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# EFFECTS OF OCCUPATIONAL EXPOSURE TO A MIXTURE OF SOLVENTS ON THE INNER EAR: A FIELD STUDY

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**Abstract.** Some clinical and laboratory studies indicate that industrial solvents such as toluene, styrene, xylene, trichloroethylene and carbon disulfide or their mixtures may affect the inner ear, although the mechanism of this process is still not well understood. The aim of this investigation was to assess the incidence of hearing and vestibular disorders (using modern audiological and vestibular tests) in 61 workers exposed to a mixture of organic solvents at the production of paints and varnishes; the control group included 40 age-matched non-exposed subjects. Environmental and biological monitoring revealed that the most significant exposure can be attributed to the following mixture constituents: ethylbenzene, xylene and trimethylbenzene isomers such as pseudocumene, mesitylene and hemimellitene. Electronystagmographic examinations showed the symptoms of vestibular dysfunction, as well as the decreased duration, amplitude and slow phase angular velocity of induced nystagmus in 47.5% of the subjects exposed versus 5% of controls. This was accompanied by sensorineural high frequency hearing loss, identified by means of pure tone audiometry in 42% of those exposed versus 5% controls, and reduced amplitudes of transiently evoked and distortion-product otoacoustic emissions. The findings closely correspond with the rate of the total exposure to the solvent mixture. A possible mechanism responsible for ototoxicity of solvents is discussed.

**Key words:**
**Organic solvent mixture, Environmental and biological monitoring, Pure tone audiometry, Otoacoustic emissions, Electronystagmography, Hearing and vestibular disorders**

## INTRODUCTION

The assessment of health effects of occupational exposure to organic solvents has recently been an important problem for occupational medicine specialists and numerous toxicological research centers dealing mainly with neurology and otoneurology. The reason is that organic solvents, chemicals widely spread in industry, are characterized by high volatility and lipid solubility, which enhance their absorption in tissues and their binding to lipids. As the nervous tissue is mostly composed of lipids, it is particularly sensitive to solvent toxicity.

Chronic exposure to vapors of solvents, frequently a mixture of different compounds, may lead to long-term or even permanent functional pathology in the central and peripheral nervous systems, especially in workers exposed to high concentrations of these chemicals [1,2]. Some studies [3,4] report that solvents at low doses, below the recommended threshold limit values, may produce mild but clinically detectable sensory impairments. However, the quantitative data on exposure have not been available to allow the dose-response relationship to be characterized.

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**Table 1.** References on ototoxic effects of exposure to solvent in animals

| Author | Effect | Toxicant |
|---|---|---|
| Bushnell, et al. [5] | ABR: increased latencies across toluene concentration growth | Toluene |
| Campo, et al. [6] | Cochlear lesion in measurements of near field potentials from the inferior colliculus | Toluene |
| Crofton, Lassiter and Rebert [7] | Mid-frequency hearing loss (8–16 kHz) in reflex audiometry | Styrene, xylene mixture, n-butanol |
| Fechter, et al. [8] | Mid-frequency hearing loss (8–16 kHz) in reflex audiometry and in cochlear action potentials | Trichloroethylene |
| Gagnaire, et al. [9] | ABR: time– and dose-dependent increase in the peak latencies, as well as in interpeak I-V differences, and decrease in amplitudes | Diethylbenzene and diacethylbenzene |
| Johnson [10] | Frequency specific ABR: maximal threshold shifts between 6.3–12.5 kHz; DPOAE: lowered amplitudes | Toluene |
| Niklasson, et al. [11] | ENG: central vestibular system disorders | Toluene, styrene, trichloroethane |
| Rebert, et al. [12] | ABR: decreased amplitudes correlated with blood levels of solvents | Styrene, trichloroethylene |
| Rebert, et al. [13] | ABR: increased latencies as a dose increased | Mixture of solvents (xylene, chlorobenzene, trichloroethylene) |

**Table 2.** References on ototoxic effects of exposure to solvents in humans

| Author | Effect | Toxicant |
|---|---|---|
| Abbate et al. [14] | ABR: alteration in electric responses | Toluene |
| Hirata et al. [15] | ABR: delayed latencies of main components | Carbon disulfide |
| Laukli and Hansen [16] | Sensorineural hearing loss or central auditory disorders in the test battery (PTA HFA, SRT, ABR, filtred speech) | Various industrial solvents |
| Morata et al. [17] | Central auditory lesion in stapedius reflex testing (reflex threshold and decay) | Toluene |
| Odkvist et al. [18] | Auditory and vestibular lesions of a central origin found in cortical response audiometry and dynamic posturography | Industrial solvents |
| Pollastrini et al. [19] | ENG: assymetry in vestibular reactions, abnormal saccades, spontaneous nystagmus<br>Auditory tests: central lesion | Benzene derivatives |
| Sułkowski [20] | ENG: positional nystagmus, abnormalities in eye-tracking and optokinetic tests | Carbon disulfide |

Nowadays, a lot of data provide evidence that the subtle sensorineural elements of the inner ear may also be damaged by solvents.

A recent literature review on the ototoxic effect of exposure to solvents in both laboratory animals and humans is given in Table 1 [5–13] and Table 2 [14–20]; it suggests two distinct patterns of cochlear dysfunction.

One pattern produced by toluene involves the impairment of outer hair cells that normally encode middle frequency tones located in the middle turns [21]. The ototoxicity appears to stem from a preferential perturbation in motility of these cells and, thereby of sensitivity to sound. Preferential dysmorphia in these cells and impaired regulation of free intracellular calcium level occur rapidly and at low concentrations of toluene predicted to occur in the brain of humans exposed to its permissible levels. Because the outer hair cell alone shows rapid electromotility, a process sensitive to [Cai2+], it may particularly be vulnerable to ototoxic agents that disrupt intracellular calcium regulation. The second pattern produced by trichloroethylene, unlike toluene, impairs preferentially inner hair cell-spiral ganglion cell function. It is yet to be determined whether this reflects excitotoxic injury at this synapse [5].

There is still a lack of well documented investigations trying to explain the mechanism of ototoxicity of the solvent mixture and evaluate the function of both the parts of the

inner ear (cochlear and vestibular) at large in workers employed in real industrial conditions.

The major objective of this study was to examine the physiological effects of occupational exposure to a mixture of organic solvents on the auditory and vestibular systems in the factory workers involved in the production of paints and varnishes.

## MATERIALS AND METHODS

Of the 95 workers exposed to a mixture of organic solvents, a final sample of 61 subjects (only men, aged 22–58 years; mean, 39.8 ± 11.2) was selected following a questionnaire survey and otolaryngological examinations. Those with middle ear pathology, past ear surgery, head injuries, ototoxic drug treatment, diabetes, hypertension, neurologic diseases, alcohol abuse and history of noise exposure were excluded from the study. The duration of employment and exposure to the mixture of solvents in the study group ranged from 2 to 34 years (mean, 15.8 ± 9.1).

People working in direct contact with solvent vapors, such as resin synthesis analyzers, dry component mixers, mill operators, dispenser operators, colorists and packers of final products were only eligible for the study.

The control group consisted of 40 non-exposed healthy workers, aged 25–56 years (mean 39.2 ± 10.5), employed in the administration and transport service of the same factory.

In order to identify the work environment pollutants, individual dosimeters were used for air sampling at all workposts; the workers were provided with personal pumps which they carried during all daily routine operations, and the duration of sampling was always close to the nominal working time, usually not shorter than 80% of an eight-hour working shift. The ventilation systems were in use at the time of the study.

Biological monitoring of exposure to solvents involved the analysis of their blood levels and urinary excretion of the relevant metabolites, performed by gas chromatography with a flame-ionizing detector; the capillary blood samples were collected within 15–20 min after working shift; urine fractions were taken from the last 4 h of the shift.

Clinical examinations were carried out mostly in audiobus, a mobile audiological vehicle equipped with a sound-proof cabin and diagnostic apparatus for a comprehensive evaluation of hearing [22]; only electronystagmographic (ENG) investigations with use of the electronically steered rotatory armchair, optokinetic projector and Enthermo system for caloric stimulation were performed in the out-patient clinic laboratory.

The following audiological tests preceded by anamnesis and otolaryngological checking were applied in all subjects: air and bone pure tone audiometry (PTA), impedance audiometry with tympanometry (T), acoustic reflex threshold (ART) measurement, and otoacoustic emissions (OAE), both transiently evoked emissions (TEOAE) and distortion product otoacoustic emissions (DPOAE) if present, spontaneous emissions were also recorded.

The ENG investigations included a battery of tests, including: saccadic and eye-tracking test, spontaneous and positional nystagmus, optokinetic test, rotatory ($2°/sec^2$–90°/sec) and bithermal (30 and 44°C) caloric test.

Both the clinical data and exposure measurements were assessed and interpreted according to the routine obligatory rules and procedures published earlier [23, 24].

In the statistical analysis of the data, the t-Student test, calculation of means and linear regression analysis were used.

## RESULTS

Different solvents were identified in the breathing zone of workers (Table 3). Only concentrations of xylene (about 20% of solvent mixture) exceeded slightly the MAC values binding in Poland (100 $mg/m^3$); the concentrations of remaining mixture constituents: toluene, ethyltoluene, styrene, n-propylbenzene, ethylbenzene and trimethylbenzene isomers (the latter about 42% of solvent mixture) were lower or within the MAC values.

However, the calculated rate of combined total exposure (the sum of quotients of individual compounds concentrations by respective exposure limit values) amounted to 0.94–3.73 $mg/m^3$ (the geometric means) and fluctuated within max-min values of 12.38–0.30 (hygiene norm = 1), depending on individual workposts.

**Table 3.** Results of environmental monitoring (individual dosimetry)

- The following substances were identified in the workplaces air :
  - Xylene
  - Toluene· Ethyltoluene
  - Styrene· n-propylbenzene
  - and (mostly) trimethylbenzene isomers:
  - pseudocumene
  - mesitylene
  - hemimetillene
- Concentrations of solvent mixture calculated as the geometric means of combined total exposure = 0.83–1.3 (max-min 2.9–0.4)

**Table 4.** Study groups and characteristics of exposure to a mixture of organic solvents

| Age of subjects, duration and magnitude of exposure | Statistical parameters | Groups of subjects according to cumulative dose of exposure (n = 61) | | | Controls (n = 40) |
|---|---|---|---|---|---|
| | | Group I (n = 20) Cumulative dose ≤ 10 | Group II (n = 23) Cumulative dose 10-20 | Group III (n = 18) Cumulative dose > 20 | |
| Age (yr) | X ± SD | 35 ± 11.4 | 36.3 ± 8.6 | 41.4± 11.2 | 39.2 ± 10.5 |
| Duration of exposure (yr) | Min | 22.0 | 26.0 | 24.0 | 25.0 |
| | Max | 55.0 | 57.0 | 58.0 | 56.0 |
| | X ± SD | 7.0 ± 4.1 | 11.2 ± 4.1 | 15.8 ± 9.1 | |
| | Min | 2.0 | 6.0 | 3.0 | |
| | Max | 19.0 | 25.0 | 34.0 | |
| Cumulative dose | X ± SD | 5.46 ± 2.48 | 15.18 ± 3.43 | 41.88 ± 14.36 | |
| | Min | 1.40 | 10.08 | 21.60 | |
| | Max | 9.50 | 19.80 | 68.40 | |
| | X ± SD | 0.94 ± 0.75 | 1.48 ± 0.45 | 3.73 ± 2.87 | |
| Rate of total exposure | Min | 0.30 | 0.50 | 1.00 | |
| | Max | 3.97 | 1.94 | 12.38 | |

A more detailed characteristics of exposure and subjects are shown in Table 4; the so called cumulative dose of exposure, i.e. the product of exposure duration in years and of the total exposure rate was coined and the exposed subjects were categorized into three groups (I, II, III) accordingly to its value.

Interestingly, the measured levels of noise associated with the production process in workrooms were low (within $Leq_{60-75}$ dBA), considerably below the permissible hygiene standard (85 dBA).

The blood and urine concentrations of solvents and urinary excretion of their metabolites are given in Table 5; although they did not exceed the limit values, they confirmed a direct contact of the workers under study with industrial solvents.

One may presume, bearing in mind the rigid criteria for selecting study subjects, that hearing loss recognized in

**Table 5.** Results of biological monitoring (gas chromatography)

- Blood
  - The highest concentrations of solvents were found for:
  - Xylene (14.54—348.28 µg/dm$^3$)
  - Toluene (0.95—56.27 µg/dm$^3$)
  - N-propylbenzene (11.28—89.26 µg/dm$^3$)
  - Mesitylene (0,99—70.14 µg/dm$^3$)
  - Pseudocumene (0.80—53.12 µg/dm$^3$)
  - Hemimellitene (0.60—48.24 µg/dm$^3$)
- Urine

Concentrations:
Methylbenzoic acid (15.4—1054.6 mg/dm$^3$)

Excretion rate of metabolites:
- Benzoic acid (6.0—68.8 mg/h)
- Mandelic acid (0.1—3.0 mg/h)
- 2,4-; 2,5-; 3,4 dimethylbenzoic acid (0.2—8.2 mg/h)
- 3,5- dimethylbenzoic acid (0.01—1.67 mg/h)
- 2,3-2,6 dimethylbenzoic acid (0.02—0.93 mg/h)

**Table 6.** Auditory findings in the study group (n = 61) exposed to organic solvents versus controls (n = 40)

| Exposed group accordingly to cumulative dose of exposure | Results of audiological examinations | | | | | |
|---|---|---|---|---|---|---|
| | Pure-tone audiogram* | Tympanogram type | Occurrence of otoacoustic emissions | | | Tinnitus |
| | | | SOAE | TEOAE | DPOAE | |
| | Normal hearing (thresholds in the range of 0.25-8 kHz ≤ 15 dB) n = 35 (57%) | A | **2 (3.2%)** | **35 (57%)** | **35 (57.0%)** | **2 (3.2%)** |
| I | 32 (52%) | | 1 (1.6%) | 30 (49%) | 33 (54.0%) | 2 (3.2%) |
| II | 3 (4.9%) | | 1 (1.6%) | 4 (6.5%) | 1 (1.6%) | – |
| III | – | | – | 1 (1.6%) | 1 (1.6%) | – |
| | Hearing loss 16-30 dB n = 10 (16%) | A | **2 (3.2%)** | **3 (4.9%)** | **4 (6.5%)** | **2 (3.2%)** |
| I | 1 (1.5%) | | 1 (1.6%) | – | – | – |
| II | 5 (8.0%) | | 1 (1.6%) | 3 (4.9%) | 2 (3.2%) | – |
| III | 4 (6.5%) | | – | – | 2 (3.2%) | 2 (3.2%) |
| | Hearing loss 31-40 dB n = 6 (9.8%) | | | | | |
| I | – | A | – | – | **1 (1.6%)** | **1 (1.6%)** |
| II | 3 (4.9%) | | | | – | – |
| III | 3 (4.9%) | | | | 1 (1.6%) | – |
| | Hearing loss 41–50 dB n = 5 (8,1%) | A | – | – | – | 1 (1.6%) |
| I | 1 (1.6%) | | | | | |
| II | 2 (3.3%) | | | | | |
| III | 2 (3.3%) | | | | | |
| | Hearing loss 51–60 dB n = 5 (8.1%) | A | – | – | – | – |
| I | – | | | | | |
| II | 3 (4.9%) | | | | | |
| III | 2 (3.3%) | | | | | |
| Controls n = 40 | Hearing loss 16–30 dB n = 2 (5.0%) | A | 1 (2.5%) | 8 (95%) | 40 (100%) | – |

* age-adjusted data.

42% of the exposed subjects (*v* 5% of controls) and other audiological findings (Table 6) are the effects of exposure to industrial solvents.

The solvent mixture-induced hearing loss was a sensorineural high frequency (above 1 kHz) loss of various degrees with significantly reduced amplitudes of otoacoustic emissions as exemplified in Fig. 1.

The crude audiometric data were finally age-adjusted according to ISO-7029 [25] and then subjected to an analysis.

Both the hearing thresholds defined in pure tone audiometry and amplitudes of otoacoustic emissions closely corresponded with cumulative dose of exposure; the more increased dose, the more lowered amplitudes and the highest thresholds were observed, as illustrated by the DPOAE data in Table 7. Similar relations also applied to TEOAE amplitudes.

The most significant relationships between DPOAE amplitudes and exposure were found in the subjects' breathing zone, in which trimethylbenzene isomers (pseudocumene, mesitylene and hemimellitene) predominated as the main constituents of the solvent mixture (Figs. 2, 3 and 4).

The ENG tests yielded interesting findings; they demonstrated the presence of vestibular disorders of mild or advanced degree inasmuch as 47.5% of workers employed at the production of paints and varnishes (*v* 5% of controls) as shown in Table 8. The comparative analysis of

**Table 7.** DPOAE amplitudes (dB SPL) in subjects exposed to a mixture of organic solvents versus controls

| Statistical parameters | Groups of subjects according to cumulative dose of exposure (n = 61) | | | Controls (n = 40) |
|---|---|---|---|---|
| | Group I (n = 20) | Group II (n = 23) | Group III (n = 18) | |
| X | 1.99 ± 6.14 | -0.31 ± 10.90 | -2.87 ± 9.06 | 7.48 ± 4.67 |
| Min | -6.65 | -27.85 | -18.75 | -9.15 |
| Max | 9.30 | 16.25 | 16.20 | 9.59 |

mean parameters of vestibular-oculomotor induced reactions revealed the significantly decreased duration, amplitude and slow phase angular velocity of nystagmus versus normal values in the control group of non-exposed sub-

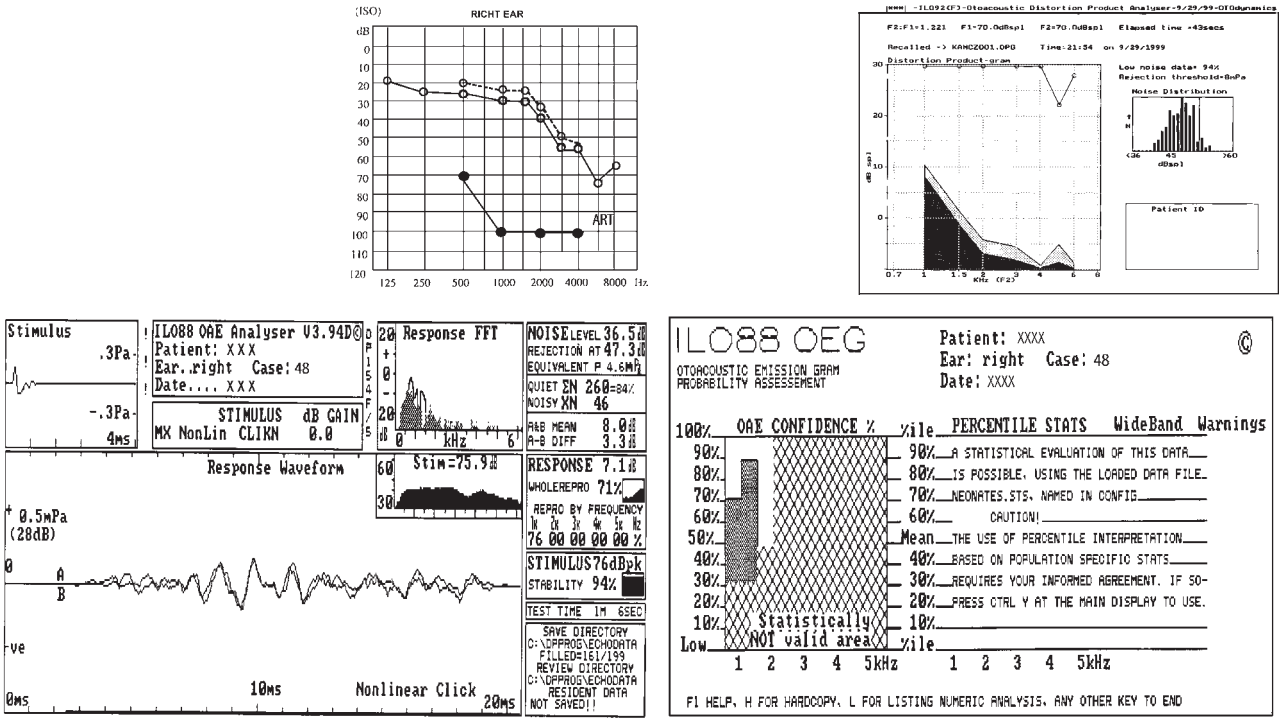


**Fig. 1.** Pure-tone audiogram and otoacoustic emissions registered in one of the subjects exposed (group II, mill operator, aged 46 years, exposure duration of 15 years).

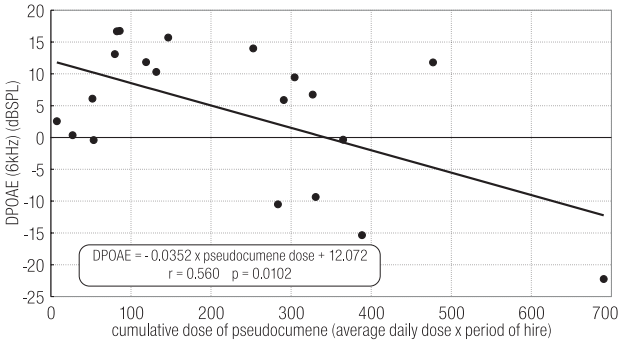


**Fig. 2.** Linear relationship between DPOAE amplitude and cumulative dose of pseudocumene.

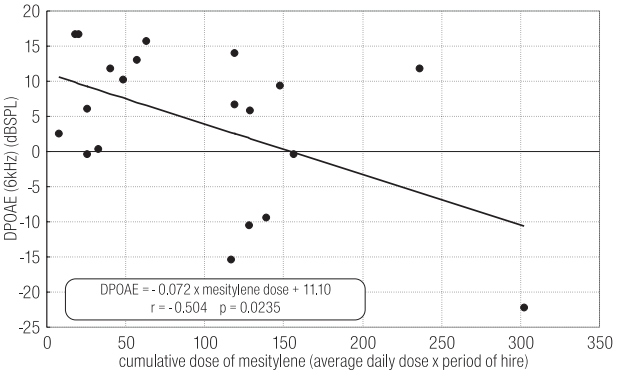


**Fig. 3.** Linear relationship between DPOAE amplitude and cumulative dose of mesitylene.

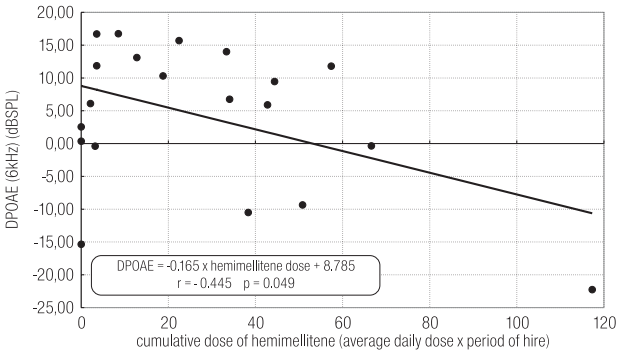


**Fig. 4.** Linear relationship between DPOAE amplitued and cumulative dose of hemimellitene.

jects. An example of abnormalities in the ENG tracings is presented in Fig. 5.

## DISCUSSION AND CONCLUSION

An increasing interest in biological effects imposed by a mixture of organic solvents in general, and their influence on hearing and balance in particular, results from a growing use of these chemicals in various branches of industry. This entails the need for recognizing thoroughly early preclinical symptoms of possible intoxication in order to establish the relevant MAC values, especially for individual constituents of the mixture in the combined exposure to solvents.

Although organic solvents have been used in industrial production for over 150 years, serious concern for their ototoxic effect on the exposed workers began to grow only about 15 years ago. A lot of research data have been gathered to date and all of them provide evidence that solvents can induce permanent hearing loss in both experimental animals (Table 1) and humans (Table 2).

The problem was neglected due to the fact that substantial noise is often present in most occupational settings where solvent exposures occur, and thereby hearing impairments observed in these situations have been attributed exclusively to noise exposure. On the other hand, some recent studies suggest that the combined exposure to noise and ototoxic chemical compounds induces hearing loss more severe than that evoked by one of these agents acting alone [26,27].

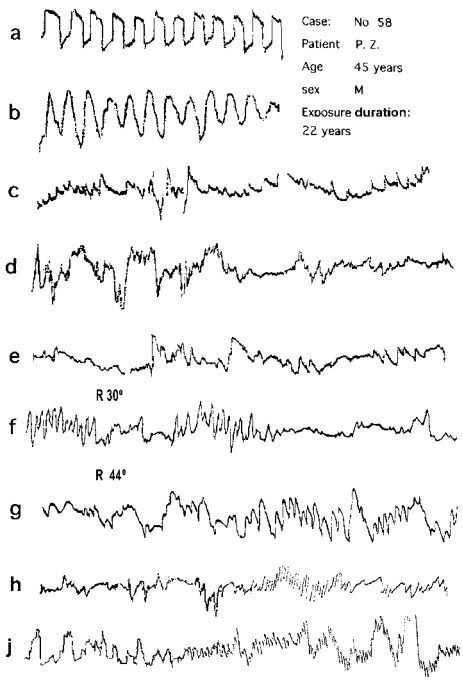


**Fig. 5.** ENG tracings recorded in one of the subjects exposed (group III, colorist, aged 45 years, exposure duration of 22 years): a – saccadic test; b – eye-tracking tests; c – spontaneous nystagmus; d, e – rotary test (2°/sek$^2$–90°/sekŻ; f, g – caloric test; h, j – optokinetic test.

The explanation of this possible synergistic effect is the objective of the "NoiseChem" research project just developed by the European Commission [5]. The US National Institute for Occupational Safety and Health (NIOSH) is also involved in the project. The Institute has initiated much earlier studies of the effects of noise and solvents occurring alone, and in a combined exposure (Fig. 6) [28]. The study reported here was focused on the assessment of ototoxicity of the mixture of organic solvents identified in the factory of paints and varnishes, therefore only those subjects who were employed at workposts with the low noise levels, not hazardous to hearing (60–75 dBA), were eligible for the study. An audiological testing was extended to include ENG investigations to check the function of vestibular organ of the inner ear, seldom examined in the solvent exposed workers because of the difficulties faced in the use of the sophisticated ENG set in the field conditions.

The results of our study showed a significant prevalence of ENG abnormalities (47.5% in the exposed group vs 5%

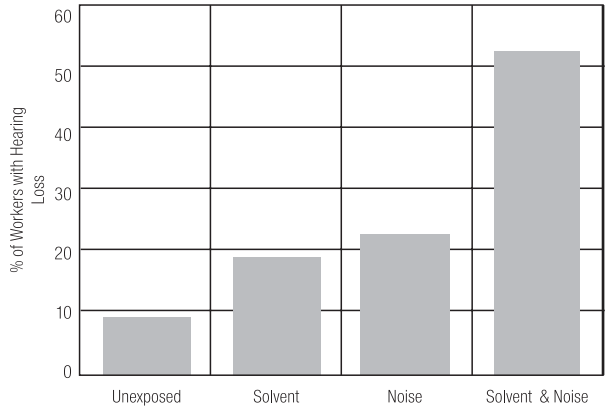


**Fig. 6.** The effect of solvent and noise exposure on hearing loss (acc. to NIOSH).

of controls), although complaints of vertigo were reported by only 26.1 % of study subjects. This may be explained by a very well known high sensitivity of the method that enables us to detect slight preclinical signs of vestibular dysfunction.

A predominant number of complaints of vertigo in employees of the paint and lacquer industry (40.5%) were found in the neurological screening carried out by Indulski et al. [29].

The ENG findings similar to ours (Table 8) were reported by Pollastrini et al. [19] who examined a group of 53 industrial painters exposed to benzene derivatives. They detected asymmetric post-rotatory and/or caloric reactions, disordered saccades and spontaneous nystagmus in the study subjects. The frequency and advancement of these and other pathologies, revealed in our material, markedly increased with growing cumulative dose of the exposure defined as a product of exposure duration in years and of the calculated total exposure rate for the mixture of solvents·.

The qualitative and quantitative evaluation of the ENG findings allows to assume that they are possibly due to toxic lesions in the peripheral (reflected *inter alia* by the canal paresis) and central vestibular (evidenced for example by abnormalities in saccadic, eye-tracking and optokinetic tests) systems; they probably depend on the predominating components of the mixture.

Also, the auditory findings of this study (Table 6) correspond closely with a cumulative dose of exposure to the mixture of solvents. They showed mainly a high frequency (above 1 kHz) sensorineural hearing loss, identified in 42% of those exposed versus 3% of non-exposed subjects. Adjusted accordingly to the presbyacusis data, proposed in ISO-7029 [9], the hearing loss in the exposed group seemed to be of the mild or moderate degree and the exposed-non-exposed hearing thresholds differed significantly. This was accompanied by the lowered amplitudes of otoacoustic emissions, both TEOAE and DPOAE, or their absence if hearing loss exceeded 40–50 dB. Similar

**Table 8.** Vestibular findings in the study groups

| Study groups | Vertigo (%) | Abnormalities in morphology of ENG tracings | | | | | | Mean values of induced nystagmus | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Nystagmus spontaneous or positional (%) | Saccadic test (%) | Eye tracking test (%) | Optokinetic test (%) | Directional preponderance (%) | Canal paresis (%) | Duration | Amplitude | Slow phase angular velocity |
| Exposed: | | | | | | | | | | |
| Group I (n = 20) | 4 (6.5) | 2 (3.3) | 1 (1.6) | 2 (3.3) | 3 (4.9) | 1 (1.6) | – | 25.1–0.2 | 3.0–3.7 | 18.6–21.0 |
| Group II (n = 23) | 6 (9.8) | 6 (9.8) | 7 (11.5) | 2 (3.3) | 5 (8.2) | 6 (9.8) | 2 (3.3) | 25.2–29.8 | 2.1–3.9 | 18.6–21.9 |
| Group III (n = 18) | 6 (9.8) | 6 (9.8) | 11 (48.0) | 4 (6.5) | 7 (11.5) | 8 (13.1) | 6 (9.8) | 25.3–30.1 | 3.3–3.9 | 19.9–22.6 |
| Totally I+II=III (n = 61) | 16 (26.1) | 14 (22.9) | 19 (31.1) | 8 (13.1) | 15 (24.6) | 15 (24.5) | 8 (13.1) | 26.3–32.1 | 3.5–4.2 | 20.2–23.5 |
| Controls (n = 40) | 2 (5.0) | – | 2 (5.0) | 2 (5.0) | – | – | – | 34.6–38.7 | 4.6–5.7 | 25.5–27.5 |

findings were disclosed in animals intoxicated with toluene by Johnson [10].

The peripheral or central auditory disorders in people working in contact with various solvent vapors were reported among others by Odkvist et al. (18), Morata et al. [17], Laukli and Hansen [16] and Śliwińska-Kowalska et al. [30]. Thus, it appears again that the site of hearing lesion due to solvent exposure, like in the vestibular deficit, may be associated with individual constituents of solvent mixtures.

The results of the present study provide convincing evidence that occupational exposure to a mixture of organic solvents is ototoxic.

All confounding factors (past and current noise exposure, past and current middle and inner ear pathology, presbyacusis and presbyastasis, head injuries, neurological and metabolic diseases, medication, abuse of alcohol, tobacco and drugs, chemicals used in hobbies) were excluded following a thorough analysis of medical and occupational history and ENT examinations), therefore the observed symptoms of the inner ear damage in the subjects under study can be attributed to the long-term exposure to mixtures of solvents.

Since the mean concentrations of individual solvents fell rather within the MAC limits or slightly exceeded them, the total rate of the combined exposure to the mixture seems to be responsible for the findings. It could be explained by the additivity rule of health effects that is often used to cope with the problem of combined exposure to solvents [2].

As proved by environmental and biological monitoring, as well as by the measurements of otoacoustic emissions, the exposure to trimethylbenzene isomers: pseudocumene, mesitylene and hemimetillene, the main components of the mixture solvents, contributed most significantly to the development of clinically detectable inner ear disorders in the workers employed in the factory of paints and varnishes.

The precise mechanism by which some toxicants exert their detrimental effect on the internal ear has not as yet been fully elucidated; perhaps it is due to their direct assault upon the sensory cells of the cochlear and vestibular neuroepithelia, followed by the effect of solvents on metabolic processes and enzymatic systems, which probably inhibit the protein synthesis.

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