RELATIONSHIP BETWEEN STYRENE EXPOSURE AND HEARING LOSS: REVIEW OF HUMAN STUDIES

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Abstract

Styrene is an aromatic solvent belonging to the alkylbenzene family. Occupational exposure to styrene occurs mainly in the manufacturing of fiberglass-reinforced polyester products, e.g. reinforced plastics and composites. Since 1988, nine studies have been published on the relationship between occupational exposure to styrene and hearing loss. All studies were the cross-sectional epidemiological studies or clinical studies from occupational health clinics. A total of more than 1000 workers exposed to styrene, both with and without concurrent noise exposure, were examined using different outcome measures for hearing loss.

Exposure assessment was usually based on styrene measurements in the breathing zone during several hours of one working day. Some of the studies employed also the biological monitoring of styrene exposure based on determination of its urinary metabolites. The current exposures to styrene varied between 2 and 35 ppm. In some studies, lifetime exposure was calculated using company records and questionnaire data. The current exposure to noise was estimated by noise dosimetry or standard noise measurements. Lifetime noise exposure was assessed using questionnaire data and occupational noise estimates. In many studies, noise-exposed groups were used as controls together with the unexposed workers.

Of the nine studies, seven show some effects on the auditory system that were associated with styrene-alone exposure. These effects are examined using different outcome measures such as pure tone audiometry, high frequency hearing loss, and central hearing tests. In some studies, an increased risk for hearing loss was associated with exposure estimates.

Key words: Styrene, Hearing loss, Occupational exposure, Human

INTRODUCTION

Occupational hearing loss has traditionally been considered the same as noise-induced hearing loss. Some early studies hypothesized about the potential damage caused by chemicals such as organic solvents to the auditory system, since solvents are known for their neurotoxic effects both on the central and peripheral nervous system [1,2].

The hearing loss associated with chemical exposure was often attributed to noise exposure, since noise is often present in the workplaces where chemical exposures occur as well. Thus, the potential risk of hearing loss due to chemical exposure has not been acknowledged until recent years.

Over the last decades, several studies have reported on the effects of occupational chemicals on the auditory system and their interaction with noise in animals [3–5] and in man [6–8]. Both animal and human studies have shown that the audiometric frequency range affected by solvents is not limited to the range affected by noise [9,10]. Nevertheless, if careful analyses are not performed and attention is not given to all the exposure conditions, the observed hearing disorders can be erroneously attributed to noise or completely unnoticed among the workers who are not included in the hearing conservation programs.

Styrene has been investigated in several human studies seeking for a relationship between occupational exposure...
and hearing loss. The objective of the present review is to evaluate the currently available evidence regarding workplace exposure to styrene and auditory effects in humans.

**STYRENE**

Styrene is an aromatic solvent belonging to the alkylbenzene family. Styrene is produced in large quantities from oil or petroleum gas and is used as an intermediate chemical for polymers in the manufacture of plastics, resins, coatings, and paints.

The major route of exposure is through the respiratory system, and liquid styrene is also rapidly absorbed through the skin [11]. The dermal absorption of styrene, however, is negligible compared to the uptake via the lung. Some 90 to 97% of the styrene absorbed by humans is eliminated as urinary metabolites, with only a small fraction eliminated as parent compound in expired air or urine [12].

Occupational exposures to styrene occur mainly in the manufacturing of fiberglass-reinforced (GRP) polyester products, e.g. reinforced plastics and composites used among others in the boat building industry [11]. In Europe and the US, the occupational exposure limits (OEL) for styrene in the air vary from 10 to 100 ppm and are set primarily to prevent the neurotoxic effects such as changes in neurobehavioral performance [11]. The OELs in selected countries are displayed in Table 1.

**Table 1. Styrene OEL values in selected countries**

<table>
<thead>
<tr>
<th>Country</th>
<th>8 h values (ppm)</th>
<th>8 h values (mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>100</td>
<td>430</td>
</tr>
<tr>
<td>USA</td>
<td>100</td>
<td>420</td>
</tr>
<tr>
<td>France</td>
<td>50</td>
<td>210</td>
</tr>
<tr>
<td>Japan</td>
<td>50</td>
<td>210</td>
</tr>
<tr>
<td>Denmark</td>
<td>25</td>
<td>105</td>
</tr>
<tr>
<td>Finland</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Germany</td>
<td>20</td>
<td>86</td>
</tr>
<tr>
<td>Sweden</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Poland</td>
<td>12</td>
<td>50</td>
</tr>
</tbody>
</table>

Styrene exposure is sometimes monitored also with biological monitoring. The biological exposure indices (BEIs) are the two major urinary metabolites: mandelic acid (MA) and phenylglyoxylic acid (PGA) [12]. The American Conference of Governmental Industrial Hygienists (ACGIH) has set a BEI limit value for styrene for MA + PGA in urine at 400 mg/g creatinine at the end of the shift. This corresponds approximately to 25 ppm in the air.

The OELs have been reduced in several countries in the second part of the 20th century. Owing to this policy as well as the development of new technologies in the manufacturing industry, the exposure levels have decreased [13]. In a recent study aimed at investigating the olfactory function in styrene workers, Lees [14] assessed styrene exposure in four American factories making reinforced plastics [14]. The current styrene exposure was around 20 ppm. The mean post-shift MA and PGA concentrations were 580 and 170 mg/g creatinine, respectively. These values highly correlated with styrene concentrations in the air. Low levels of current exposure to styrene were also found in several of the studies reviewed in this paper.

However, certain jobs in the GRP industry still require manual lamination and spray painting, which may give rise to higher exposures.

**HUMAN STUDIES ON THE EFFECTS OF OCCUPATIONAL EXPOSURE TO STYRENE ON THE AUDITORY SYSTEM**

Several studies have been conducted regarding the effects of occupational exposure to styrene on the auditory system, as well as the interaction between styrene and noise. Since 1988, nine studies have been published (in 10 publications) investigating the relationship between occupational exposure to styrene and hearing loss. All the studies were the cross-sectional epidemiological studies or clinical studies from occupational health clinics.

There are no studies on workers exposed to styrene alone in a totally quiet environment. However, in several studies described below, it was possible to investigate the groups
of workers exposed to styrene when the noise levels were below 85 dBA.
Each study will be summarized below and some of the findings will be compared in Table 2.

In this cross-sectional study, audiometric measurements in 59 workers exposed to styrene in a GRP plant were compared with the results for 94 controls working in the production industry where no chemical exposure was present.
Air styrene concentration was measured on three consecutive days. The results made the workers to be classified into two groups depending on current styrene exposure levels. The different levels depended on specific job tasks for the different groups of workers. In the group exposed to higher styrene levels, the mean exposure was 32 ppm and the group with a lower exposure level had a mean exposure of 14 ppm. Noise exposure was measured in each plant and was found to be somewhat different. The controls were exposed to high-frequency noise at levels between 80–85 dBA. The styrene workers were exposed to a background noise between 66–70 dBA, but there were short periods of time when the noise from noisy equipment increased the exposure to the levels between 70 to 104 dBA.
Multivariate comparisons of the audiometry thresholds were made between styrene-exposed workers and controls, between the group with the highest exposure level and the controls, and between the two groups exposed to different styrene concentrations. No significant differences were noted between all the styrene-exposed workers and the control group. The only significant difference in the hearing threshold values was found between the group with higher styrene exposure compared to the group with lower exposure level. The difference referred to 8 kHz and was evident both in the high-frequency measurements and conventional audiometry.
At the time the study was conducted, the findings of animal studies indicated that organic solvents could produce a high-frequency hearing loss. This was the main reason for choosing the high-frequency audiology as the outcome measure. Further animal studies have shown that the cochlear damage in rats refers to the low- and mid-frequency region of the cochlea [9,10]. In view of these data, the results from the study by Muijser et al.[15] are less surprising than it seemed at the time they were published.

Möller C, Ödkvist L, Larsby B, Tham R, Ledin T, Bergholtz LM. Otoneurological findings in workers exposed to styrene (1990) [16]
This study concerned 18 workers exposed to styrene in a Swedish boat building plant for a period of 6–15 years. Styrene exposure was assessed based on archive company records and occupational health inspections. During 8 h sampling, the mean concentrations ranged from 35 ppm to 15 ppm over a 10 year period (1976 to 1987). Most of the exposure was below the Swedish OEL at that time. Biological monitoring was not used for routine exposure assessment, hence such data were not available.
An extensive otoneurological test battery, comprising standard clinical tests, was used to investigate the effect of styrene exposure on hearing and balance. Both the peripheral and central functions were tested. The hearing tests consisted of pure tone audiogram, speech discrimination, interrupted speech and cortical response audiometry. The findings were compared with those for the reference group. The results of pure tone audiometry and maximum speech discrimination did not indicate hearing loss that could be attributed to noise exposure. However, 7 of 18 workers presented abnormal results in the central auditory system examinations, such as the interrupted speech test and especially the cortical evoked auditory response test, and 16 workers showed abnormal results in the tests investigating the central part of the balance system, such as posturography and rotatory visual suppression.
This study revealed the effects on the auditory system after low-level exposure to styrene despite the limited number of workers examined. The effects on the balance system were even more common in this group. It was not possible to investigate the dose-response relationship due to the small size of the study population. The difficulty in
It would be interesting to perform such a comparison also in the present study to see whether a more conservative approach using estimated lifetime styrene exposure as the only styrene factor included in the multivariate model, is the only way to analyze the data.

Sass-Kortsak AM, Corey PN, Robertson JM. 
An investigation of the association between exposure to styrene and hearing loss (1995) [17] 
Styrene and noise exposures were meticulously assessed, using personal dosimetry for both solvents and noise, in 299 workers at reinforced fibre industry in Canada. Workers were divided into three different groups according to current exposure measurements. The current mean styrene exposure for the directly exposed group (n = 170) was 26 ppm at the noise level of 89 dBA, the indirectly exposed group (n = 86) had the mean styrene concentration of 9 ppm and the noise level of 89 dBA, and 73 of the subjects were not exposed either to styrene or noise (level measured 80 dBA). Measurements of pure tone audiometric threshold were made before and after the shift. Based on current exposure estimates from the different plants and work history, a lifetime exposure estimate was calculated for both styrene and noise. The values were adjusted for the self-reported use of respiratory protection devices and hearing protectors. 
A multiple linear regression model was used to investigate the association between these lifetime exposures and hearing thresholds at 3, 4, 6 and 8 kHz. Also the subjects’ age and some other factors such as years of smoking and free-time exposure were considered in the model. The association between noise exposure, based on estimated lifetime exposure, and hearing loss (assessed by averaging pure tone thresholds) was significant, and so were the expected associations with age. No such relationship was found for styrene exposure. Styrene exposure approached the level of significance for hearing loss only at specific frequencies (4 and 6 kHz in the left ear). The conclusion of this study [17] was that no significant relationship could be found between styrene exposure and hearing loss. Some of the studies reviewed below compared different exposure groups by current exposure measurements.

In this study, 20 GRP industry workers were examined using an otoneurological test battery. Exposure assessment was based on personal sampling (8 h values) as well as biological monitoring data. Styrene concentrations in the air ranged between 3–54 ppm and only four of the workers were exposed at levels above 50 ppm. The levels of mandelic acid and phenylglyoxylic acid in urine varied between 80–942 mg/g creatinine (corresponding to approx. max value of 350 ppm). No hearing loss could be detected with pure tone audiometry or stapedius reflex measurements, whereas 17 out of 20 subjects showed abnormal vestibulo-ocular reflex results and six had abnormal results on the rotating chair test.
The results indicate that although no effects on hearing could be found in this small group of workers, an impact on the vestibular system was evident even though it was a subclinical effect [18].

Morioka I, Kuroda M, Miyashita K, Takeda S. 
Evaluation of organic solvent ototoxicity by the upper limit of hearing (1999) [19] 
The effects of styrene on hearing were investigated in male workers exposed in factories that produced plastic buttons or bathtubs. 93 workers participated in the study. They were exposed to a mixture of solvents, mainly styrene and toluene. 44 of the workers were exposed to styrene in combination with acetone. Solvent exposure was measured by personal air sampling. Of the 93 participants, only 6 were exposed to styrene levels that exceeded the 50 ppm Japanese exposure limit. Biological monitoring of exposure that employed mandelic acid in urine at the end of the shift was also used in exposure assessment. The workers...
whose noise exposures exceeded 85 dBA were excluded from the study population.

In early detection of noise-induced hearing loss, a special technique was used for determining the upper frequency limit of human hearing. This parameter was measured using a sweeping tone from 50 kHz downwards to 0.5 kHz (stimuli level 75±10 dB). The frequency at which the subjects first perceived the tone was noted. The results were compared with the standard values of the upper frequency limit of human hearing established for normal population of different age. Apart from the high frequency hearing test, the conventional pure tone audiometry (between 0.5–8 kHz) was also performed.

The measurement results showed that the prevalence of subjects with an upper limit of hearing below the 75th percentile of the standard values of the upper frequency limit for the normal population, correlated both with the measured styrene concentration in the air and the biological measure of mandelic acid in urine. The conclusion was that styrene exposure even below 50 ppm might cause a decrease in the upper limit of hearing. This outcome measure is not a sole indication of hearing loss but is considered to be an early sign of hearing loss. No effects were found in pure tone audiometric measurements.

The workers in this study were not exposed to styrene alone, but for most of the subjects styrene was the major component of the mixture. Also another potential ototoxic solvent, toluene, was present in the workplace, but a negative correlation was found between this exposure and the upper limit of hearing. However, it cannot be excluded that toluene exposure may also have had some influence on the results of the study [19].


In this follow-up study, 48 workers at a GRP plant were divided into three subgroups by their exposure conditions: an unexposed group (controls), a group exposed to low levels of styrene (2.9 to 28.9 ppm) and low levels of noise (69 to 76 dBA), and a group exposed to noise levels ranging from 82 to 86 dBA. The same outcome measure, the upper limit of hearing was used, as described in the study above [19], along with normal pure tone audiometry. No effects of solvent exposure were detected by audiometric testing up to 8 kHz in any of the groups.

There was a significantly higher prevalence of subjects with an upper limit of hearing below the 75th percentile of the normal population in the group exposed to styrene, compared to the controls and to the noise-exposed group. In the group exposed to styrene, the upper limit of hearing fell below the 75th percentile in 50% of the subjects.

This finding is remarkable in such a small group of workers, especially if one considers that both the noise levels and styrene concentrations in the air were within the limits recommended by several international agencies [20].


These two papers describe the same cross-sectional study, each one reporting the findings of either of the two separate parts of the audiological test battery used in the study. Morata et al. [21] describe the details of exposure measurement, present the results of audiometric measurement (pure tone audiometry), and report the results of a multiple regression analysis. Johnson et al. [22] discuss the results of the other audiological tests included in the test battery. Since the study population in both papers is the same, they are reviewed below as one study, with reference given in the text to respective publication.

An association between the biological determinant of styrene exposure and the auditory dysfunction was also observed in a cross-sectional study conducted in Sweden, which aimed at investigating the effects of occupational exposure to low levels of styrene and noise [21,22]. Styrene measurements were carried out for all the exposed workers, by means of air sample analysis and biological monitoring of mandelic acid in urine. Noise dosimetry
was conducted for a majority of the workers and covered all the different jobs performed in the plant. The workers not included in the noise dosimetry measurements were assigned the mean exposure values for the workers doing the same tasks. About 60% of the participants in both the groups exposed to noise (styrene and noise, and noise alone) were exposed to noise levels above the Swedish occupational exposure limit (OEL) (85 dBA/3 dB exchange rate), and the range of exposure was also similar in these groups (75–116 dB(A)). Styrene exposures were low, averaging 3.5 ppm, with a maximum level of 22 ppm (8 h values) [21,22].

Audiometric tests were used as outcome measures, including pure tone audiometry [21], central hearing tests, and otoacoustic emissions [22].

Air concentrations of styrene correlated with the biological measure of mandelic acid in urine [21].

Workers exposed to noise and styrene, and styrene alone had significantly worse pure-tone thresholds at 2, 3, 4, and 6 kHz when the group mean for each frequency was compared with the values for noise-exposed or non-exposed workers. The percentage of subjects with hearing levels (dB HL) above the median of age-correlated levels for the normal population in Sweden was significantly higher at 4, 6 and 8 kHz for both the groups exposed to styrene, whereas in the noise-exposed groups, a higher percentage of subjects with elevated hearing levels was found only at 6 and 8 kHz [21].

Speech-in-noise perception was also tested, and significantly worse results were found in all the exposed groups compared to controls. The central auditory evoked responses showed prolonged latencies in exposed workers [22].

A test of the ability to hear interrupted speech was used to examine the central part of the auditory system. In this test, only the workers exposed to styrene, with or without noise exposure, presented significantly worse results. The classification criterion of the normal values for this test was a score above the median of 93% of correct responses and the criterion for abnormal values, a score of 78% and below. A significantly lower percentage of subjects in both the groups exposed to styrene showed values above the normal median result (p < 0.05), and significantly more subjects in these groups had values below the criterion for abnormal results (p < 0.05). This finding indicates an effect on the central part of the auditory system that was not present among the noise-exposed workers [22].

Multiple regression analysis was also carried out to find the variables that contributed to the development of hearing loss (measured as pure tone thresholds) [21]. Age, noise exposure (past and current), and mandelic acid levels were the only variables that reached the level of statistical significance. The odds ratio estimates for hearing loss were 2.44 times higher for each mmol of mandelic acid per gram of creatinine (95% CI: 1.01–5.88), 1.18 times higher for each dB of current noise exposure (cumulative exposure index, 95% CI: 1.01–1.38), and 1.19 times higher for each year of age (95% CI: 1.11–1.28). The result of testing for interaction between noise and styrene exposure was not significant, suggesting an additive effect between the two agents [21].

These studies [21,22] included a relatively large population exposed to styrene and the results show the effects on the hearing system, evident at the group level.


As a part of a comprehensive project conducted in Poland to study the auditory effects of several solvents and noise, a group of workers exposed to styrene alone (n = 194) was compared with the groups of workers exposed to styrene and noise (n = 56); styrene and toluene (n = 26); styrene, toluene and noise (n = 14); and noise alone (n = 66), or unexposed workers (n=157). The participants from the styrene-alone group were exposed to noise levels of 80.3±3.0 dBA, whereas in the styrene and noise group, the noise level was 88.6±2.4 dBA. Styrene exposure was assessed as the averaged individual worklife exposure. Biological monitoring was not reported in this paper. Individual averaged worklife exposure to solvents was calculated from company measurements and detailed
questionnaire data, using the measured solvent exposure multiplied by years of exposure at different workplace and then divided by the total years of exposure. The worklife exposure level was 15 ± 9.5 ppm in the styrene-alone group and 8.4 ± 6 ppm in the styrene and noise group.

Pure tone audiometry was used for hearing assessment. Conductive hearing loss was excluded by using bone conduction audiometry measurements. Hearing loss (> 25 dB at more than one frequency above 2 kHz) was observed in 76% of the workers exposed to styrene and noise or styrene and toluene, in 57% of the styrene-alone group, 56% in the noise exposed group, and 33% in the unexposed group. Significantly higher mean audiometric thresholds (p < 0.05) were found among the styrene exposed workers at 2, 4 and 6 kHz, when compared to the noise-exposed and unexposed groups. When compared to the solvent-exposed groups, the mean thresholds were also significantly higher at the frequencies of 4 and 8 kHz.

A multiple logistic regression analysis for the risk of hearing loss was performed. The odds ratio (OR) for hearing loss after styrene exposure was 3.9 (95% CI: 2.4–6.2; adjusted for age and current and lifetime noise exposure). When all the subgroups were analyzed (adjusted for age), the ORs were 3.4 (95% CI: 1.7–6.4) for noise-alone group, 5.2 (95% CI: 2.9–8.9) for styrene-alone group, and 10.9 (95% CI: 4.9–24.2) for the group exposed to styrene and noise. In the subgroups for which exposure to toluene with or without noise was also included in the model, the OR was even higher, despite a smaller number of subjects in these groups.

Further analyses using multiple linear regressions revealed a significant relationship between the average worklife styrene concentration and hearing loss at the highest frequencies measured, 6 and 8 kHz.

This study [23] concerned a large cohort of workers and demonstrated a clear relationship, especially between styrene exposure and hearing loss. The effect was increased and potentiated both by coherent noise exposure and exposure to other solvents such as toluene. The effect shown is of outmost importance, the more so that the standard test for hearing, pure-tone audiometry, was used as an outcome measure.

**Hoffmann J, Ihrig A, Hoth S, Triebig G. Field study to explore possible effects of styrene on auditory function in exposed workers (2006) [24]**

In this study, 16 styrene-exposed workers in a boat building plant were compared with a control group of 16 workers, matched for age and noise exposure history, but not directly exposed to chemicals.

Styrene exposure was assessed by biological monitoring; styrene metabolites in urine were determined. The levels of mandelic acid (MA) and phenylglykoxylic acid (PA) in urine varied between 72–2213 mg/g creatinine, with a mean of 656 mg for the directly exposed workers. This mean value corresponds to approximately 25 ppm. For the controls, the mean of 130 mg MA+PA/g creatinine (approx. 5 ppm; range 25–478 mg/g creatinine) was determined.

Hearing ability was investigated by pure tone audiometry and transient evoked otoacoustic emissions (TEOAE). No differences between the two groups were found with respect to hearing thresholds at any frequency, or amplitude, or reproducibility of TEOAE.

The correlation of the duration of styrene exposure and exposure measurements with the hearing levels was investigated. Only single significant results were found at 1000 Hz for styrene exposure duration and at 500 Hz for urinary MA+PA.

The conclusion of this study [24] was that styrene exposure did not have any effect on the hearing level of the workers. This could be due to the small number of subjects examined or to the fact that also the controls were exposed to low levels of styrene.

**COMPARISON OF REVIEWED STUDIES**

As an overview, some exposure data and major findings of the studies discussed above are summarized in Table 2. Several differences between the studies can be noted. The size of the study populations varied from 16 up to over 500 workers. When the number of workers is too small, the results are less convincing than the effects on hearing detected in a larger exposed group.
studies differed in whether and how a historical exposure assessment had been made. Furthermore, different outcome measures were used to test the effects on the auditory and vestibular system, thus making the comparison of the effects somewhat difficult.

The current exposure levels for styrene vary between the studies from a mean of 4 ppm up to approximately 50 ppm. In most cases, the current exposures were reported to be below the threshold limit values. However, not only the current exposure levels did influence the results, and the

### Table 2. Summary of reviewed studies

<table>
<thead>
<tr>
<th>Exposure levels</th>
<th>Study groups</th>
<th>Results</th>
<th>Strength of evidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>S: &lt; 35 ppm</td>
<td>156 workers</td>
<td>Difference in hearing thresholds at 8 kHz between least exposed and most exposed workers</td>
<td>+</td>
<td>Muijser et al., 1988 [15]</td>
</tr>
<tr>
<td>N: &lt; 85 dBA</td>
<td>(59 S; 94 not exposed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S: &lt; 25 ppm</td>
<td>18 S</td>
<td>7 workers showed impairment of central hearing pathways. 16 workers showed abnormalities in vestibular tests</td>
<td>+ hear + bal</td>
<td>Möller et al., 1990 [16]</td>
</tr>
<tr>
<td>N: Estimated &lt; 85 dBA TWA</td>
<td>comp. to reference group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S: &lt; 26 ppm</td>
<td>299 workers</td>
<td>N and S exposures were highly correlated. Age and noise exposures were significantly associated with hearing loss</td>
<td>–</td>
<td>Sass-Kortsak et al., 1995 [17]</td>
</tr>
<tr>
<td>N: 80–89 dBA</td>
<td>(170 directly exposed; 86 indirectly exposed; 43 not exposed to S)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S: &lt; 54 ppm</td>
<td>20 workers all S exposed</td>
<td>No effects in hearing tests (PTA). 17 workers showed abnormalities in vestibular tests</td>
<td>– hear + + bal</td>
<td>Calabrese et al., 1996 [18]</td>
</tr>
<tr>
<td>N: not known</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S: Mean 8 ppm (1–93 ppm)</td>
<td>93 workers</td>
<td>No effect in PTA. Detection of high frequency tones was poorer in workers exposed to S &gt; 5 y. Reduction dose-dependent and correlated with S in air and biological exposure measures of S</td>
<td>++</td>
<td>Moroika et al., 1999 [19]</td>
</tr>
<tr>
<td>N: &lt; 85 dB</td>
<td>(44 S; 49 S in mixtures)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>S: Mean 22 ppm</td>
<td>54 workers</td>
<td>No effect in PTA. S exposed workers had poorer detection of high frequency tones than N exposed or unexposed</td>
<td>++</td>
<td>Moroika et al., 2000 [20]</td>
</tr>
<tr>
<td>N: S+N group = 76 dBA</td>
<td>(23 S and N; 19 N and 12 not exposed)</td>
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<tr>
<td>N: 86 dBA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>S: &lt; 4 ppm</td>
<td>313 workers</td>
<td>S exposed, and S and N exposed had worse PTA and lower scores in speech tests. Biological exposure measures of S correlated with hearing loss</td>
<td>++</td>
<td>Moroata et al., 2002 [21]</td>
</tr>
<tr>
<td>N: S group = 84 dBA</td>
<td>(89, S and N; 65 S; 78 N and 81 not exposed)</td>
<td></td>
<td>Johnson et al., 2006 [22]</td>
<td></td>
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<tr>
<td>N: S+N group = 89 dBA TWA</td>
<td></td>
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<tr>
<td>N group: 86 dB TWA</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Lifetime S: estimated to 15 ppm;</td>
<td>513 workers</td>
<td>4-fold (OR = 3.9; 95% CI: 2.4-6.2) increase in the odds of developing hearing loss related to S exposure. 2 to 3-fold increase in odds ratio in S and N, compared to S-only and N-only exposed subjects</td>
<td>+++</td>
<td>Śliwińska-Kowalska et al., 2005 [23]</td>
</tr>
<tr>
<td>(1–73 ppm)</td>
<td>(56, S and N; 194 S; 66 N; 26 S and toluene (T); 14 S, T &amp; N, and 157 not exposed).</td>
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<td></td>
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<tr>
<td>N: 70–93 dBA</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>S: approx 26 ppm (biolog. monit)</td>
<td>32 workers</td>
<td>Isolated correlations but inconsistent relationships between impaired hearing and exposure measures</td>
<td>–</td>
<td>Hoffman et al., 2006 [24]</td>
</tr>
<tr>
<td>N: not known</td>
<td>(16 S, 16 not exposed)</td>
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</table>

Abbreviations used: S — styrene, N — noise, ppm — parts per million, dBA — decibel A-weighted, TWA — Time Weighted Average (8 hours), kHz — kilohertz, PTA — pure tone audiogram, y — years, CI — Confidence Interval, hear — hearing, bal — balance.


The current exposure levels for styrene vary between the studies from a mean of 4 ppm up to approximately 50 ppm. In most cases, the current exposures were reported to be below the threshold limit values. However, not only the current exposure levels did influence the results, and the studies differed in whether and how a historical exposure assessment had been made. Furthermore, different outcome measures were used to test the effects on the auditory and vestibular system, thus making the comparison of the effects somewhat difficult.
The current level of exposure was low in all studies and especially low in the recent studies covering the largest number of workers exposed to styrene [19,21,23]. In some studies, the styrene-exposed workers were also exposed to noise at the level well below the current threshold limit value (85 dBA) [19,20,23], showing that noise does not seem to be a factor necessary for inducing the effects on the auditory system under conditions of styrene exposure. However, when the noise levels were above 85 dBA, an interaction between styrene and noise was detected [23]. High noise exposure can cause noise-induced hearing loss, which makes it impossible to detect any hearing loss caused by styrene exposure, as shown by Sass-Kortsak et al. [17]. When other solvents, such as toluene and n-hexane, are involved as well, the risk for hearing loss increases even further [23].

As there were many differences between the nine different populations, an attempt was made to compare some aspect of the methods used and the results (Table 3).

**CONCLUSIONS AND RISK EVALUATION FOR STYRENE AND EFFECTS ON THE AUDITORY SYSTEM**

The reviewed human studies provide evidence for the ototoxicity of styrene. The majority of these studies show effects on the auditory or the balance system. The effects are negligible and usually of a sub-clinical nature. In most cases, they cannot be shown at an individual level, but significant results are found in comparison with unexposed workers. Dose-relationships cannot be established from these data, since the exposure assessments differ between the studies. A meta-analysis of the raw-data from several of the study groups is currently under way and maybe this study will reveal some dose-response data.

Different methods were used for analysis of results. In some studies, the results were compared between different exposed groups and controls with or without noise exposure, some smaller studies compared the results to normal clinical values, while other studies correlated the effects on the auditory system to styrene exposure in different ways. In some of the larger studies, more than one of these methods was used.

As there were many differences between the nine different populations, an attempt was made to compare some aspect of the methods used and the results (Table 3).

**Table 3. Comparison of the results and methods used for the nine different study groups**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Used in N studies</th>
<th>N Positive studies</th>
<th>N Negative studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA</td>
<td>9</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>High frequency hearing</td>
<td>3</td>
<td>2–3?</td>
<td>0–1?</td>
</tr>
<tr>
<td>Central auditory tests</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Balance tests (central and peripheral)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>OAEs</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Result analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group comparison</td>
<td>6</td>
<td>4–5?</td>
<td>1–2?</td>
</tr>
<tr>
<td>Multiple regression</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Correlation with exposure</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Significant between-group differences, significant correlation with exposure, or abnormal values compared to reference values was considered a positive result. Varying numbers and the ‘?’ sign indicate that the result can be interpreted in different ways and that the study was counted both as positive and negative. Note that some studies use more than one method and/or analysis.
The evidence from these studies indicates that workers exposed to styrene, even below the current TLV values (of around 20–50 ppm), might be at risk for hearing loss. This means that actions should be taken and these workers should be included in the hearing conservation programs regardless of the noise levels in workplace. Such recommendations already exist in the new Noise Directive 2003/10/EC [25], on minimum health and safety requirements regarding the exposure of workers to the risks arising from noise. In Article 4 of Section II, Obligations of Employers, the Directive states that when carrying out risk assessments, the employers should “[…] give particular attention to: any effects on worker’s health and safety resulting from interactions between noise and work-related ototoxic substances […]” [25]. In 2003, the US Army published a factsheet on Occupational Ototoxins and Hearing Loss which argued that since the exposure threshold for ototoxic effects is not known, audiometric monitoring is necessary to determine whether the substance affects the hearing of the exposed workers [26]. Best practice guidelines addressing the auditory risks of chemicals were also published in Australia [27]. The European Directive should have been implemented in all the Member States by 2006.

More research and practical testing is necessary to develop better testing instruments for screening the hearing of these workers. However, a test of the speech or listening ability of the central auditory system should be instantly included in the hearing conservation program.

REFERENCES


