Exposure of workers to a mixture of toluene and xylenes. II Effects

Zhen Chen, Shi-Jie Liu, Shi-Xiong Cai, Yi-Min Yao, Hong Yin, Hirohiko Ukai, Yoko Uchida, Haruo Nakatsuka, Takao Watanabe, Masayuki Ikeda

Abstract

The health effects of exposure to a mixture of toluene and xylene isomers was studied on the fourth or fifth day of a working week. The criteria of selection were that (1) the workers participated in the whole examination (personal diffusive sampling); (2) analysis of urine for monitoring of exposure, a questionnaire, haematology, and serum biochemistry for examination of effects on health), and (2) exposure was almost exclusively to toluene and xylenes (>90%), but not toluene alone (no more than 90% toluene), xylenes alone (not more than 70% xylenes), or gasoline.

It was not possible beforehand to identify the workers who met the criteria. Accordingly, almost 1000 exposed workers were examined, of whom 233 subjects (122 men and 111 women) satisfied the two selection criteria. Some of them were exposed also to a few ppm ethylbenzene, but none was exposed to benzene.

Toluene (methylbenzene) and xylene (three isomers of dimethylbenzene) are often present in combination in organic solvent preparations. Many reports from various countries have been published on exposure of workers, or of the general population. Whereas the toxicity of toluene has been extensively studied, reports on the health effects of xylene alone are few; publications of the effects of toluene-xylene combinations on factory workers are rare, despite their wide use.

More than 200 workers exposed to toluene and xylene in combination were examined in our study and compared with a similar number of non-exposed controls in a search for possible effects on the central nervous system, as well as haematological and serum biochemical effects. The lack of metabolic interaction between the solvents is reported separately.

Materials and methods

SELECTION OF WORKERS AND DESIGN OF HEALTH EXAMINATION

The study was carried out in China on the fourth or fifth day of a working week. The criteria of selection were that (1) the workers participated in the whole examination (personal diffusive sampling); (2) analysis of urine for monitoring of exposure, a questionnaire, haematology, and serum biochemistry for examination of effects on health), and (2) exposure was almost exclusively to toluene and xylenes (>90%), but not toluene alone (no more than 90% toluene), xylenes alone (not more than 70% xylenes), or gasoline.

It was not possible beforehand to identify the workers who met the criteria. Accordingly, almost 1000 exposed workers were examined, of whom 233 subjects (122 men and 111 women) satisfied the two selection criteria. Some of them were exposed also to a few ppm ethylbenzene, but none was exposed to benzene.

Toluene (methylbenzene) and xylene (three isomers of dimethylbenzene) are often present in combination in organic solvent preparations. Many reports from various countries have been published on exposure of workers, or of the general population. Whereas the toxicity of toluene has been extensively studied, reports on the health effects of xylene alone are few; publications of the effects of toluene-xylene combinations on factory workers are rare, despite their wide use.

More than 200 workers exposed to toluene and xylene in combination were examined in our study and compared with a similar number of non-exposed controls in a search for possible effects on the central nervous system, as well as haematological and serum biochemical effects. The lack of metabolic interaction between the solvents is reported separately.

Materials and methods

SELECTION OF WORKERS AND DESIGN OF HEALTH EXAMINATION

The study was carried out in China on the fourth or fifth day of a working week. The criteria of selection were that (1) the workers participated in the whole examination (personal diffusive sampling); (2) analysis of urine for monitoring of exposure, a questionnaire, haematology, and serum biochemistry for examination of effects on health), and (2) exposure was almost exclusively to toluene and xylenes (>90%), but not toluene alone (no more than 90% toluene), xylenes alone (not more than 70% xylenes), or gasoline.

It was not possible beforehand to identify the workers who met the criteria. Accordingly, almost 1000 exposed workers were examined, of whom 233 subjects (122 men and 111 women) satisfied the two selection criteria. Some of them were exposed also to a few ppm ethylbenzene, but none was exposed to benzene.

Toluene (methylbenzene) and xylene (three isomers of dimethylbenzene) are often present in combination in organic solvent preparations. Many reports from various countries have been published on exposure of workers, or of the general population. Whereas the toxicity of toluene has been extensively studied, reports on the health effects of xylene alone are few; publications of the effects of toluene-xylene combinations on factory workers are rare, despite their wide use.

More than 200 workers exposed to toluene and xylene in combination were examined in our study and compared with a similar number of non-exposed controls in a search for possible effects on the central nervous system, as well as haematological and serum biochemical effects. The lack of metabolic interaction between the solvents is reported separately.

Materials and methods

SELECTION OF WORKERS AND DESIGN OF HEALTH EXAMINATION

The study was carried out in China on the fourth or fifth day of a working week. The criteria of selection were that (1) the workers participated in the whole examination (personal diffusive sampling); (2) analysis of urine for monitoring of exposure, a questionnaire, haematology, and serum biochemistry for examination of effects on health), and (2) exposure was almost exclusively to toluene and xylenes (>90%), but not toluene alone (no more than 90% toluene), xylenes alone (not more than 70% xylenes), or gasoline.

It was not possible beforehand to identify the workers who met the criteria. Accordingly, almost 1000 exposed workers were examined, of whom 233 subjects (122 men and 111 women) satisfied the two selection criteria. Some of them were exposed also to a few ppm ethylbenzene, but none was exposed to benzene.

Toluene (methylbenzene) and xylene (three isomers of dimethylbenzene) are often present in combination in organic solvent preparations. Many reports from various countries have been published on exposure of workers, or of the general population. Whereas the toxicity of toluene has been extensively studied, reports on the health effects of xylene alone are few; publications of the effects of toluene-xylene combinations on factory workers are rare, despite their wide use.

More than 200 workers exposed to toluene and xylene in combination were examined in our study and compared with a similar number of non-exposed controls in a search for possible effects on the central nervous system, as well as haematological and serum biochemical effects. The lack of metabolic interaction between the solvents is reported separately.

Materials and methods

SELECTION OF WORKERS AND DESIGN OF HEALTH EXAMINATION

The study was carried out in China on the fourth or fifth day of a working week. The criteria of selection were that (1) the workers participated in the whole examination (personal diffusive sampling); (2) analysis of urine for monitoring of exposure, a questionnaire, haematology, and serum biochemistry for examination of effects on health), and (2) exposure was almost exclusively to toluene and xylenes (>90%), but not toluene alone (no more than 90% toluene), xylenes alone (not more than 70% xylenes), or gasoline.

It was not possible beforehand to identify the workers who met the criteria. Accordingly, almost 1000 exposed workers were examined, of whom 233 subjects (122 men and 111 women) satisfied the two selection criteria. Some of them were exposed also to a few ppm ethylbenzene, but none was exposed to benzene.

Toluene (methylbenzene) and xylene (three isomers of dimethylbenzene) are often present in combination in organic solvent preparations. Many reports from various countries have been published on exposure of workers, or of the general population. Whereas the toxicity of toluene has been extensively studied, reports on the health effects of xylene alone are few; publications of the effects of toluene-xylene combinations on factory workers are rare, despite their wide use.

More than 200 workers exposed to toluene and xylene in combination were examined in our study and compared with a similar number of non-exposed controls in a search for possible effects on the central nervous system, as well as haematological and serum biochemical effects. The lack of metabolic interaction between the solvents is reported separately.
### Table 2  Prevalence of subjective symptoms

<table>
<thead>
<tr>
<th>Subjective symptoms</th>
<th>Exposed to toluene and xylene</th>
<th>Controls</th>
<th>Exposed</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>1–20 ppm</td>
<td>&gt;21 ppm</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>944 (244): 21:5**</td>
<td>825 (181): 17:1</td>
<td>277 (52): 9:0</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0:01 to controls.

Values in the table are number of affirmative answers (number of subjects)/percentage prevalence.

### Table 3  Frequency distribution of subjective symptoms

<table>
<thead>
<tr>
<th>Subjective symptoms</th>
<th>Controls</th>
<th>Exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>II</td>
</tr>
</tbody>
</table>

### Table 4  Symptoms with significant difference (p < 0:01) in percentage prevalence (%) for men and women combined

<table>
<thead>
<tr>
<th>Code</th>
<th>No symptom</th>
<th>Control</th>
<th>Exposed</th>
<th>E/C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eye irritation</td>
<td>6-2</td>
<td>28-6</td>
<td>4-6</td>
</tr>
<tr>
<td>2</td>
<td>Dimmed vision</td>
<td>3-1</td>
<td>22-2</td>
<td>7-2</td>
</tr>
<tr>
<td>3</td>
<td>Nasal irritation</td>
<td>8-3</td>
<td>28-2</td>
<td>5-4</td>
</tr>
<tr>
<td>4</td>
<td>Sore throat</td>
<td>5-2</td>
<td>40-2</td>
<td>7-7</td>
</tr>
<tr>
<td>5</td>
<td>Unusual taste</td>
<td>0-4</td>
<td>14-2</td>
<td>35-5</td>
</tr>
<tr>
<td>6</td>
<td>Face flushing</td>
<td>2-1</td>
<td>3-6</td>
<td>4-1</td>
</tr>
<tr>
<td>7</td>
<td>Dizziness</td>
<td>2-8</td>
<td>14-1</td>
<td>5-0</td>
</tr>
<tr>
<td>8</td>
<td>Floating sensation</td>
<td>7-9</td>
<td>55-1</td>
<td>7-0</td>
</tr>
<tr>
<td>9</td>
<td>Heavy feeling in the head</td>
<td>2-4</td>
<td>14-1</td>
<td>5-9</td>
</tr>
<tr>
<td>10</td>
<td>Headache</td>
<td>6-9</td>
<td>32-9</td>
<td>4-8</td>
</tr>
</tbody>
</table>

### Table 5  Comparison of haematology and serum biochemistry values

<table>
<thead>
<tr>
<th>Item (Units)</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposed</td>
<td>Controls</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>116</td>
<td>125</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01.

Values for haemoglobin, leucocytes, total protein, total bilirubin and creatinine are arithmetic mean (ASD), whereas those for γ-GTP, ASAT, ALAT, ALP, and LAP are geometric mean (GSD) with assumptions of normal and log normal distributions, respectively.

### Results

**PREVALENCE OF SUBJECTIVE SYMPTOMS**

Table 2 shows that the prevalence of symptoms during work was significantly (p < 0.01) higher in the exposed than in the control group regardless of sex. This was also true for the prevalence of the symptoms in the past three months. As the response to two questions related to menstruation did not differ between exposed and control groups, the two sexes were combined after the exclusion of these questions.

When both exposed and non-exposed subjects were classified by the number of symptoms per person, the frequency distribution was significantly (p < 0.01) different for both symptoms during work and in the past three months (table 3).

Table 4 gives prevalences for each symptom with a significant increase (p < 0.01) in the exposed population. Most of the symptoms during work related depressive effects on the central nervous system (such as codes 9 and 11) or local irritation (codes 1, 3, and 5), whereas those in the past three month period were less specific. The exposed to control ratio (E/C) ranged from 35-5 to 3-4 for the work period and 8-9 to 1-9 for the past three months and was significantly higher (p < 0.05 by U test) in the work period than in the past three months.

For the detection of possible dose dependency, exposed workers were classified into two subgroups by exposure intensities of 1 to 20 ppm and 21 ppm or more. Comparison of prevalences indicated no dose dependent increase either during work or in the past three months (table 2).

### Haematology and Serum Biochemistry

Table 5 shows the results of haematology and serum biochemistry tests. Because haemoglobin concentrations are known to be different in the two sexes the findings were treated separately for men and for women. Differences between exposed and control groups were not significant for most of the items, and none of the statistically significant differences were clinically relevant.

### Discussion

The health examination of 233 Chinese solvent workers occupationally exposed to a mixture of toluene and three xylene isomers at low concentration ratio and 241 controls showed that the prevalences of some subjec-
Exposure of workers to a mixture of toluene and xylenes. II Effects

tive symptoms were significantly increased in the study population. The symptom profiles were similar to those found after occupational exposure to toluene or xylenes, and focused on depression of the central nervous system and local irritation. In agreement with other observations, haematology and serum biochemistry did not show noteworthy changes: this was also the case for workers exposed to toluene or xylenes.

The toxicity profiles are essentially the same for toluene, xylenes, and the mixture of the two, the central nervous system being the primary target. This suggests that it is justified when evaluating the toxicity of mixtures of toluene and xylenes at such low levels of occupational exposure, to add the effects. The current occupational exposure limits for toluene and three xylene isomers are set at 100 ppm, indicating that their potencies are essentially equal in their ability to depress the central nervous system.

We thank Professor C Jin of the Institute of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, China, Professor T Suzuki (the former Director), and Professor K Yoshinaga of Tohoku Rosai Hospital, Sendai 980, Japan for their support to this study.


4 Ogata M, Takamatsu Y, Tomokuni K. Excretion of hippuric acid and m- or p-methylhippuric acid in the urine of persons exposed to vapours of toluene and m- or p-xylene in an exposure chamber and in workshops, with specific reference to repeated exposures. Br J Ind Med 1971;28:382-5.


