Subclinical Increases in Serum Transaminase Activities among Female Workers Exposed to Toluene at Sub-OEL Levels

Key words: GOT—GPT—Hepatic function—Toluene

Despite the general belief that toluene is not very hepatotoxic under occupational conditions\textsuperscript{1,2}, hepatic damage was sometimes reported among glue sniffers\textsuperscript{3–5}, accident victims\textsuperscript{6} and laboratory animals\textsuperscript{7,8} exposed either to toluene or its homologue xylene. Trials are made in the present study to examine if there are any detectable changes in hepatic functions in relation to the intensity of the exposure to toluene in occupational settings.

Three groups of female subjects were examined. Those in Group A were female workers in a rubber-bag container plant where toluene was the sole organic solvent present in the glue. Group B consisted of 18 female employees engaged in the production of rubber boots utilizing the glue containing toluene as a major solvent together with minute amount of methyl ethyl ketone. Hospital nurses, 50 in total, served as controls.

Time-weighted average of exposure to toluene was determined using carbon felt dosimeters as personal samplers\textsuperscript{9,10}. Urine samples, collected from the exposed groups at the end of the afternoon shifts, were subjected to the analyses for hippuric acid and o-cresol as the indices of exposure to toluene by the methods previously reported\textsuperscript{11}. Hepatic function tests and hematological examinations were carried out by the conventional methods with blood samples collected during the morning shifts. Statistical evaluations were made with Student’s t-test with an assumption of normal distribution, except for urinary metabolites for which a log-normal distribution was assumed\textsuperscript{12}.

In Table 1 are summarized the results of hepatic function tests together with the intensities of exposure to toluene. The time-weighted average exposure concentration of toluene as measured by personal sampling was 69 ppm for Group A and 45 ppm for Group B, both being well below the current occupational exposure limit (OEL) of 100 ppm\textsuperscript{13}. Such exposures could be confirmed by the elevated levels of the two metabolites in urine. No hematological abnormalities were detected in any groups.

When hepatic functions were examined, elevations of both GOT and GPT levels were detected; the increases were, even though subclinical, statistically significant (\(p<0.01\)) and dose-dependent. Possible effect of alcohol intake could be ruled

\textsuperscript{This work was supported in part by a Grant-in-aid for 1981 from the Occupational Health Promotion Foundation, Tokyo, Japan.}
out as the $\gamma$-GTP level remained unchanged\textsuperscript{14}. Other indices were essentially normal except that LDH and LAP were higher in Group A but not in Group B. It should be added that industrial hygiene survey failed to detect any hepatotoxic chemicals other than toluene in the work environments.

The present findings, together with other equivocal observations among toluene-exposed workers\textsuperscript{1,15,16}, suggest that possible hepatotoxicity of this most popular solvent\textsuperscript{17,18} deserves further attention.

### Table 1. Hepatic functions in relation to the intensity of exposure to toluene

<table>
<thead>
<tr>
<th>Item (Unit)</th>
<th>Exposed</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of examinees</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toluene in breath zone air (ppm)</td>
<td>69±24</td>
<td>45±42</td>
</tr>
<tr>
<td>Hippuric acid in urine (GM, mg/l: GSD)</td>
<td>1594 (1.44)</td>
<td>659 (2.84)</td>
</tr>
<tr>
<td>o-Cresol in urine (GM, ng/l: GSD)</td>
<td>893 (1.63)</td>
<td>329 (3.09)</td>
</tr>
<tr>
<td>Hepatic functions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOT [EC2.6.1.1.] (Karmen unit)</td>
<td>21.7±39**</td>
<td>19.8±3.6**</td>
</tr>
<tr>
<td>GPT [EC2.6.1.2.] (Karmen unit)</td>
<td>15.0±5.2**</td>
<td>15.1±5.5**</td>
</tr>
<tr>
<td>$\gamma$-GTP [EC2.3.2.1.] (m unit/ml)</td>
<td>7.2±3.2</td>
<td>7.1±5.1</td>
</tr>
<tr>
<td>ALP [EC3.1.3.1.] (King-Armstrong unit)</td>
<td>5.7±1.5</td>
<td>6.1±2.0</td>
</tr>
<tr>
<td>CHE [EC3.1.1.8.] (4pH)</td>
<td>1.08±0.22</td>
<td>0.97±0.13</td>
</tr>
<tr>
<td>LDH [EC1.1.1.27.] (Cabaud—Wroblewski unit)</td>
<td>412±32**,** ††</td>
<td>326±45</td>
</tr>
<tr>
<td>LAP [EC3.4.1.1.] (Goldbarg unit)</td>
<td>141±23*</td>
<td>131±14</td>
</tr>
<tr>
<td>Thymol turbidity test (Kunkel unit)</td>
<td>1.2±1.0</td>
<td>1.2±0.9</td>
</tr>
<tr>
<td>Zinc turbidity test (Kunkel unit)</td>
<td>7.2±2.2††</td>
<td>9.4±2.8**</td>
</tr>
<tr>
<td>Total bilirubin (mg/100 ml)</td>
<td>0.45±0.10*</td>
<td>0.41±0.14</td>
</tr>
</tbody>
</table>

Unless otherwise specified, the numbers in the table show mean±SD; the concentrations of hippuric acid and o-cresol in urine are expressed in terms of geometric means (GM; unit, mg/l for the former and ng/l for the latter) and geometric standard deviations (GSD), with an assumption of log-normal distribution\textsuperscript{10}.

a Either cited or recalculated from Ref. 11.
b Numbers in the parentheses indicate normal ranges.
**, * The difference from the controls is statistically significant (**, p<0.01: *, p<0.05).
††, † The difference between the two exposed groups is statistically significant (††, p<0.01; †, p<0.05).
REFERENCES


Center of Occupational Medicine, 
Tohoku Rosai Hospital, 
Dainohara 4-chome, Sendai 980, Japan

Shoji SHIOJIMA, 
Kenji HASEGAWA and 
Nobuo ISHIHARA
Department of Environmental Health, Tohoku University School of Medicine, Seiryocho, Sendai 980, Japan

(Received January 13, 1983)