168</td>
<td>389</td>
<td>Wood dust 38.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Germany</td>
<td>Men</td>
<td>229</td>
<td>493</td>
<td>Formaldehyde 52.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sweden</td>
<td></td>
<td>26</td>
<td>42</td>
<td>Leather dust 5.9</td>
</tr>
</tbody>
</table>

$\sim$, not stipulated.

*aCase–control study included in the meta-analysis.
without chromium; no reduction was observed in recent years. Olsen [20] analysed 382 cases of sino-nasal cancer in the Danish cancer registry and showed an excess risk in men and women working in the shoemaking and leather industries using a little-used epidemiological instrument, the standardized proportional incidence ratio (SPIR = 1386). Analysis of a series of 110 successive cases of sino-nasal cancer conducted from 1990 to 1993 in five Italian hospitals [21] found 26 people who had worked in the leather industry, including 23 who had worked as shoemakers or cloggers.

A histological classification is provided in a number of studies which focus on the shoe trades: adenocarcinoma accounts for 80% of cases according to Battista et al. [21], 88% according to Acheson et al. [19] and 75% according to Cecchi et al. [11]. This histological type appears to dominate sino-nasal cancer related to leather dust (as with wood dust) [12] whereas, in the Italian study (all different types of exposure taken together), it only represents 25% of cases in men and 14% in women [7]. According to the results of the meta-analysis [12], smoking is linked with the squamous cell carcinoma form and not adenocarcinoma.

### Discussion

This review of epidemiological surveys suggests that there is a major excess risk of sino-nasal cancer in the shoe-making and shoe-repair industries, especially for those involved in finishing operations (stitching, buffing and polishing) in which exposure levels to leather dust are particularly high [8,13,19]. The incidence of sino-nasal cancer is estimated at 7/100 000 in those involved in finishing shoes, and 1/100 000 for other jobs in the industry [21]. The study of Merler shows a significant dose–response effect in the profession (all histological types taken together).

The leather industry employs a total of 1.62% of French workers. Of these 5% are tanners, 64% shoe-makers and 25% involved in the manufacture of other leather goods [22]. The job–exposure matrix in the population as a whole compiled by the National Health Monitoring Institute (Institut National de Veille Sanitaire, the Matgéne Programme) [23] provides information on the levels of exposure to leather dust in France: 27% of employees in the leather industry are exposed to, 1 mg/m³, 40.2% to between 1 and 37 mg/m³, 14% to between 3 and 77 mg/m³ and 18% to >7 mg/m³; for 41% of these workers, the probability of exposure is >90%. It should be noted that exposure times tend to be short: 53% of those exposed endure 5 years of exposure or less. Applying this matrix to the 1999 French Census, it seems that 0.24% of men and 0.38% of women in the working population are exposed to leather dust. Estimates of the fraction of risk of sino-nasal cancer which can be attributed to leather dust ranges from 2.8 to 12.8% depending on the

### Table 3. Cohorts of leather workers and sino-nasal cancer

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Town</th>
<th>Cohort</th>
<th>Type of cancer</th>
<th>Observed cases</th>
<th>Expected cases</th>
<th>Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality Pippard</td>
<td>1939</td>
<td>England</td>
<td>5017</td>
<td>Shoemakers</td>
<td>2</td>
<td>0.51</td>
<td>SMR: 5.03 (0.61–18.18)</td>
</tr>
<tr>
<td>and Acheson [14]</td>
<td>1982</td>
<td>Shoe finishers</td>
<td>5</td>
<td>Sino-nasal cancer</td>
<td>5</td>
<td>0.36</td>
<td>SMR: 14.08 (4.57–32.86)</td>
</tr>
<tr>
<td>Costantini et al.</td>
<td>Italy</td>
<td>–</td>
<td>14</td>
<td>Shoemakers</td>
<td>14</td>
<td>2.25</td>
<td>SMR: 6.22 (3.7–9.7)</td>
</tr>
<tr>
<td>et al. [15]</td>
<td></td>
<td>Report of Baldasseroni study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fu [13]</td>
<td>1940</td>
<td>USA</td>
<td>4215</td>
<td>Shoemakers</td>
<td>12</td>
<td></td>
<td>SMR: 7.41 (3.8–12.9)</td>
</tr>
<tr>
<td>Italy (Firenze)</td>
<td>1993</td>
<td>Tanners</td>
<td>5</td>
<td>Sino-nasal cancer</td>
<td>1</td>
<td>1</td>
<td>SMR: 1</td>
</tr>
<tr>
<td>Incidence Andersen</td>
<td>1998</td>
<td>Finland</td>
<td>2026</td>
<td>Tanners</td>
<td>2</td>
<td>0.5</td>
<td>SIR: 3.77 (0.46–13.6)</td>
</tr>
<tr>
<td>et al. [17]</td>
<td>1989</td>
<td>Norway</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mikoczy et al.</td>
<td>1998</td>
<td>Sweden</td>
<td>10224</td>
<td>Tanners</td>
<td>2</td>
<td>0.5</td>
<td>SIR: 3.77 (0.46–13.6)</td>
</tr>
</tbody>
</table>

–, not stipulated; SIR, Standardized Incidence Ratio.
level of risk under consideration [3–7]. In the meta-analysis of five European studies [12], this attributable risk fraction (both genders and all histological types taken together) is estimated at 3% for leather dust and 18% for wood dust. According to Comba et al. [7], the fraction is 8% among leather workers and 21% among wood workers.

A meta-analysis was not performed as the review includes three different types of studies (case–control, mortality and cancer incidence). Moreover, within the same type of study, data risk levels differ depending on the occupational activities and histological types of nasal cancer detected; there are not sufficient data to provide an overall estimate of risk in each condition. However the meta-analysis carried out by t’Mannetje (Table 2) shows a statistically significant estimate of the risk from two European case–control studies in men.

No risk of sino-nasal cancer is found in the tanning industry in which operations are carried out in a damp environment [24]. However, there may be an excess risk for other forms of cancer, e.g. lung cancer (possibly due to chromium and arsenic-containing substances [25,26]) and soft tissue sarcoma (possibly related to chlorophenols) [14,18].

The RNV3P registry does not contain a single case of sino-nasal cancer in employees of the leather industries out of >22 000 occupational diseases referred to University Hospitals >4 years in all the countries: This is probably a reflection of the lack of awareness of such an association among physicians, who did not think of referring their patients to a specialist occupational physician. This situation is also compounded by the fact that the link has no medicolegal status. Another epidemiological factor to take into consideration is the fact that the cumulative duration of exposure among French workers is short.

In terms of aetiology, plant-derived tannins (which are also found in tree bark) may be a causative agent of ethmoid adenocarcinoma in wood workers, and also in leather workers [21].

Geographical differences in the risk of sino-nasal cancer have been attributed to the fact that the leather used in Britain is tanned using mineral oil and in the USA using vegetable oil [27]. Mention has been made of the presence of chromium salts carried over from the tanning process but there is still a risk of cancer in those working with leather tanned without any chromium salts [19]. Particle sizes have been measured in the dusts generated at various workstations in the shoe trade [28]. Although the mean concentrations of inhalable particles taken >8 h are of the order of 0.12–0.91 mg/m³, there may be high short-term (>1 min) fluctuations, e.g. 0.62–6.4 mg/m³ at finishing stations, and 0.1–14.57 mg/m³ in small shoe-repair units. The median particle diameter is of the order of 10 μm so the proportion of extra-thoracic particles which would lodge in the nasal fossae is high (35–52% depending on the job). Although the dust level seems moderate in the light of the occupational threshold for particles with no special toxicity [29] (Threshold Limit Value – Time Weighted Average = 10 mg/m³ for 8 h of work per day in France), exposure peaks seem to be high, particularly with respect to the occupational threshold for wood dust of 1 mg/m³.

In conclusion in the light of this review, greater awareness is required of the carcinogenicity of leather dust as has already been achieved for wood dust: physicians with respect to the occupational aetiology, occupational health experts for medical monitoring and industry professionals to implement technical solutions and discuss setting occupational threshold exposure levels. It is likely that the failure to recognize sino-nasal cancer as an occupational disease in the shoe trades in France and elsewhere, together with the different ways in which OHPs are dealt with in Europe [30] both contribute to our poor understanding and failure to implement effective preventive measures.

This is a serious form of cancer with high levels of mortality and sequelae, and one which significantly compromises quality of life. As it is a rare cancer—even in this high-risk group—addressing it should not represent a major economic problem.

Conflicts of interest
None declared.

References


