To the Editor. Materljan et al (1) provided interesting information on the epidemiology of central nervous system (CNS) tumors in an area of Croatia. They observed a higher incidence rate of neuroepithelial, meningeal, metastatic intracranial, and metastatic intraspinal tumors in men than women. We would like to suggest that the increased incidence of these types of tumors might be related to occupational exposure, although the authors’ do mention that exposure to tumorigenic factors may explain the increase for intracranial tumors. A previous study (2) suggested that male mortality, with cancer being a primary cause, from exposure to hazardous substances is 4 times greater than that for women. Previous studies (3-5) have reported that those in occupational settings (e.g. agricultural and wood workers) with exposure to hazardous materials may experience a higher incidence of “brain” tumors than controls. However, reporting of increased incidences of brain tumors and exposure to hazardous materials (e.g. chemical industry) is not consistent (6); yet the hypothesis that such exposures carry an increased risk is worth exploring. Although the population in the Materljan study is small, it may be worth exploring if a relationship exists between occupation and CNS tumors. This could be accomplished by questionnaire completion by the next of kin.

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4 Heineman EF, Cocco P, Gomez MR, Dosemeci M, Stewart PA, Hayes RB, et al. Occupational exposure to


In Reply: Dr. Lange and colleagues suggest that the increased incidence of the central nervous system (CNS) tumors found in the Labin area, Croatia (1) might be related to the occupational exposure to hazardous substances. We pointed out that one of the limitations of our study was the fact that for most patients with CNS tumors, we were not able to collect any information on the social status, employment, and other data that would allow us to discuss the etiological hypothesis (1). Also, we detected too small a number of registered single type-tumors in order to seriously consider their etiology. However, we analyzed the epidemiological characteristics of glioblastoma, the most frequent type of CNS tumor (22 men and 8 women) in the Labin area during the period 1974-2001 (2). The spatial distribution was inhomogenous and the mean annual incidence between the single municipalities differed significantly (chi square = 10.288; df = 4; p = 0.036), being the highest in Kršan and Sv. Nedelja (Fig. 1). Six patients (5 men, 1 woman) out of 9 (7 men, 2 women) were residents of Kršan, the municipality with the highest mean annual incidence, living in the farming areas of Čepić and Kožljak (difference statistically significant for men; chi square = 4.541; df = 1; p = 0.033). This suggests a possible relation between glioblastoma and exposure to hazardous agricultural substances, mostly pesticides. Moreover, two of us (E.M. and B.M.) have been working as practitioners in this area for more than 15 years, and in many cases we have witnessed pesticide poisoning in local farmers because of improper use. However, none of the poisoned farmers have later developed any type of CNS tumor.

The etiology of brain tumors, including glioblastoma, is unknown. Up till now, the defined risks derive from ionizing radiation and hereditary syndromes, but their contribution in these types of tumors is less than 5% (3). Particular occupations have a higher risk of getting this disease: electricians, petrochemical workers (linked to solvents), and farmers (linked to pesticides), although published reports are sometimes inconsistent (1-3).

If any relation between glioblastoma and occupation indeed exists in our study, it is very weak, as indicated in Table 1. The most frequent occupations are mining and office work. These and other mentioned occupations are consistent with the known risks. The exploitation of the coalmine was once the main activity in the Labin area, and it is known that a higher exposure to natural radiation was present in these circumstances (4). However, the number of those employed in mining, particularly those linked to coal extraction, varied considerably during the period of active mining (from hundreds to thousands during 1974-1999), not allowing a thorough analysis.

Finally, any analysis of the relation between exposure to hazards and the disease have to take into account the cumulative influence of both occupational and residential exposure. In our case, a high voltage air power-transmission network (nowadays fortuna-

Table 1. Occupations of glioblastoma patients in Labin area, Croatia, 1974-2001

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coal mining</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Office worker</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Catering and tourism</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Textile industry</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Thermoelectric power plant</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Driver</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Housewife</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>8</td>
</tr>
</tbody>
</table>
tely mostly interred) crossed the settlements of Labin, Potpićan, Raša, and Tupljak. Also, high voltage power-transmission lines were installed near or cross the settlements in the above mentioned farming area with the highest incidence of glioblastoma. Some studies support the hypothesis that occupational and less residential magnetic field exposure play a role in the etiology of glioblastoma (5,6).

All these facts complicate further debates on etiological hypothesis related to occupational or environmental hazard, and the small sample in our study (1) allows us only to guess about role of hazardous or possible causative factors.

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