Melanoma and occupation: results of a case-control study in The Netherlands


Abstract

Several studies have reported excesses of risk of melanoma in specific industries. Data from a case-control study in The Netherlands, including 140 cases with a cutaneous melanoma and 181 controls with other types of malignancy, were used to evaluate whether the reported associations with these specific industries could be reproduced. Adjustment for characteristics of pigmentation and exposure to sunlight was made. Increased risks of cutaneous melanoma were found for subjects who had ever worked in the electronics industry (odds ratio (OR) = 2.03, 95% confidence interval (95% CI) 0.63-6.62), in the metal industry (OR = 2.61, 95% CI 0.96-7.10), and in the transport and communication branch (OR = 1.92, 95% CI 0.84-4.35). These ORs were adjusted for age, sex, education, hair colour, tendency to burn, freckling, and exposure to sunlight. No increased risks were seen for workers in the chemical industry, the textile industry, and among health care workers. Analyses according to duration and latency of exposure did not give consistent results, but existing patterns may be obscured by the imprecision of the estimates.

(British Journal of Industrial Medicine 1993;50:642-646)

Incidence of cutaneous melanoma has been increasing rapidly in the past decades and a doubling of incidence every decade has been found. Exposure to sunlight is considered to be the most important environmental risk factor, but exposure to occupational hazards may also play a part in the aetiology. In recent years several melanoma clusters have been reported to occur in certain industries, such as the petrochemical, chemical, electronics, and vinyl chloride and rubber industries. Increased risks have also been reported for workers in the printing industry, in the textile industry, and in the manufacture of synthetic fibres. A few case-control studies reported increased odds ratios (ORs) associated with exposure to specific compounds, such as organic chemicals and cutting oils. Magnani et al found an increased risk in “furnace, forge, foundry, and rolling mill workers” and for exposure to lead and mercury compounds. Other occupational groups, in which more or less consistently increased risks of melanoma have been found, are firemen, the armed forces, and health care workers such as veterinarians, dentists, pharmacists, and doctors.

Most of these studies evaluated relations between multiple cancers and multiple occupational exposures, however, and several significant associations are expected to occur from chance alone. Often, these studies were merely hypothesis generating. Adjustment for pigmentation characteristics and exposure to ultraviolet rays was seldom feasible and duration and latency analyses were not always performed. More evidence on the causality of the reported associations is needed.

Therefore, data from a case-control study were used to reevaluate the reported associations between risk of cutaneous melanoma and specific industries. An important advantage of this study is the availability of detailed information about other risk factors for melanoma, such as pigmentation characteristics and exposure to sunlight.

Material and methods

The case-control study was performed in The Netherlands and included 140 cases with superficial spreading or nodular melanoma and 181 controls with other types of malignancy. Table 1 gives the diagnoses among control patients. Both cases and controls were derived from the same cancer registry, the Comprehensive Cancer Centre, IKO, which covers the midwestern part of The Netherlands.
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Information on occupational exposure was collected by interview. The respondents were asked about all jobs they had had for at least six months. Recorded were type of job, type of industry, and first and last year of employment. The subjects also received a list of specific groups of chemicals, on which they indicated whether they had ever been exposed to them.

To be able to adjust for potential confounders, information was obtained about age at diagnosis, sex, education as an indicator of socioeconomic state, and reaction of the skin to sunlight measured by tendency to burn and ability to tan. Subjects also gave detailed information about exposure to sunlight. A distinction was made between exposure to the sun during work (chronic exposure) and exposure during leisure time activities (intermittent exposure). The second type of exposure, which is supposed to be more irregular than occupational exposure to sunlight, is considered an important risk factor for melanoma, whereas chronic exposure is believed to have a neutral or even a protective effect. Physical examination of the respondents was also accomplished and included assessment of skin, hair, and eye colour, degree of freckling, and number of naevi on the back.

Crude ORs were calculated for all industries that have been reported to be associated with increased risk of melanoma. Subjects were considered exposed to a specific industry if they had ever worked in that industry. Next, all ORs were adjusted for age, sex, education, hair colour, tendency to burn, freckling, and chronic and intermittent exposure to sunlight by use of multivariate logistic regression models. Finally, duration and latency analyses were performed to assess whether more detailed specification of occupational exposure would reveal other or stronger associations with risk of melanoma.

Results

Table 2 presents numbers of cases and controls who ever worked in specific industries. The ORs are given only if the number of cases or controls exceeded five. Two types of analyses with different definitions of non-exposure were performed. Firstly, non-exposure was defined as never having worked in the specific industry for which the OR was calculated. Secondly, non-exposed subjects were defined as those persons who had never worked in any of the industries mentioned in the table (53 cases and 78 controls). The second method revealed consistently higher ORs. With the exception of the risk estimates for workers in the chemical industry (OR = 1.03), the ORs for all industries with potential risk were slightly increased.

<table>
<thead>
<tr>
<th>Industry</th>
<th>No of cases</th>
<th>No of controls</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR† (95% CI)</th>
<th>Crude OR‡ (95% CI)</th>
<th>Adjusted OR‡ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrochemical</td>
<td>1</td>
<td>2</td>
<td>0.90 (0.33-2.43)</td>
<td>0.31 (0.10-0.98)</td>
<td>1.03</td>
<td>0.42</td>
</tr>
<tr>
<td>Chemical</td>
<td>7</td>
<td>10</td>
<td>1.47 (0.58-3.70)</td>
<td>1.51 (0.52-4.35)</td>
<td>1.64</td>
<td>2.03</td>
</tr>
<tr>
<td>Electronics</td>
<td>10</td>
<td>9</td>
<td>1.09 (0.53-2.24)</td>
<td>1.08 (0.49-2.41)</td>
<td>1.23</td>
<td>1.14</td>
</tr>
<tr>
<td>Rubber and plastics</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Printing</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Textile</td>
<td>15</td>
<td>18</td>
<td>1.34 (0.68-2.64)</td>
<td>2.48 (1.09-5.64)</td>
<td>1.47</td>
<td>2.61</td>
</tr>
<tr>
<td>Synthetic fibres</td>
<td>2</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metal</td>
<td>19</td>
<td>19</td>
<td>1.49 (0.82-2.70)</td>
<td>0.97 (0.48-1.97)</td>
<td>1.59</td>
<td>1.00</td>
</tr>
<tr>
<td>Health care</td>
<td>27</td>
<td>25</td>
<td>1.14 (0.70-1.84)</td>
<td>1.70 (0.84-3.46)</td>
<td>1.25</td>
<td>1.92</td>
</tr>
<tr>
<td>Transport and communication</td>
<td>44</td>
<td>52</td>
<td>1.49 (0.82-2.70)</td>
<td>0.97 (0.48-1.97)</td>
<td>1.59</td>
<td>1.00</td>
</tr>
</tbody>
</table>

ORs and 95% CIs are given only if more than five subjects are available.

* Subjects who never worked in the specific industry for which the OR is given are regarded as non-exposed.
† Subjects who never worked in any of the industries mentioned in the table are regarded as non-exposed.
‡ Adjusted for age, sex, education, hair colour, tendency to burn, freckling, and chronic and intermittent exposure to sunlight.
Table 3 Exposure to groups of chemicals reported by workers in the electronics and metal industries, and in transport and communication, compared with exposure of subjects who had never worked in these industries

<table>
<thead>
<tr>
<th>Group of chemicals</th>
<th>Electronics (%)</th>
<th>Metal industry (%)</th>
<th>Transport and communication (%)</th>
<th>Other (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tar products</td>
<td>26</td>
<td>16</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Cleaning agents/solvents</td>
<td>58</td>
<td>63</td>
<td>43</td>
<td>38</td>
</tr>
<tr>
<td>Paints/lacquers/varnishes</td>
<td>11</td>
<td>26</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Paint removers</td>
<td>11</td>
<td>21</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Printing inks</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Glues</td>
<td>16</td>
<td>29</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Cutting oils/coolants</td>
<td>0</td>
<td>29</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Lubricating oils</td>
<td>26</td>
<td>40</td>
<td>21</td>
<td>6</td>
</tr>
<tr>
<td>Condensator and insulator fluids</td>
<td>21</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Plastic monomers</td>
<td>21</td>
<td>11</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Plastic polymerisation products</td>
<td>21</td>
<td>24</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Insecticide</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Insulating materials</td>
<td>42</td>
<td>34</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>Preservatives</td>
<td>16</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Explosives</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

Compared with control patients, cases of melanoma were younger, more often female, better educated, and more often had red or blond hair. Moreover, they burnt and freckled more easily, participated more often in sunbathing during leisure time, and were less often exposed to sunlight during work. Therefore, ORs were adjusted for the potential confounding effect of these risk factors (table 2).

If non-exposure was defined as never having worked in any of the potentially risk generating industries, ORs increased for the electronics industry (OR = 2.03), the metal industry (OR = 2.61), and the transport and communication branch, which includes the armed forces and firemen (OR = 1.92). The OR decreased for workers in the chemical industry (OR = 0.42), for workers in textile industry (OR = 1.14), and for those in health care professions including veterinarians and people working in the pharmaceutical industry (OR = 1.00).

Stratification by duration of industrial exposure did not result in increases in ORs with longer duration of exposure. In the electronics and metal industry the crude ORs were higher for persons who had worked there for one to five years than for persons with longer duration of employment. Analyses according to latency period (< 20 years and ≥ 20 years) suggested higher risks of melanoma with a latency of < 20 years; crude ORs were 2.23 in the metal industry, 1.32 in the electronics industry, and 1.85 in the transport and communication branch. With a latency of more than 20 years the OR for the electronics industry remained 1.32; for the metal industry and the transport and communication branch the ORs decreased to 1.17 and 0.98 respectively. Adjustment for potential confounders was no longer feasible because of the low numbers in each category of duration and latency.

Table 3 shows that, when compared with the other industries, in the three industries with increased risk of melanoma higher proportions of workers were exposed to tar products, cleaning agents and solvents, paint removers, glues, lubricating oils, plastics, and insulating materials.

Discussion

Cutaneous melanoma constitutes a growing threat to public health. A critical evaluation of the potential effects of occupational hazards is warranted. The results of this study corroborate previously reported positive associations between risk of cutaneous melanoma and employment in the electronics industry, in metal working, and in the transport and communication branch.

The availability of detailed information about other risk factors for melanoma made it possible to assess the independent effect of industrial exposures. After adjustment for age, sex, education, pigmentation characteristics, and intermittent sunlight exposure habits, the ORs remained high. These results indicate that confounding by established risk factors for melanoma does not explain the positive associations.

Recall bias seems a very unlikely explanation for the increased ORs for workers in the electronics and metal industries and in the transport and communication branch. The respondents and the interviewers were not aware of possible associations between these specific industries and risk of melanoma. Furthermore, the control group also consisted of patients with a malignancy, who, like the cases with melanoma, will meditate about the possible causes of their disease. Therefore, they are comparable with respect to their inclination to attribute their disease to occupational exposures.

Theoretically, the use of control patients with other types of malignancy could have obscured existing positive associations between specific industries and risk of melanoma. This would be the case if employment in these industries actually
caused one of more of the cancers of the control group. Because of this danger, we chose a control group consisting of patients with a variety of malignancies, such that any association between one of these cancers and a specific industrial exposure would have little overall effect on the results.28 As can be seen in table 1, patients with bladder cancer or non-Hodgkin's lymphoma constitute the largest proportions of the control group. Because bladder cancer is known to be associated with occupational exposures, including patients with bladder cancer in the control group could have resulted in dilution of existing associations between melanoma and the industries under study. Therefore, the analyses were repeated after exclusion of the controls with bladder cancer. These analyses gave similar results and did not reveal stronger or new associations.

Other sources of failure to detect any existent relations between occupational hazards and risk of melanoma may be the low number of exposed subjects and the rather crude definition of occupational exposure. No increased risks were seen for workers in the chemical industry, the textile industry, and among health care workers. Based on the numbers of exposed controls, however, and assuming an a error of 0.05, the power of detecting ORs of 2.0 was rather low: 66% for health care workers, 54% for the textile industry, and 36% for the chemical industry.29 Distinction of ever v never employed in a particular industry is only a crude characterisation of occupational exposure, which could also have obscured any existing relations. Because of the low numbers of cases and controls in each industry, analysis according to job categories was not feasible; nor did stratification by duration and latency of industrial exposure show any consistent patterns.

We tried to obtain more specific information about occupational exposures in the industries that were associated with increased risk of melanoma. Occupations of cases with melanoma ever employed in metal working were engineering fitter (four), tool maker (two), crane engineer (one), mechanic (two), welder (one), sheet metal worker (one), production worker (three), driver (one), and administrator (four). Jobs reported by melanoma cases in the electronics industry were electrical engineer (one), engineering fitter (two), mechanic (three), production worker (one), installer (one), drawer (one), and administrator (one). The large number of cases in the transport and communication branch was mostly due to serving in the army. None of the melanoma patients were firefighters. The increased OR associated with the transport and communication branch might partly be explained by the fact that 24% of subjects ever employed in this branch had also worked in the metal industry.

Information about contact with groups of chemicals indicates that in the electronics industry, the metal industry, and the communication and transport branch higher proportions of workers were exposed to tar products, cleaning agents and solvents, paint removers, glues, lubricating oils, plastics, and insulating materials (table 3). Unfortunately, the results of this and other studies do not allow more detailed identification of the agents responsible for the excess risk. A solvent often used in metal cleaning is methylene chloride, which was reported by Lanes et al30 to be positively associated with risk of melanoma. Furthermore, Bell et al reported a twofold increased risk for contact with cutting oils.19 More evidence about the effect of these chemicals on risk of melanoma is lacking.

In conclusion, the results of this study indicate that the risk of cutaneous melanoma for workers in the electronics and metal industries needs further appraisal. Confounding by other known risk factors for melanoma did not explain the positive associations. As other studies also found an increased risk of melanoma in the electronics industry, it seems unlikely that the positive associations are due to chance. Cohort studies are necessary to further clarify the specific exposures responsible for the excesses of melanoma found.

We thank Dr N Roeleveld for her consent to use part of a questionnaire on occupational risk factors and Professor D M Elwood for his consent to use part of the questionnaire developed for the Western Canada Melanoma Study.

10 De Guire L, Theriault G, Iturra H, Provencher S, Cyr D, Case BW. Increased incidence of malignant melanoma of...


Accepted 5 October 1992