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Hearing loss among workers exposed to moderate concentrations of solvents

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Objectives It is known that some industrial organic solvents are ototoxic. This study was aimed at evaluating the hearing effects of a mixture of organic solvents alone or in combination with noise on employees in paint and lacquer enterprises. The concentration of solvents was below the occupational exposure limits (OEL) for most of the subjects.

Methods Altogether 517 subjects were divided into the following three groups: persons with no risk due to noise or organic solvent exposure at the workplace, workers exposed to organic solvents only, and workers exposed to both organic solvents and noise.

Results The relative risk (RR) of hearing loss in the solvent-only exposure group was significantly increased (RR 4.4 and RR 2.8 for noise exposure of < 80 dB-A and < 85 dB-A, respectively) in a wide range of frequencies (2–8 kHz). No additional risk in the solvent + noise exposure group was found (RR 2.8). Hearing thresholds were significantly poorer in a wide range of frequencies (1–8 kHz) for both groups exposed to solvents, when compared with the reference group. The mean hearing thresholds at frequencies of 2–4 kHz were poorer for workers exposed to solvents + noise than for the solvent-only group; this finding suggests an additional effect for noise. However, there was no correlation between hearing loss and the extent of solvent exposure.

Conclusions The results indicate that occupational organic solvent exposure at moderate concentrations increases the risk of hearing loss, and the ototoxic effects should be considered when the health effects of exposed workers are monitored.

Key terms noise, occupational exposure level, relative risk, xylene.

Noise exposure has been commonly regarded as the main hazard of occupational hearing loss. Other ototoxic factors associated with industrial environments, both of a physical and chemical nature, are often neglected. However, the information currently available indicates that several chemicals, including organic solvents such as xylene, toluene, styrene, n-hexane, and trichloroethylene, have noxious, neurotoxic, and ototoxic effects. These substances and their mixtures are common in industrial environments.

In the early 1980s, Rebert et al (1) were the first to provide evidence on organic solvent ototoxicity in rats. Later, the case study of Barregård & Axelsson (2) reported enhanced hearing loss in four subjects exposed to noise and solvent chemicals — the hearing damage was higher than the one expected in cases of sole exposure to noise. Later studies, on a remarkably larger population, confirmed that exposure to organic solvents is associated with excessive hearing loss (3, 4). The results published by Morata et al in 1997 (5) and by

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Morioka in 2000 (6) are even more alarming, suggesting that such solvents may be harmful at concentrations within the limits recommended by international agencies. Moreover, organic solvents may increase the noise effect on hearing, as they cannot only damage widespread regions of the cochlea, but also more central auditory pathways and the cortex (4). Currently, the population of workers exposed to organic solvents is not included in hearing conservation programs, since occupational legislation does not consider environmental chemicals hazardous to the auditory system.

This study was aimed at evaluating the hearing of employees exposed to a mixture of organic solvents at a moderate, anticipated as safe, concentration in paint and lacquer enterprises. Since some workers were not only exposed to organic solvents, but also to noise, we further attempted to investigate the effect of combined exposure to organic solvents and noise. Finally, the relation between the amount of exposure and hearing loss was assessed.

Subjects and methods

Study population

The study population included workers of four Polish paint and lacquer enterprises. Data on the exposure to organic solvents have been collected by one of the coauthors for the last 5 years. For all the subjects, the estimation of exposure hazards within the last 20 years was based on data provided by local authorities responsible for hygiene and safety at enterprises. For a few of the workers exposed to solvents for more than 20 years, the estimation was based on the oldest data available. After 1960, the industry was modernized, and the technological processes were vent-controlled. Since then, exposures have remained at a constant level. Four enterprises applied similar technologies and used an organic solvent mixture of similar composition. Some employees were not only exposed to organic solvents, but also had exposure to noise at levels up to 100 dB-A.

The workers were included in the study according to the following inclusion criteria: at least 6 months of exposure to solvents, no history of middle-ear diseases, normal tympanic membrane appearance when examined, no air-bone gap in audiometric tests, tympanogram type A, and present ipsilateral stapedius reflex.

Altogether, 517 subjects were included and divided into three groups.

The reference group contained 214 subjects (113 men and 101 women), primarily white-collar workers with a few other employees, aged 19 to 72 (mean 38.5, SD 10.6) years, with no hazardous noise or organic solvent exposure. The exposure to noise was below or equal to a sound pressure level of 80 dB-A for 174 of the 214 persons, and it ranged from 81 to 85 dB-A for the remaining 40 subjects.

The solvent-only exposure group contained 207 subjects, including 121 men and 86 women, aged 22 to 63 (mean 39.3, SD 9.5) years. Their responsibilities required direct exposure to resin paint chemicals manufactured at different sites, including the mechanical service of factory machines, the preparation of paint mixtures, and the supervision of the quality laboratory. For 104 of the 207 workers the noise exposure was ≤ 80 dB-A, and for 103 workers it was in the range of 81 to 85 dB-A. The time of employment was 0.5 to 39 (mean 12.8, SD 8.2) years.

The solvent + noise exposure group included 96 subjects, 77 men and 19 women, aged 20 to 58 (mean 38.4, SD 9.1) years. These persons also manufactured resin-based paints, similar to those in the solvent-only exposure group, but they operated other machines. The exposure to noise was > 85 dB-A. The time of employment ranged from 0.5 to 39 (mean 12.2, SD 8.5) years. All the workers exposed to noise had been enlisted into a hearing protection program, and they wore hearing protectors regularly.

To determine whether underlying differences may have existed between the groups, the subjects' previous exposure to noise, previous exposure to chemicals, medical and audiological history, hobbies, and prior military service were assessed in detail. Data were collected in an interview based on a questionnaire with approximately 20 questions on work and medical history, current health status, occupational and nonoccupational exposure, and life-style (including alcohol and tobacco consumption). The interview protocol included questions concerning demographic data, health information that focused on events that could be related to hearing status, and nonoccupational noise exposure data. The self-reported medical history included data on diabetes, high blood pressure, serum cholesterol, prior ear surgery, head injury, high fever, measles, mumps, ear infections, family history of hearing loss, use of ototoxic medication, and tinnitus. Diabetes and high blood pressure were reported as positive if an employee had received or was receiving treatment for this condition.

The differences were related to gender (the group exposed to solvents and noise included more men), pigment concentration (more blond and reddish haired subjects in the reference group), medical history of acoustic trauma (more common in the group exposed to solvents only), and head trauma (more often in both groups exposed to solvents). Furthermore, symptoms suggesting inner-ear and central-nervous-system damage, such as tinnitus or vertigo, were more often noted in the group exposed to solvents. A higher percentage of subjects in

the reference group reported therapy with ototoxic antibiotics in the past.

Solvent exposure assessment

Personal monitoring with the dosimetry method was used for the air sampling. The subjects were provided with personal sampling pumps that they carried during all daily routine operations. The sampling duration was always close to the normal worktime, not shorter than 75% of an 8-hour workshift, in accordance with adopted uniform criteria for work environment monitoring (Polish Standard PN–89/Z–04008.07). Air was sampled by passing a known volume of air through sorbent tubes containing two sections of charcoal using SKC personal sampling pumps (model 222–4, SKC Inc, Eighty Four Pennsylvania, United States). Both sections of charcoal were eluted with 1 ml of carbon disulfide. The eluate was analyzed with gas chromatography (gas chromatograph HP-5890 series II). A detailed description of the solvent assessment procedure is available elsewhere (7).

In the companies manufacturing paint and lacquer, the subjects were exposed to a solvent mixture with mixed xylene isomers (ortho, meta and para) always as one of the predominant ingredients (ie, in 1999 the xylene fraction varied from 13.6% to 55.6% of the entire mixture, depending on the manufacturing site). Furthermore, the content of ethyl acetate and white spirit was notable, and there were detectable concentrations of toluene, butyl acetate, and ethyl benzene. The content of the remaining chemicals constituted a very low percentage of the entire mixture weight.

The xylene air concentration in 1999 ranged from 0 to a maximum of 290 mg/m^3, and the arithmetic and geometric means did not exceed the Polish occupational exposure limit (OEL 100 mg/m^3) in any of the factories. In addition, the exposure index for the mixture, calculated as the sum of the fractions (concentration of given chemical by its normative limit) of all the compounds of the mixture, did not exceed the limit (value 1) in any of the companies studied. The highest solvent concentration was observed in the department that manufactured resin-based paint and in the local laboratories, where the upper limit of exposure was exceeded at times.

Since the employees were exposed to different solvent concentrations at different workplaces during different employment periods, we calculated the average exposure over each employee's worklife using the following equation:

$$[(a_1 \times b_1) + \ldots (a_n \times b_n)] / (b_1 + \ldots b_n),$$

where a_i (i = 1...n) = solvent concentration (or exposure index) at a given place of work over the time period between two consecutive measurements of exposure, b_i (i = 1...n) = period of employment (in years) with solvent concentration (or exposure index) of a_i.

The lifetime exposure average concentration of solvent above the OEL or an exposure index value of >1 indicated overexposure to solvents. As the contact of the reference subjects with trace quantities of organic solvent mixtures in the place of employment could not be excluded and as there was a possibility of contact with paints and varnishes in everyday life, the critical limit value for solvents between two distinctive groups of exposed and unexposed subjects was based on the mean individual exposure index for the mixture equal to 0.25 (< 0.25 = unexposed, ≥ 0.25 = exposed to solvents).

Table 1 presents the workers' exposure to organic solvents. The mean xylene and ethyl benzene concentrations were similar in the solvent-only and solvents + noise exposure groups, whereas the ethyl acetate, white spirit, toluene, and butyl acetate concentrations, as well

Table 1. Lifetime average exposure to solvents in the study groups. (OEL = occupational exposure limit)

Organic solvent	Exposure level (mg/m^3)						OEL[a]
	Solvent-only exposure group			Solvent + noise exposure group			
	Mean	SD	Range	Mean	SD	Range	
Xylene	28.7	22.3	1.0 – 110.0	28.3	18.7	1.0 – 86.4	100
Ethyl acetate	11.5	23.8	10.8 – 61.6	7.7	23.8	0.0 – 120.0	200
White spirit	11.7	61.6	0.0 – 563.0	7.0	12.2	0.0 – 64.4	300
Toluene	8.4	10.4	0.0 – 92.5	5.8	7.9	0.0 – 48.0	100
Butyl acetate	8.3	35.9	0.0 – 285.5	1.8	4.4	0.0 – 16.6	100
Ethyl benzene	7.7	10.8	0.0 – 65.6	7.9	4.4	0.3 – 65.6	100
Exposure index[b]	0.8	0.5	0.3 – 3.0	0.6	0.3	0.3 – 1.6	1

[a] Values above the OEL indicate overexposure to solvents. Some OEL values are lower in other countries (ie, the OEL value for xylene is 50 mg/m^3 in Sweden, and the toluene OEL is 50 mg/m^3 in many countries).
[b] Sum of the fractions (concentration of given chemical by its normative value) of all the compounds in the mixture; values above 1 indicate overexposure to a mixture of solvents.

as the exposure index, were slightly higher in the solvent-only group. Neither did the mean value exceed the limits.

Table 2 illustrates the distribution of the study population in relation to the level of solvent exposure. The solvent-only group included a higher percentage of persons overexposed to the mixture of solvents (indicated by the exposure index) and its main compound xylene, and the time of exposure of these workers was longer if compared with that of the solvent + noise group.

Noise exposure assessment

Sound pressure measurements were conducted with a sound pressure level meter (model 2231, Brüel & Kjær). These measurements were performed according to the 1994 Polish standard (PN–N–01307:1994) and with reference to the Polish standard PN–N–01307:1994 and standard ISO 9612:1997 of the International Organization for Standardization (ISO). The assessment of occupational exposure to noise was based on the noise exposure level averaged over the total time of exposure.

The critical limit for noise between two distinctive groups of exposed and unexposed subjects was based on the admissible A-weighted sound pressure level of 85 dB-A (≤ 85 dB-A = unexposed, > 85 dB-A = exposed to noise).

The analysis of noise exposure indicated that 78% of the solvent + noise exposure group was exposed to moderate levels of noise (86–90 dB-A) and 2% was exposed to extreme levels of noise (around 100 dB-A).

Testing procedures

To assess the workers' hearing status, otoscopy, puretone audiometry, and immittance audiometry were performed by an audiologist. Otoscopy and audiometry (using a Madsen-type Zodiac 901 immittance audiometer) were performed to screen for conditions that would require that the subject be excluded from the study (ie, external otitis, otitis media or a perforated tympanic membrane).

Pure-tone audiometry was performed for all the subjects at the frequencies of 1, 2, 3, 4, 6 and 8 kHz. Bone conduction testing was performed at the affected frequencies in the range of 1 to 4 kHz. The subjects were tested in a quiet room that met the requirements of the ANSI S 3.1–1991 standard of the American National Standards Institute for audiometric testing environments, at least 14 hours after the last exposure to noise. The interacoustic type AC 40 audiometer was calibrated according to the ISO R389–1964 norm prior to the data collection. Daily biological calibration checks were also performed immediately before the testing. Audiograms were classified as normal if none of the single hearing thresholds exceeded hearing loss of 25 dB for either ear.

Table 2. Study population by exposure to solvents.[a]

Exposure indices	Solvent-only exposure group			Solvent + noise exposure group		
	Workers		Mean duration of exposure (years)	Workers		Mean duration of exposure (years)
	N	%		N	%	
Xylene concentration						
≤ 50 mg/m³	170	82	13.1	85	89	12.8
50–100 mg/m³	29	14	10.2	11	12	7.5
>100 mg/m³	8	4	20.3	-	-	-
Exposure index for the mixture[b]						
≤ 0.5	57	28	13.0	53	56	12.5
0.51–1.0	92	44	12.9	34	35	13.8
> 1.0	58	28	12.4	9	9	4.7

[a] Only xylene and the exposure index.
[b] Above 1 indicates overexposure to solvents.

Data analysis strategies

Extensive checks and rechecks were made for invalid codes or consistency errors. The data were analyzed with SPSS® for Windows and EGRET® software. The statistical analysis was based on the following tests: one-way analysis of variance with the multiple comparisons test to determine the mean hearing loss at respective frequencies and multiple logistic regression to model relative risk in relation to the study parameters and the covariates of age and gender. The multiple logistic regression model was used to identify any relation between solvent exposure (substance concentration, exposure indices) and the probability of hearing loss. Furthermore, a multiple linear regression model was used to determine the relation between the amount of exposure and the profoundness of hearing loss.

Results

Incidence and risk of hearing loss

The highest incidence of hearing loss (61.5%) was found in the solvent + noise exposure group. For the solvent-only exposed subjects, this value was slightly lower (57.5%). Differences between the solvent-only group and solvent + noise group were noted for the right ear (hearing loss more common in the solvent + noise group — 54% versus 45%). No difference of this type was found for the left ear (in both groups the incidence was 49%). The incidence of hearing loss in both of the exposed groups was significantly increased when compared with that of the referents (36%).

The relative risk of hearing loss in the two groups exposed to solvents was significantly higher than in the reference group, and no apparent difference was found between the solvent-only group and the solvent + noise group (RR 2.8, 95% CI 1.8–4.3 and RR 2.8, 95% CI 1.6–4.9, respectively). The relative risk of hearing loss was calculated separately for the subgroup of solvent-only exposed workers, whose occupational exposure to noise was equal to or below 80 dB-A (considered to be a level fully safe for the auditory system). The probability of hearing loss was significantly elevated in this subgroup and 4.4 times higher than in the noise-matched reference subgroup (95% CI 2.3–8.1).

Risk of hearing loss at specific frequencies

The analysis for relative risk of hearing loss at respective frequencies proved that there was a hazard of hearing impairment for both ears within the wide range of frequencies. For the right ear the odds ratios matched the significance in the range of frequencies from 2–8 kHz in both groups exposed to organic solvents. For the left ear these values were significantly elevated within the range of frequencies from 2 to 8 kHz in the solvent-only group and from 2 to 6 kHz in the solvent + noise exposure group. At all the studied frequencies the risk of hearing loss was slightly higher in the solvent + noise group when this group was compared with the solvent-only group (figure 1).

Extent of hearing loss

Averaged air-conduction audiometric curves are presented in figure 2. As hearing loss of sensory origin was the only one analyzed, bone-conduction audiometric curves were disregarded to clarify this figure.

The hearing threshold values were significantly increased (ie, worsened) in both groups exposed to organic solvents in a comparison with the referents at all the frequencies tested. The hearing loss was essentially poorer in the solvent + noise group than in the solvent-only group, matching significance for frequencies 3 and 4 kHz for the right ear and 2, 3 and 4 kHz for the left ear.

Correlation between exposure indices and hearing loss

The correlation between the exposure indices and hearing loss was determined in the group exposed to solvents only. There was no linear correlation between the risk of hearing loss and the individual solvent exposure indices (ie, mean concentration of solvents and the exposure index for the mixture). A positive linear correlation was found between some exposure indices and the hearing audiometric thresholds at single frequencies only, including the mean toluene concentration and hearing loss in the right ear at frequencies 4 and 6 kHz, the mean toluene concentration and hearing loss in the left ear at frequencies 3, 4 and 6 kHz, the mean xylene concentration and hearing loss at 3 kHz in the right ear,

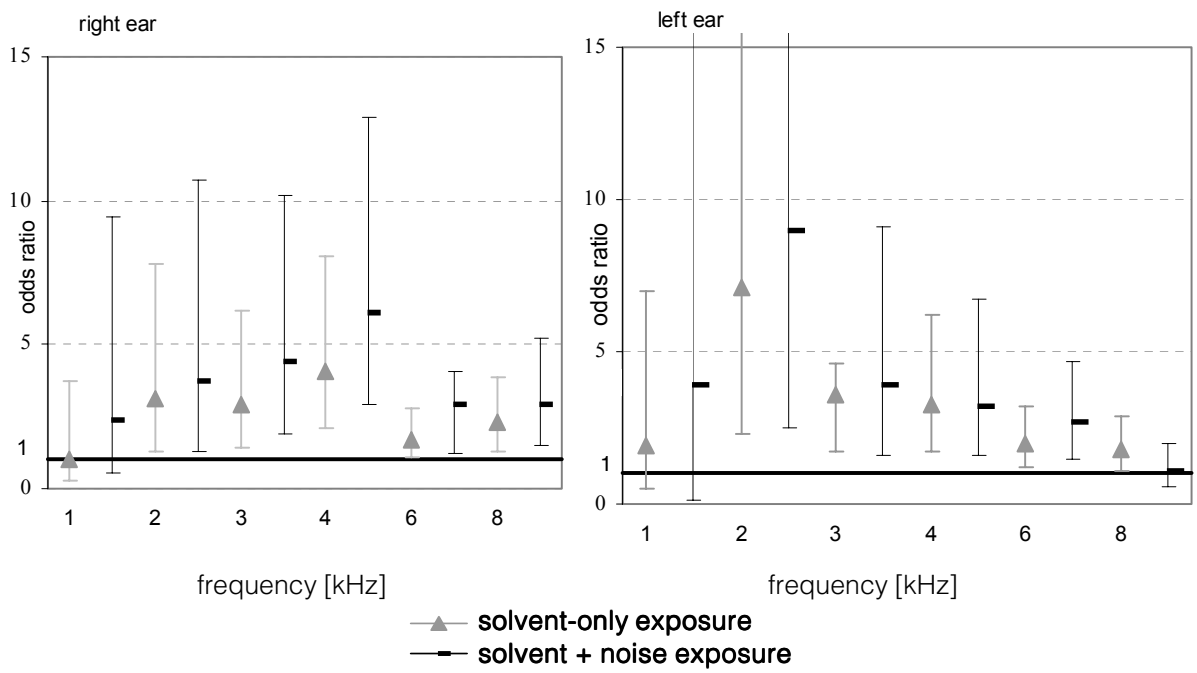

Figure 1. Odds ratios for hearing loss at specific frequencies in the solvent-only exposure group and the solvent + noise exposure group in relation to the reference group. (If the lower end of the 95% confidence interval is above 1, the odds ratio reaches the level of significance)

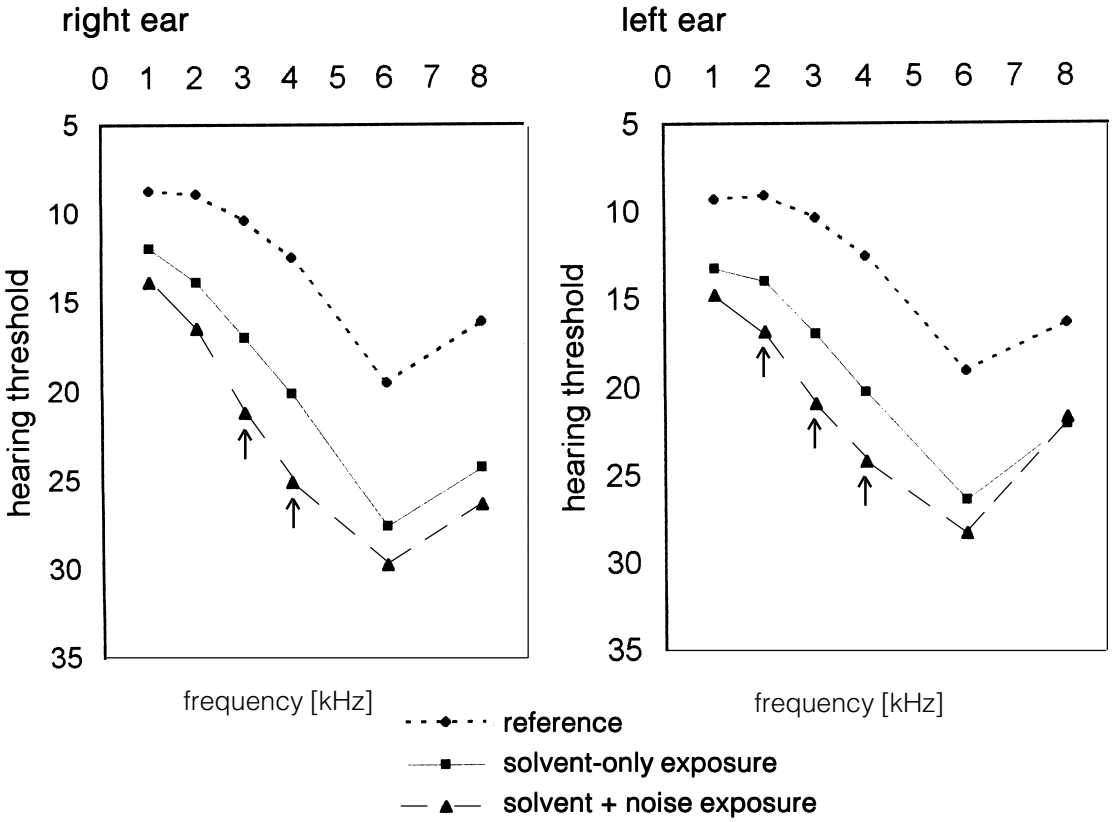

Figure 2. Mean air-conduction audiometric curves of the study groups. [Arrows indicate where the mean hearing thresholds in the solvent + noise exposure group and the solvent-only exposure group differ significantly ($P < 0.05$)]

and the mean index for the mixture of solvents and hearing loss in the left ear at 2 kHz.

Discussion

Previous reports for humans indicate that occupational exposure to a mixture of organic solvents (with or without noise) increases hearing loss. The 20-year prospective studies by Bergström et al (3) indicated that the incidence of social-disability-related hearing loss among employees exposed to organic solvents and noise was significantly higher (23%) if compared with that of subjects exposed to noise but not exposed to chemicals (5–8%). These effects were found even though the noise level in the chemical division had been lower (80–90 dB-A) than that in other branches (95–100 dB-A). A cross-sectional design study (8) with more than 3000 male subjects showed that exposure to solvents, without noise, for over 5 years, resulted in an adjusted relative risk of 1.4 for self-assessed hearing impairment. The data from Morata et al (4) demonstrated that the isolated exposure of workers to a mixture of organic solvents containing mainly toluene, xylene, benzene, methyl ethyl ketone, methyl isobutyl ketone, and ethanol (in a printing plant) was associated with a more than fivefold increased risk of hearing impairment. Furthermore, another Morata et al (5) study on the cohort of petrochemical workers exposed to various levels of noise and solvent mixtures estimated the adjusted odds ratios of 1.8–3.0 for high-frequency hearing loss, depending on the specific department.

Our study population included employees exposed to solvents in the paint and lacquer industry. The concentration of the solvent mixture was comparable to that of the study by Morata et al (4) on solvent concentrations in a paint filling division. The level of noise depended on a given place of work and its mean level exceeded the permissible value of 85 dB-A equivalent sound pressure level for about one-third of the persons studied. To assess the effects of solvents and noise on hearing separately, this population was divided into two groups, a solvent-only exposure group and a solvent + noise exposure group. Other occupational risk factors related to hearing loss were surveyed and carefully

searched for with the use of a questionnaire. No differences were revealed that might impair hearing in the groups exposed to organic solvents. These results imply that the incidence of hearing loss was elevated in the solvent-only group when compared with that of the unexposed reference group. Thus the relative risk of hearing loss was 2.8–4.4 times higher (depending on whether the 85 dB-A or 80 dB-A cut-off point was used for noise exposure). This range is similar to that found by Morata et al (5). Since noise levels below 80 dB-A are considered safe for the auditory system, these data imply that the increased risk of hearing loss was due to occupational exposure to organic solvents. The increased risk of hearing loss was found for nearly the entire range of analyzed frequencies (2–8 kHz). Furthermore, pure-tone audiometry showed significantly higher mean hearing thresholds in the solvent-only group when it was compared with the referents at all the frequencies tested (from 1–8 kHz). It is possible that solvent exposure alone affects a wide range of frequencies, including the middle frequencies, not only the high frequencies, as in the case of noise (3).

It should be noted that most of our subjects were exposed to concentrations below the permissible level (generally accepted as safe for the nervous system). This finding confirms the previous suggestion of Morata et al (4) and Morioka et al (6) that moderate occupational exposure to solvents may enhance the risk of hearing loss, even when differences in the composition of applied mixtures are to be considered.

The data from previous studies on animals (9–14), along with the findings among substance abusers (15), may imply that the most potent ototoxic solvents among those used in the lacquer and paint industry are xylene, toluene, ethyl benzene, and white spirit. Exposure to xylene was earlier demonstrated to impair hearing at middle and high frequencies in rats (16) and to cause vestibuloocular disturbances (17). It has also been proposed that xylene may display a more enhanced ototoxicity than toluene (13). Toluene (but not its metabolite) damages both cochlea and the retrocochlear auditory pathway as assessed by auditory brainstem responses (18) and distortion product otoacustic emission (19–20). Exposure to ethyl benzene in rats resulted in an increase in the threshold for the compound action potential by up to 30 dB in a large frequency range (1–24 kHz), due to outer hair cell loss (21). White spirit exposure also led to a dose-dependent increase in the amplitude of the auditory brainstem response of the same strain of animals (22). No data on the ototoxicity of isolated exposure to ethyl acetate and butyl acetate are yet available.

In industrial environments, exposure to organic solvents often occurs simultaneously with noise. This could be a confounding factor in assessments of the solvent influence on hearing. Synergistic or additive effects of solvents and noise have been demonstrated in animal studies (23, 24). The levels of exposure in these studies were, however, remarkably higher than those at the workplace. Thus no apparent conclusions can be drawn as to whether or not the interaction would have occurred at lower, more occupationally relevant, levels of exposure.

Research data on the combined effects of noise and organic solvents on human hearing are difficult to analyze due to the numerous confounding factors. Morata et al indicated that simultaneous exposure to noise and toluene brings about an over 11-fold increase in the risk of hearing impairment in comparison with the 5-fold increase due to exposure to a solvent mixture only and the 4-fold increase due to exposure to noise only (4). However, the interpretation of these results should consider the quantitative and structural differences of the groups. The employees exposed to noise and toluene, especially prior to the installation of air conditioning, were exposed to an extremely high concentration of toluene, while those included in the group exposed to solvents without noise were exposed to an organic solvent mixture, including toluene among other compounds, but at much lower levels. Thus the toluene effect in the first group could have been much more pronounced than the mixture effect in the second group, regardless of the influence of the noise itself. The retrospective epidemiologic studies (8) on the effects of mixed solvent and noise exposure, as well as those by Sass-Korsak (25) on noise and styrene, indicate that, in the case of combined exposure, noise effects are dominant. These authors did not observe any additional (synergistic or additive) effect of solvents. On the other hand, Morioka at al (6) provided data on the probable combined effects of organic solvents and noise by exploring the upper limit of hearing among exposed and unexposed persons.

Our data showed that the incidence of hearing loss was slightly higher in the solvent + noise group than in the solvent-only group. However, the adjusted odds ratio was similar in both groups. The additive effect of the combined exposure group may have been hidden in our study due to more extensive solvent exposure in the solvent-only exposed group. It should be also emphasized that solvents make people more susceptible to hearing loss at lower levels (80–85 dB-A) that influence the hearing loss pattern. On the other hand, the hearing thresholds were significantly worsened in the range of 2–4 kHz in the group exposed to organic solvents and noise as compared with the solvent-only exposure group; this finding suggests the possibility of an interaction between the hazards. There is no doubt that the accurate identification of involvement of each risk factor in the case of combined exposure to chemical and physical hazards merits further studies on large, properly randomized populations, including noise-only exposure groups, which were not available in our study.

Thus far, epidemiologic data have not succeeded in demonstrating a correlation between the solvent exposure level and the risk or the probability of hearing loss. In our study, we did not find any correlation between the indices of inhaled exposure and the risk of hearing loss. However, we demonstrated a linear correlation between the extent of hearing loss and some exposure indices; this result suggests a possible relationship between these parameters. Biological monitoring seemed to be more adequate for this purpose, as Morata at al were able to demonstrate a correlation between hearing loss and hippuric acid, the biological marker for toluene, in urine. According to this report, odds ratio estimates were 1.76 times greater for each increment of hippuric acid per gram of creatinine in urine (95% CI 1.00–2.98) (26). Further studies on the dose-response relationship should be performed.

Currently, assessing the safety of organic solvents for humans is based on psychological, hepatotoxic, and respiratory symptoms. The results of this study show that workers exposed to a mixture of organic solvents at moderate concentrations have an increased risk of hearing loss. Thus the ototoxic effect of organic solvents should be considered in the monitoring of health effects on exposed workers.

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