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Ototoxicity of industrial chemicals alone or in combination with noise**

Styrene (monomer)

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Introduction

There is increasing epidemiological evidence that exposure to some solvents, metals, asphyxiants and other substances is associated in humans with a risk of hearing loss. On the contrary, the interaction of chemicals and noise has received little attention. This project was undertaken to develop a database of toxicological data from the primary literature, allowing the identification of ototoxic substances and substances that interact with the noise present in the work environment. Critical toxicological data were compiled for chemical substances included in the Quebec regulation (Regulation Respecting Occupational Health and Safety).

Methods

The data were evaluated only for realistic exposure concentrations up to:
- the short-term exposure limit value, or
- the ceiling value, or
- 5 times the 8-h time weighted average exposure limit value (TWAEV) for human data, or
- 100 times the 8-h TWAEV or the ceiling value for animal studies.

We took into consideration the number of studies and for each study the following parameters: studied species, number of subjects or animals, exposure route, characteristics of control groups, exposure levels, audiometric and statistical tests, dose/effect relationship and when available, mechanisms of action.

Using a systematic weight of evidence approach, the information from both human and animal studies was examined. At first, a weight of evidence qualifier was given for both the ototoxicity and the interaction with noise : "strong", "medium", "weak", "absent" or "no study found". Note that weight of evidence qualifier "absent" should not be regarded as evidence that a substance is not ototoxic or that it does not interact with noise.

We built a weight of evidence table (see Table 1) that allowed us to combine the information from both human and animal studies on ototoxicity of chemicals and their interaction with noise. Human data were given more weight in the overall assessment. For example, a "strong" evidence from animal studies combined with an "absence" of evidence from the available human studies yielded a "medium" evidence overall.

Regarding the final conclusion about the ototoxic potential of substances or their interaction with noise, a substance bearing an overall qualifier of "strong evidence" of ototoxicity or interaction with noise was considered as an "ototoxic substance" or as a substance for which there is an "evidence of interaction" with noise. Those with "medium evidence" overall were rated "possibly ototoxic" or "possible interaction". We considered the ototoxic potential of those with only "weak evidence" as "non conclusive". Finally, those for which there was absence of evidence bore the mention "no evidence" of ototoxicity or interaction with noise.

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Table 1

Weight of evidence approach for the assessment of ototoxicity and interaction with noise of industrial chemicals

Weight of evidence of studies			Conclusion about ototoxicity	Conclusion about the interaction substance / noise
Human studies	**Animal studies**	**Overall**		
S	S	S	O	I
S	M	S	O	I
S	W	S	O	I
S	A	S	O	I
S	X	S	O	I
M	S	S	O	I
M	M	M	PO	PI
M	W	M	PO	PI
M	A	M	PO	PI
M	X	M	PO	PI
W	S	M	PO	PI
W	M	W	NC	NC
W	W	W	NC	NC
W	A	W	NC	NC
W	X	W	NC	NC
A	S	M	PO	PI
A	M	W	NC	NC
A	W	W	NC	NC
A	A	A	NE	NE
A	X	A	NE	NE
X	S	M	PO	PI
X	M	W	NC	NC
X	W	W	NC	NC
X	A	A	NE	NE
X	X	X	X	X

Strength of evidence about otoxicity or interaction substance / noise

S = Strong, M = Medium, W = Weak, A = Absent, X = No study found

Conclusion about ototoxicity

O=Ototoxic substance, PO=Possibly ototoxic substance, NC=Non conclusive, NE=No evidence, X=No documentation

Conclusion about the interaction substance / noise

I=Evidence of interaction, PI=Possible interaction, NC=Non conclusive, NE=No evidence, X=No documentation

Abbreviations

TWAEV : 8 h time weighed average exposure [limit] value in Quebec

D-TWAEV : Calculated inhaled dose for pulmonary ventilation of 10 m^3/d and body weight of 70 kg

Ceiling : Ceiling exposure [limit] value in Quebec

D-Ceiling : Calculated inhaled dose for pulmonary ventilation of 10 m^3/d and body weight of 70 kg

STEV : Short term exposure [limit] value in Quebec

C/D reported : Reported concentration or reported dose

CSU/DSU : Reported concentration expressed in standard units of mg/m^3 or reported dose expressed in standard units of mg/kg/d

Ratio : For concentrations CSU/TWAEV or CSU/Ceiling and for doses DSU/ D-TWAEV or DSU/D-Ceiling

ASM : Air sampling method

BM : Biological monitoring results

NSM: Noise sampling method

NL: Noise levels

SPL : Sound pressure level

Styrene (monomer)

Quebec's Occupational exposure limits: TWAEV: 213 mg/m³ (50 ppm). STEV: 426 mg/m³ (100 ppm)

Conclusion about ototoxicity **Ototoxic substance**	Strength of evidence From human studies: **Medium** From animal studies: **Strong** Overall: **Strong**
Conclusion about interaction with noise **Non conclusive**	Strength of evidence From human studies: **Weak** From animal studies: **Medium** Overall: **Weak**

Ototoxicity - Analysis of human studies

Recently, Lawton et al. (2006) reviewed a number of occupational investigations of the exposure and relation between inhaled styrene and hearing loss. Our conclusions are in agreement with theirs. We have added several recent studies. Twelve studies used threshold differences to differentiate between styrene exposed and non-exposed workers. Of the twelve studies, four found no evidence to support an effect of styrene on the thresholds of hearing (Möller 1990, Sass-Kortsak 1995, Calabrese 1996, Hoffman 2006). Two studies were limited to styrene effects in the very high frequency region (Muijser 1988, Morioka 1999) and in one of them the workers were exposed also to other solvents (Morioka 1999). In contrast, six studies report styrene-induced hearing losses (Sliwinska-Kowalska 2003, Morata 2002, Sliwinska-Kowalska 2005, Morioka 1999, Mascagni 2007, Triebig 2008). However, a dose-response relationship was only found in the study by Morioka (1999).

Ototoxicity - Analysis of animal studies

There are numerous studies demonstrating that styrene by inhalation is ototoxic in laboratory animals. Susceptibility to solvents is species dependent. Styrene causes a permanent damage to auditory system mainly of the rat. The auditory system of the guinea-pig is not injured by styrene as much as that of the rat (Lataye 2003, Fechter 1993). Styrene damages hair cells in the cochleae of rats, and the spiral ganglions are not spared. The important characteristic of styrene is higher susceptibility of outer hair cells compared to inner hair cells (Lataye 2003). The effect is dose-related. One study suggested that Dieters cells are the most vulnerable target of styrene and that styrene-related cell death occurs primarly by apoptosis (Chen 2007). Subacute styrene exposure seems not to damage the hair cells; long-term exposure does. For chronic exposure, higher styrene concentrations lead to greater hair cell mortality. The mid-frequency hearing loss is most often reported. Morphologic examination determined a corresponding loss of OHC in the middle frequency region of the rat cochlea (Yano 1992). Hair cell deaths are not closely related to hearing threshold shifts in the rat.
There is no styrene induced hearing loss for chronic exposure of rats up to about 600 ppm. Concentrations greater than 600 ppm show threshold shifts directly related to styrene concentration.

Interaction with noise - Analysis of human studies

Six studies have investigated workers exposed to both noise and styrene. Two studies found no interaction between styrene and noise. Due to confounding factors, however, it was concluded that the data were inadequate for assessing the combined effects of noise and chemical exposure on hearing (Morata 2002, Sass-Kortsak 1995). In one study Muijser (1988) the control group was exposed to much higher level of noise than the group exposed to styrene precluding evaluation of interaction between noise and styrene. Three studies from the same laboratory demonstrated additive or infraadditive effects (Sliwinska-Kowalska 2001, Sliwinska-Kowalska 2003, Sliwinska-Kowalska 2005). No dose-response relationship between styrene exposure and hearing thresholds was found and only the abstract was available in English for the third study.

Interaction with noise - Analysis of animal studies

Four animal studies were evaluated. Susceptibility to solvents is species dependent. The auditory system of the guinea-pig is not injured by styrene as much as that of the rat. One study on guinea pigs exposed simultaneously to 500 or 1200 ppm styrene and 95 dBA noise for 7 h provided no evidence of interaction between the two agents (Fechter 1993). Three studies in rats demonstrated an ototoxic interaction between styrene and noise. The potentiation of styrene-induced hearing loss by noise was found in one study after exposure to 400 ppm styrene (Lataye 2005) and synergism was observed in two studies after simultaneous exposure to 300-750 ppm styrene and 100 dB noise (Lataye 2000, Mäkitie 2003).

Discussion

Although certain ototoxic effects were reported in workers, other human studies are necessary to further

support the current incomplete evidence. In rats, styrene clearly affects the auditive function mainly in the range of the mid frequencies of the cochlea. There is weak evidence of an ototoxic interaction with noise in workers. In rats, a synergistic interaction was found in two studies, as well as a potentiation of noise-induced hearing loss in another study. Further studies are necessary to draw a conclusion about interaction with noise. We recommend, by taking account of the results of the human studies and the evidence brought by the animal studies, to regard styrene as an ototoxic agent.

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : 20 Sex : Not reported
Age : 32 (24-52) years

Exposure

Route : Inhalation
Duration : 7.6 (2 - 23) years
C/D reported : 14 – 416 mg/m³ (average over 8 h)
CSU/DSU :
Ratio : 0.06 - 2
ASM : Passive absorption badges 8 hours
BM : Mandelic acid + phenylglyoxylic acid : 81-943 mg/g creatinine
NSM :
NL : NR
Remarks : Urine collected before the start of work on the next day

Tests

9 subjects also tested after a recovery period of 3 weeks without exposure. Results compared with reference values

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	
• No abnormalities	
Tympanometry	
• No abnormalities	
Acoustic reflex	
• No abnormalities	
Auditory brainstem responses	Clicks of 115 dB SPL
• No abnormalities	

Mechanism of action

Authors' conclusion

Auditory system does not seem to be affected by the styrene at the exposure levels reported

Our conclusion

Auditory system does not seem to be affected by the styrene at the exposure levels reported

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 12 - 16 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 1 to 4 w
C/D reported : 1000 ppm
CSU/DSU :
Ratio : 20
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Hearing loss of 35-40 dB at 16 kHz - Hearing loss of 20 dB at 4-5 kHz - No effect of the exposure duration	• Test performed immediately and 6 weeks after the end of exposure
Light and electron microscopy	Cochleogram
• - Outer hair cell loss observed throughout the entire range of damaged frequencies - Toxic process continued even after the end of exposure - Supporting cells are the first targets. Then, outer hair cells of the third row (OHC3) are disrupted followed successively by OHC2 and OHC1 from the middle (20 kHz) to the upper turn (4 kHz) of the cochlea	• Histology performed immediately and 6 weeks after the end of exposure

Mechanism of action

Disorganization of the membranous structures could be the starting point for the cochlear injury induced by styrene

Authors' conclusion

Ototoxic effect at 1000 ppm in rats

Our conclusion

Ototoxic effect at 1000 ppm in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : E1 = 13; E2 = 14 Sex : Males

Age : E1 = 3 months; E2 = 24 - 26 months

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 700 ppm
CSU/DSU :
Ratio : 14
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Significant hearing loss in young rats only. Young animals showed threshold shifts only at high frequencies. - 15 dB hearing loss was located in the region of 16-20 kHz immediately after the end and 6 week after exposure	• Audiometry tests performed prior to styrene exposure, at the end of exposure and 6 weeks after exposure
Light and electron microscopy	
• - Aged rats had minimal outer hair cell loss - Young rats showed significant outer hair cell loss, particularly in the third row	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Authors' conclusion

Ototoxic effect at 700 ppm in rats. There is an influence of age on styrene –induced threshold shift and hair cell loss in rats

Our conclusion

Ototoxic effect at 700 ppm in rats. There is an influence of age on styrene –induced threshold shift and hair cell loss in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 7 Sex : Males
Age : NR - see remarks

Exposure

Route : Gavage
Duration : Single dose
C/D reported : 800 mg/kg
CSU/DSU :
Ratio : 26.7
ASM :
BM :
NSM :
NL :
Remarks : Weight of 330 ± 32 g

Tests

histology

Test type • Effects reported	Details on test • Remarks
Light microscopy • - Styrene concentration in the apical turn of the cochlea : 12.5 ± 3.0 µg/g - Styrene concentration in the middle turn of the cochlea : 7.4 ± 1.6 µg/g - Styrene concentration in the basal turn of the cochlea : 4.8 ± 1.0 µg/g - Styrene concentration in the perilymph of the cochlea : 3.1 ± 0.6 µg/g	Cochleae were removed and dissected 3 hours after gavage. • Styrene measurements were made by gas chromatography

Mechanism of action

Authors' conclusion

Styrene is more concentrated in apical and middle cells compared to basal cochlea cells. This could be because of a lesser washout efficiency in the apical region

Our conclusion

Styrene is more concentrated in apical and middle cells compared to basal cochlea cells. This could be because of a lesser washout efficiency in the apical region

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans
: E1 = 6; E2 = 6; E3 = 9; E4 = 10; E5 = 12
Sex : Males
Age : NR - see remarks

Exposure

Route : Gavage
Duration : 5 d/w; 3 w
C/D reported : E1 = 0 ; E2 = 200 ; E3 = 300 ; E4 = 400 ; E5 = 800 mg/kg/d
CSU/DSU :
Ratio : 6.7-26.7
ASM :
BM :
NSM :
NL :
Remarks : Weight of 330 ± 32 g

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses • - Threshold shifts were styrene dose and frequency dependent with the largest threshold shift occuring at the midfrequencies (10-20 kHz) - The threshold shifts were permanent and were similar 12 hours and 3 weeks after exposure	Tone pips at 2.5, 5, 10, 20 and 40 kHz • Auditory thresholds were determined 12 h and 3 weeks after the last day of styrene exposure
Light microscopy • Styrene-induced OHC loss was dose and location-dependent, with OHC loss starting from the middle turn of the cochlea.	

Mechanism of action

Hearing loss in the midfrequency region is caused by apoptotic cell death in the middle turn of the cochlea

Authors' conclusion

Higher middle turn cell death is caused by higher styrene concentration than in the basal turn in association with lower glutathione levels than in the apical turn of the cochlea

Our conclusion

Higher middle turn cell death is caused by higher styrene concentration than in the basal turn in association with lower glutathione levels than in the apical turn of the cochlea

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : E1 = 4; E2 = 3; E3 = 6; E4 = 3; E5 = 6 Sex : Males
Age : NR - see remarks

Exposure

Route : Gavage
Duration : 5 d/w; E1 = 3 d; E2 = 5 d; E3 = 7 d; E4 = 9 d; E5 = 3 w
C/D reported : 800 mg/kg/d
CSU/DSU :
Ratio : 26.7
ASM :
BM :
NSM :
NL :
Remarks : Weight of 330 ± 32 g

Tests

Test type	Details on test
• Effects reported	• Remarks
Light microscopy	
• - Significant OHC loss was observed only when the styrene exposure exceeded 3-5 days - Traumatic changes in Deiters cells were observed after only 3 days and some cells went through apoptotic cell death	• Cochleae were removed 12 h after the last exposure

Mechanism of action

Authors' conclusion

Dieters cells appeared to be the most vulnerable target of styrene

Our conclusion

Dieters cells appeared to be the most vulnerable target of styrene

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 4 Sex : Males
Age : NR - see remarks

Exposure

Route : Gavage
Duration : 7 d
C/D reported : 800 mg/kg/d
CSU/DSU :
Ratio : 26.7
ASM :
BM :
NSM :
NL :
Remarks : Weight of 330 ± 32 g

Tests

Test type	Details on test
• Effects reported	• Remarks

Light microscopy

- - Condensed nuclei in Deiters cells after exposure
  - While Deiters cells are injured by styrene exposure, Hensen cells can be intact
  - Active caspases-9 and 8 were observed in Deiters cells, which is indicative of apoptosis
  - Condensed nuclei in OHC cells after 3 days of exposure

Mechanism of action

Authors' conclusion

The majority of dead cochlear cells went through apoptosis. Both mitochondria-mediated pathway and the death receptor-mediated pathway were involved in the styrene ototoxic effect

Our conclusion

The majority of dead cochlear cells went through apoptosis. Both mitochondria-mediated pathway and the death receptor-mediated pathway were involved in the styrene ototoxic effect

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 7 - 8 Sex : Males
Age : 60 days

Exposure

Route : Inhalation
Duration : 8 h/d; 5 d
C/D reported : 1600 ppm
CSU/DSU :
Ratio : 32
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Reflex modification audiometry	at 0.5 - 40 kHz
• Hearing loss for 8 and 16 kHz	• Test performed 5 to 8 weeks after the end of exposure

Mechanism of action

Authors' conclusion

Mid-frequency hearing loss at 1600 ppm in rats

Our conclusion

Ototoxic effect at 1600 ppm in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Guinea pig # : 3 Sex : Males
Age :

Exposure

Route : Intraperitoneal
Duration : 2 doses
C/D reported : 1.5 mL
CSU/DSU : 2813 mg/kg/d
Ratio : 94
ASM :
BM :
NSM :
NL :
Remarks : 2 injections of 0.75 mL each spaced 30 minutes apart

Tests

Test type • Effects reported	Details on test • Remarks
Electrocochleography (Compound action potential : CAP)	2 à 40 kHz, 11 frequency
• No adverse effects	• Test performed 30 minutes after the end of exposure

Mechanism of action

Authors' conclusion

No ototoxic effect at the single dose of 2813 mg/kg/d in guinea pigs

Our conclusion

No ototoxic effect at the single dose of 2813 mg/kg/d in guinea pigs

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Guinea pig # : 5 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 7 h
C/D reported : 500 ppm
CSU/DSU :
Ratio : 10
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Electrocochleography (Compound action potential : CAP)	2 à 40 kHz, 11 frequency
• No threshold shift	• Test performed 18 to 22 hours after the end of exposure

Mechanism of action

Authors' conclusion

No ototoxic effect after exposure of 7 hours at 500 ppm in guinea pigs

Our conclusion

No ototoxic effect after 7 hour exposure to 500 ppm in guinea pigs

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Guinea pig # : 5 Sex : Males
Age : adult

Exposure

Route : Inhalation
Duration : 7 h
C/D reported : 500 and 1200 ppm
CSU/DSU :
Ratio : 10 - 24
ASM :
BM :
NSM :
NL : 95 dB(A) ; White noise
Remarks : Background noise < 50 dB(A)
Simultaneous exposure to noise + styrene

Tests

Test type • Effects reported	Details on test • Remarks
Electrocochleography (Compound action potential : CAP)	2 à 40 kHz, 11 frequency Tone pips
• - An elevation of 20 dB in the auditory thresholds at 8, 12 and 16 kHz in both noise only and styrene (500 ppm) + noise groups. Styrene (500 ppm) by itself had no effect. - One week following exposure there appeared to be a small elevation in auditory threshold among subjects in the 500 ppm styrene + noise group in relation to controls. Auditory threshold in the 1200 ppm styrene + noise group was equivalent to the subjects which had been exposed to noise alone	• Test performed 18 to 22 hours (500 ppm styrene) and 1 week (500 and 1200 ppm styrene) after the end of exposure

Mechanism of action

Authors' conclusion

Subjects administered styrene and noise simultaneously did not show a greater hearing loss than those receiving noise alone during short-term exposure

Our conclusion

Subjects administered styrene and noise simultaneously did not show a greater hearing loss than those receiving noise alone during short-term exposure

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat # : 6 Sex : Males
Age : 9 weeks

Exposure

Route : Gavage
Duration : 5 d/w; 2 w
C/D reported : 8.47 mmol/kg/d
CSU/DSU : 882 mg/kg/d
Ratio : 29
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type	Details on test
• Effects reported	• Remarks
Light and electron microscopy	Cochleogram
• - Almost complete loss in the three rows of outer hair cells in the medium and apical parts of the cochlea - About 50 % of the animals had losses in the basal part of the cochlea - Inner hair cell losses in some animals	• Histology performed 10 days after the end of exposure

Mechanism of action

Authors' conclusion

High ototoxic effect of styrene in rats

Our conclusion

Ototoxic effect of styrene after exposure by oral way in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 16; E = 16 Sex : Males

Age : C = 39 ± 8; E = 41 ± 8 years

Exposure

Route : Inhalation

Duration : 8 ± 5 years

C/D reported : NR (See remarks)

CSU/DSU :

Ratio :

ASM :

BM : Mandelic + phenylglyoxylic acids : C : 130 ± 129 mg/g creatinine (Median : 76, range : 25-478) ; E : 656 ± 639 mg/g creatinine (Median : 446, range : 72-2213)

NSM :

NL :

Remarks : Exposure was measured by urinary mandelic + phenylglyoxylic acid

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	Pure tones at 0.125, 0.25, 0.5, 1, 2 and 8 kHz
• No significant differences in the mean values of hearing ability	• Tested for both ears
Transient evoked otoacoustic emissions (TEOAE)	Click level of 80 dB SPL
• No statistical differences between exposed and control group in the amplitudes of the TEOAE	

Mechanism of action

Authors' conclusion

The results of this study do not support the assumption of an ototoxic effect of chronic styrene exposure in workers

Our conclusion

The results of this study do not support the assumption of an ototoxic effect of chronic styrene exposure in workers

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 78; E = 89 Sex : Males and females

Age : C = 45 (26-62); E = 43 (21-62) years

Exposure

Route : Inhalation

Duration : C = 17 (1-39); E = 43(21-62) years

C/D reported : 16 (0.2 - 96) mg/m³

CSU/DSU :

Ratio : 0.08

ASM : Passive absorption badges

BM : Mandelic acid: 0.9 mmol/g creatinine

NSM : Noise dosimeters Bruël and Kjaer 4436

NL : C = 77 (69-86) dB; E = 82 (75-84) dB

Remarks : Urine collected over 24h, beginning with the start of the work shift
The effect of noise exposure was not considered in this study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 1, 2, 3, 4, 6 and 8 kHz
• Higher threshold at 2-6 kHz	
Psycho-acoustical modulation transfer function	at 4 kHz
• No abnormalities	
Distortion product otoacoustic emissions (DPOAE)	
• No abnormalities	
Cortical auditory evoked potentials	
• A significant effect on the latency of the cortical evoked response	
Interrupted speech	
• A significant lower score	
Speech recognition in noise	
• Significant abnormalities	

Mechanism of action

Authors' conclusion

Occupational exposure to styrene affects both the central and the peripheral auditory system even when the noise levels are low (mean of 16 mg/m³)

Our conclusion

Auditory system seems to be affected by the styrene at the low exposure concentrations

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 8 - 16 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 750 ppm
CSU/DSU :
Ratio : 15
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Hearing losses appeared between 16 and 20 kHz, with a peak of 13.5 dB at 20 kHz at the end of exposure - Six weeks after exposure, the recovery was significant from 2 to 20 kHz	• Audiometry tests performed prior to styrene exposure, the day following the end of exposure and 6 weeks after exposure
Light and electron microscopy	
• Outer hair cell losses were greatest in the third row, followed by the second and the first row. The largest losses located at the third row, 86 % at 20 kHz and 70 % at 4 kHz	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Exact mechanism of styrene toxicity is not understood, it is likely that styrene impairs preferentially the basal pole of outer hair cells and/or the supporting cells by tissue contamination. A possible route to reach the OHC is the lipid-rich content of the membranes of the different cells of the organ of Corti

Authors' conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 8 - 16 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : Styrene, noise, styrene + noise : 6 h/d; 5 d/w; 4 w
C/D reported : 750 ppm
CSU/DSU :
Ratio : 15
ASM :
BM :
NSM :
NL : 97 dB SPL at 8 kHz ; Octave band noise centerd at 8 kHz
Remarks : Background noise < 66 dB SPL

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Inferior colliculus Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Both noise and styrene alone caused permanent threshold shifts - Following the combined exposure, the threshold elevation exceeded the summed loss caused by noise and styrene alone in the range 8-20 kHz - 6 weeks after exposure, significant recovery was observed over frequency range from 2 to 24 kHz	• Audiometry tests performed prior to styrene exposure, the day following the end of exposure and 6 weeks after exposure
Light microscopy	Cochleogram
• - Both noise and styrene alone caused cell losses - Following the combined exposure, the cell losses exceeded the summed loss caused by noise and styrene alone in the range 8-20 kHz	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Noise induced hearing loss was mainly related to injuries of the stereocilia
Styrene-induced hearing loss was related to outer hair cells losses and/or supporting cells by tissue contamination

Authors' conclusion

Noise and styrene can cause a permanent synergistic loss of auditory sensitivity

Our conclusion

Synergic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 8 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 750, 1000 and 1500 ppm
CSU/DSU :
Ratio : 15 - 30
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - 1500 ppm : hearing losses appeared in all frequencies with a peak of 54.3 dB at 12 kHz - 1000 ppm : hearing losses appeared in all frequencies with a peak of 34 dB at 12–16 kHz - 750 ppm : hearing losses appeared between 16 and 24 kHz, with a peak of 10 dB at 20 kHz	• Audiometry tests performed prior to styrene exposure and 6 weeks after the end of exposure
Light and electron microscopy	
• - Outer hair cell losses were greatest in the third row, followed by the second and the first row in all doses - Inner hair cell loss observed only at 1500 ppm, where up to 35 % of losses were observed in the high frequencies - Neurons of the spiral ganglion were injured with significant losses at 1000 and 1500 ppm in the median spiral ganglion	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Authors' conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 6 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d
C/D reported : 1000 ppm
CSU/DSU :
Ratio : 20
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Distortion product otoacoustic emissions (DPOAE)	at 2, 3, 4, 5, 6, 8, 10, 12 and 16 kHz L1 = 10 to 60 dB L1 = L2 Ratio f2/f1 = 1.20
• Amplitudes depressed at 2 and 4 weeks post-exposure	• Test performed 1 week before exposure, 20 minutes, 2 and 4 weeks after the end of exposure
Light and electron microscopy	
• - Outer hair cells of the third row (OHC3) were disrupted, followed successively by OHC2 and OHC1 - Inner hair cells were relatively well preserved	• Histology performed 4 weeks after the end of exposure

Mechanism of action

Authors' conclusion

Ototoxic effect at 1000 ppm in rats

Our conclusion

Ototoxic effect at 1000 ppm in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Guinea pig # : 5 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d
C/D reported : 1000 ppm
CSU/DSU :
Ratio : 20
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Distortion product otoacoustic emissions (DPOAE)	at 2, 3, 4, 5, 6, 8, 10, 12 and 16 kHz L1 = 10 to 60 dB L1 = L2 Ratio f2/f1 = 1.20
• No changes in amplitude nor in otoacoustic emissions	• Test performed 1 week before exposure, 20 minutes, 2 and 4 weeks after the end of exposure
Light and electron microscopy	Cochleogram
• No permanent hair cell loss	• Histology performed 4 weeks after the end of exposure

Mechanism of action

Authors' conclusion

No ototoxic effect at 1000 ppm in guinea pigs. Guinea pigs appear to be resistant to styrene ototoxic effect

Our conclusion

No ototoxic effect demonstrated at 1000 ppm in guinea pigs. Guinea pigs appear to be resistant to styrene ototoxic effect

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 5 - 8 Sex : Males

Age :

Exposure

Route : Inhalation

Duration : 6 h/d; 5 d/w; 4 w

C/D reported : 700 ppm

CSU/DSU :

Ratio : 14

ASM :

BM :

NSM :

NL :

Remarks : E1 = age of 3 months and weight of 345 g ; E2 = age of 5 months and weight of 345 g ; E3 = age of 5 months and weight of 312 g ; E4 = age of 5 months and weight of 411 g

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Logons at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Hearing loss of 23.5 dB and 7.7 dB located in the region of 16 kHz in young (E1) and old (E2) rats, respectively. - Hearing loss of 7 dB obtained with the same age animals regardless of the body weight (groups E3 and E4)	• Audiometry tests performed prior to styrene exposure, at the end of exposure and 6 weeks after exposure
Light and electron microscopy	
• - In the region of 2 - 30 kHz, young and old animals showed 80.3 % outer hair cell (OHC) losses in the third row. In the second and the third row, the OHC losses were greater in the young rats than in old rats. - No large difference in OHC losses between E3 and E4 groups. The OHC losses were 58, 13 and 5 % for the third, the second and the first row, respectively, in the region of 2 - 27 kHz	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Authors' conclusion

Ototoxic effect at 700 ppm in rats. There is an influence of age on styrene –induced threshold shift and hair cell loss in rats. Young rats are more susceptible to styrene. Weight does not play a major role in styrene ototoxicity

Our conclusion

Ototoxic effect at 700 ppm in rats. There is an influence of age on styrene –induced threshold shift and hair cell loss in rats. Young rats are more susceptible to styrene. Weight does not play a major role in styrene ototoxicity

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 4 - 8 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : G1 (active rats): 300, 400, 500, 600 ppm; G2 (sedentary rats): 500, 650, 850, 1000 ppm
CSU/DSU :
Ratio : 6 - 20
ASM :
BM :
NSM :
NL :
Remarks : Groups of active (using a running wheel) and sedentary rats exposed to styrene

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Logons at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Group G1 : 8 and 7 dB hearing loss at 2 and 3 kHz with 600 ppm styrene; 14 dB hearing loss at 16-20 kHz with 500 ppm styrene; 5 dB hearing loss at 16-20 kHz with 400 ppm styrene. - Group G2 : comparable effects as in G1 but at higher styrene concentrations. 9.7 dB hearing loss at 600 ppm with active rats and 802 ppm with sedentary rats	• Test performed before and 4 weeks after the end of exposure
Light microscopy	Cochleogram
• - In both groups, outer hair cell losses (OHC) observed throughout the entire range of damaged frequencies -The most significant losses located at the third row (OHC3) starting at 400 ppm with active rats and 650 ppm with non active rats, followed successively by OHC2 and OHC1	• Histology performed 4 weeks after the end of exposure

Mechanism of action

Authors' conclusion

LOAEL of 400 ppm for ototoxic effect at in active rats and 650 ppm in sedentary rats

Our conclusion

LOAEL of 400 ppm for ototoxic effect at in active rats and 650 ppm in sedentary rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 6 Sex : Males
Age : 11 weeks

Exposure

Route : Inhalation
Duration : Styrene, noise, styrene + noise : 6 h/d; 5 d/w, 4 w
C/D reported : 400 ppm
CSU/DSU :
Ratio : 8
ASM :
BM :
NSM :
NL : 86.2 dB SPL ; Octave band noise centered on 8 kHz
Remarks : Groups of active rats (using a running wheel)

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Logons at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• No difference between the «noise» and «noise + styrene» groups	• Test performed before and 4 weeks after the end of exposure
Light microscopy	Cochleogram
• - Noise alone : no effect - Combined exposure caused an increase in outer hair cells (OHC2 and OHC3) loss at 4 to 20 kHz in comparison with exposure to styrene only	• Histology performed 4 weeks after the end of exposure

Mechanism of action

Authors' conclusion

Potentiation of styrene-induced hearing loss by noise

Our conclusion

Potentiation of styrene-induced hearing loss by noise

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 8 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 500, 650, 850, 1000 and 1500 ppm
CSU/DSU :
Ratio : 10 - 30
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Inferior colliculus Clicks at 2 - 32 kHz
• - Auditory threshold shifts increase as a function of the styrene concentration - At 850 ppm, the amplitude shift was large around 16-20 kHz (19 dB) but no hearing loss was found at higher and lower frequencies. - >1000 ppm : frequency independent hearing loss	• Test performed immediately and 6 weeks after the end of exposure
Light and electron microscopy	Cochleogram
• 650 ppm : outer hair cell losses along the organ of Corti. The outer hair cell losses most significant at the third row	• Histology performed immediately and 6 weeks after the end of exposure

Mechanism of action

Authors' conclusion

LOAEL of 570 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 570 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 5 - 11 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 750 ppm
CSU/DSU :
Ratio : 15
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Inferior colliculus Clicks from 2 to 32 kHz
• Hearing losses at 2,16 and 20 kHz (5, 7.1 and 9.2 dB, respectively)	• Audiometry tests performed prior to styrene exposure and 6 weeks after the end of exposure
Light microscopy	
• Outer hair cell (OHC) losses were greatest in the third row, followed by the second and the first row. The largest losses located at the third row, 86 % at 8 and 22 kHz	• Histology performed 6 weeks after the end of exposure

Mechanism of action

Exact mechanism of styrene toxicity is not understood. A possible route to reach the outer hair cells is the lipid-rich content of the membranes of the different cells of the organ of Corti

Authors' conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 750 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Wistar # : 7 - 12 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 12 h/d; 5 d/w; 4 w
C/D reported : 100, 300 and 600 ppm
CSU/DSU :
Ratio : 2 - 12
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Inferior colliculus Clicks and tone bursts at 1.0, 2.0, 4.0 and 8.0 kHz
• 600 ppm : threshold shift of 3 dB at 8 kHz	• Test performed over 20 to 40 days after the end of exposure
Light and electron microscopy	Cochleogram
• 600 ppm : outer hair cell losses found in the third row of upper basal and middle coil	• Histology performed over 20 to 40 days after the end of exposure

Mechanism of action

Authors' conclusion

LOAEL of 300 to 600 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 300 to 600 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Wistar # : 5 - 12 Sex : Males
Age : adult

Exposure

Route : Inhalation
Duration : 12 h/d; 5 d/w; 4 w
C/D reported : 100, 300 and 600 ppm
CSU/DSU :
Ratio : 2 - 12
ASM :
BM :
NSM :
NL : 100 - 105 dB(A) Leq 12 h
Remarks : Noise level weighting unclear(dB SPL or dB(A))

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Inferior colliculus Clicks and tone bursts at 1.0, 2.0, 4.0 and 8.0 kHz
• - Threshold shitf of 3 dB SPL at 8 kHz after exposure to 600 ppm styrene - No threshold shitf after exposure to lower styrene concentrations - Threshold shitf (2-9 dB SPL) at 8 et à 2 kHz after exposure to noise alone - Threshold shitf (23-27 dB SPL) after exposure to the combination of noise + 600 ppm styrene at all frequencies - Threshold shitf (5-10 dB SPL) after exposure to the combination of noise + lower styrene concentrations (100 and 300 ppm) was equivalent to that seen after exposure to noise alone	• Test performed immediately and 2 to 6 weeks after the end of exposure
Light microscopy	Cochleogram
• - 600 ppm styrene : substantial outer hair cell (OHC) loss - Noise : occasional loss of OHC - Noise + 100 ppm styrene : only occasional loss of OHC - Noise + 300 ppm styrene : few OHC loss located in all three rows of middle turn - Noise + 600 ppm styrene : more severe damage of the OHC than after exposure to 600 ppm styrene alone and also IHC loss in some animals	

Mechanism of action

Authors' conclusion

Ototoxic interaction between styrene and noise. Synergism is manifested only if styrene is applied in concentrations above the critical level (between 300 and 600 ppm in this study)

Our conclusion

Synergy between 300 - 600 ppm styrene and 100 dB A noise in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 60 ; E = 32 Sex : Males and females

Age : C = 22 - 65 ; E = 21 - 51 years

Exposure

Route : Inhalation

Duration : E = 7.1 years

C/D reported : NR (see remarks)

CSU/DSU : NR

Ratio :

ASM : NR

BM : Mandelic + phenylglyoxylic acids : 149 ± 80 mg/g creatinine

NSM :

NL : Noise in working places : 73 dB(A) Leq

Remarks : Exposure was measured by urinary mandelic + phenylglyoxylic acid (mean : 149 ± 80 mg/g creatinine)
The effect of noise exposure was not considered in this study
Only the abstract was available in English

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry • Exposed group showed slight higher mean audiometric thresholds compared to control for all frequencies	Pure tones at 0.5, 1, 2, 3, 4, 6 and 8 kHz

Mechanism of action

Authors' conclusion

Present experience seems to confirm the hypothesis that styrene exposure alone can determine a weak sensorineural high-frequency hearing loss

Our conclusion

Styrene exposure alone can determine a weak sensorineural high-frequency hearing loss

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C1 = 18; E = 18 Sex : Males

Age : C1 =39 (30 - 54); E = 40 (28 - 61) years

Exposure

Route : Inhalation

Duration : 10.8 (6 - 15) years

C/D reported : < 25-100 mg/m³ (average over 8 h)

CSU/DSU :

Ratio : 0.1 - 0.5

ASM : Passive absorption badges

BM :

NSM :

NL : NR

Remarks :

Tests

Results compared with reference values or control groups

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	Pure tones
• No abnormalities	
Cortical auditory evoked potentials	Frequency glides at 50 Hz et 200 Hz
• Abnormal results in 6 subjects	

Mechanism of action

Results suggest degradation in ability to discriminate frequeny changes

Authors' conclusion

At low doses, styrene causes central nervous system disturbances which can be apparent in special otoneurological tests

Our conclusion

At low doses, styrene causes central nervous system disturbances (at cortical-subcortical levels) which can be apparent in special otoneurological tests

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 81; E = 65 Sex : Males and females

Age : C = 45 (26 - 62) years; E = 43 (21 - 62) years

Exposure

Route : Inhalation

Duration : 7.6 (2 - 23) years

C/D reported : 16 (0.2-96) mg/m³ (average over 8 h + range)

CSU/DSU :

Ratio : 0.08

ASM : Passive absorption badges 7 hours

BM : Mandelic acid: 0.9 mmol/g creatinine

NSM : Personal noise dosimeter; mean 7.6 h (2.5-12 h)

NL : C = 77 (69-86) dB(A) ; E = 82 (75-84) dB(A)

Remarks : Exposed workers employed for a minimum of 1 year. Cumulative lifetime exposure of 1303 mg.yr/m³
Urine samples collected over 24 h from the beginning of the workshift under study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry • - Hearing losses at 2, 3, 4 and 6 kHz when compared with unexposed workers (> 25 dB HL) - No significant difference in prevalence of high-frequency hearing loss - Lack of dose-response relationship	at 1, 2, 3, 4, 6 and 8 kHz

Mechanism of action

Authors' conclusion

The study suggests ototoxic effect of styrene above 100 mg/m³ in workers

Our conclusion

No convincing ototoxic effect at this low concentration of styrene (average of 16 mg/m³) in the workers

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker

: C = 81; E1 (noise) = 78; E2 (styrene) = 65; E3 (styrene + noise) = 89

Sex : Males and females

Age : C = 45 years; E1 = 42; E2 = 43; E3 = 43 years

Exposure

Route : Inhalation

Duration : 1 - 39 years

C/D reported : E2 = 16 (0.2-96) mg/m³; E3 = 12 (0.03-50) mg/m³

CSU/DSU :

Ratio : 0.08

ASM : Passive absorption badges 7 hours

BM : Mandelic acid: E2 and E3 = 0.9 mmol/g creatinine

NSM : Personal noise dosimeter ; mean 7.6 h (2.5 to 12 h)

NL : C = 77 (69-86) dB(A) ; E1 = 85 (75-116) dB(A) ; E2 = 82 (75-84) dB(A) ; E3 = 89 (85-108) dB(A)

Remarks : Cumulative lifetime exposure of 1303 mg.yr/m³
Urine samples collected over 24 hours from the beginning of the workshift under study
Exposed workers employed for a minimum of 1 year

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 1, 2, 3, 4, 6 and 8 kHz
• - Significantly poorer thresholds at 2, 3, 4, 6 and 8 kHz in the group exposed to styrene compared to other groups. - Significantly poorer thresholds at 2, 3 and 8 kHz in the group exposed to styrene when compared with styrene + noise group. - However, the group exposed to styrene alone was exposed to higher concentrations of the styrene than the group exposed to styrene + noise.	

Mechanism of action

Authors' conclusion

This study found no interaction between styrene and noise in causing a hearing loss, however an additive effect was detected

Our conclusion

No interaction or additive effect in workers

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 33 ; E = 93 Sex : Males

Age : C = 50.8 ; E = 36 years

Exposure

Route : Inhalation

Duration : C = NR ; E = 9.4 ± 8.9 years

C/D reported : 8.0 (0.1-91.6) ppm (logarithmic mean)

CSU/DSU :

Ratio : 0.002-1.832

ASM : Samplers in the breathing zone

BM : Mandelic acid : 61 subjects <0.3 g/L ; 25 subjects of 0.3 - 1.0 g/L ; 7 subjects >1.0 g/L

NSM : 173 measurments with a data recorder (TEAC R-61) the day the subjects were examined

NL : 53.0 to 95.0 dB(A) with 14% of the measures in excess of 85 dB(A)

Remarks : The effect of noise exposure was not considered in this study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 0.5, 1, 2, 4 and 8 kHz
• The conventional audiometry indicated no alteration resulting from exposure to styrene	
Determination of higher audible frequency	Swept of pure times from 0.5 to 25 kHz at 75 dB(A) ± 10 dB(A) level
• The upper limit of hearing showed a dose-dependent reduction in plastic industry workers exposed below the limit of 50 ppm	

Mechanism of action

Authors' conclusion

The findings of the study show probable dose-dependant ototoxicity of styrene in humans, even at low levels

Our conclusion

Probable ototoxicity of styrene in humans, even at low levels

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 88; E1 = 28; E2 = 31; E3 = 7 Sex : Males

Age : C = 35.3 years; E = 33.8 (19-55) years

Exposure

Route : Inhalation

Duration : 8.6 years (<1 month - 24 years)

C/D reported : mean (max): E1 = 61 (138) mg/m³; E2 = 138 (361) mg/m³; E3 = 452 (716) mg/m³

CSU/DSU :

Ratio : 0.3 - 3.4

ASM : Passive absorption badges during 3 days

BM :

NSM : Sound level meter: Bruël and Kjaer type 2204 during 8 hours

NL : C = 80-85 dB(A) ; E = 66-70 dB(A)

Remarks : Control group exposed more to the noise than the group exposed to styrene ; 3 groups of exposed workers + 1 control group

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz
• No differences between the groups exposed and control	
Ultrahigh frequency audiometry	at 8, 10, 12, 14 and 16 kHz
• Difference between the groups E1 and E2 only at 8 KHz but not at 10-16 KHz	

Mechanism of action

Authors' conclusion

The study suggests ototoxic effect of styrene for high frequency tones (>8kHz) in workers

Our conclusion

No evidence that low-level styrene exposure produce threshold shifts in the low or high freqencies

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 88; E1 = 28; E2 = 31; E3 = 7 Sex : Males

Age : C = 35.3 years; E = 33.8 (19-55) years

Exposure

Route : Inhalation

Duration : 8.6 years (<1 month - 24 years)

C/D reported : mean (max): E1 = 61 (138); E2 = 138 (361); E3 = 452 (716) mg/m³

CSU/DSU :

Ratio : 0.3 - 3.4

ASM : Passive absorption badges during 3 days

BM :

NSM : Sound level meter: Bruël and Kjaer type 2204 during 8 hours

NL : C = 80-85 dB(A) ; E = 66-70 dB(A)

Remarks : Control group exposed more to the noise than the group exposed to styrene ; 3 groups of exposed workers + 1 control group
The effect of noise exposure was not considered in this study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz
• No differences between the groups exposed and control	
Ultrahigh frequency audiometry	at 8, 10, 12, 14 and 16 kHz
• Difference between the groups E1 and E2 only at 8 KHz but not at 10-16 KHz	

Mechanism of action

Authors' conclusion

The study suggests ototoxic effect of styrene for high frequency tones (>8kHz) in workers

Our conclusion

No evidence that low-level styrene exposure produce threshold shifts in the low or high freqencies

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 9 - 15 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 650, 750 ppm
CSU/DSU :
Ratio : 13 - 15
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• 650 ppm : no hearing loss 750 ppm : hearing loss observed at 2-24 kHz, with a maximum of 27 dB at 16 kHz	• Test performed only 6 weeks after the end of exposure
Light microscopy	Cochleogram
• 650 ppm : outer hair cell loss observed mainly at low frequencies of 4-6 kHz 750 ppm : outer hair cell loss observed throughout the entire range of damaged frequencies. Outer hair cells of the third row (OHC3) are the most disrupted, followed successively by OHC2 and OHC1	• Histology performed only 6 weeks after the end of exposure

Mechanism of action

Authors' conclusion

LOAEL of 650 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 650 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 5 - 13 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 6 h/d; 5 d/w; 4 w
C/D reported : 700 ppm
CSU/DSU :
Ratio : 14
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Clicks at 2, 3, 4, 5, 6, 8, 10, 12, 16, 20, 24, and 32 kHz
• - Hearing losses appeared between 10 and 24 kHz, with a peak of 14.6 dB at 20 kHz. - No significant recovery was measured six weeks after the end of exposure	• Audiometry tests performed prior to styrene exposure, at the end of exposure and 6 weeks after exposure
Light and electron microscopy	
• Outer hair cell losses were greatest in the third row, followed by the second and the first row in all doses. The largest losses located at the third row, 63 % at 2 to 32 kHz	• Histology performed 6 weeks after the end of exposure
Glutamate decarboxylase	Dosed in inferior colliculus
• No significant differences	

Mechanism of action

Authors' conclusion

LOAEL of 700 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 700 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Fisher 344 # : 12 Sex : Males
Age :

Exposure

Route : Inhalation
Duration : 14 h/d; 3 w
C/D reported : 800, 1000 and 1200 ppm
CSU/DSU :
Ratio : 16 - 24
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry • Elevation of auditory thresholds at 12 kHz and above with 800 ppm, at 4 kHz and above with 1000 ppm and at all frequences with 1200 ppm	at 2, 4, 8, 12, 16 and 20 kHz
Auditory brainstem responses • All styrene exposed rats had elevated thresholds at all frequencies tested	Inferior colliculus Tone pips of 4,8 and 16 kHz

Mechanism of action

Authors' conclusion

LOAEL of 800 ppm for ototoxic effect in rats

Our conclusion

LOAEL of 800 ppm for ototoxic effect in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Long Evans # : 6 Sex : Males
Age : 60 days

Exposure

Route : Inhalation
Duration : 18 h/d; 5 d
C/D reported : 1000 ppm
CSU/DSU :
Ratio : 20
ASM :
BM :
NSM :
NL :
Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses	Tone pips of 25 to 95 dB and 16 kHz
• Styrene exposed rats had decreased amplitude, indicative of hearing loss	• Test performed 10 days after the end of exposure

Mechanism of action

Authors' conclusion

Ototoxic effect at 1000 ppm in rats

Our conclusion

Ototoxic effect at 1000 ppm in rats

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 43; E1 = 170; E2 = 86 Sex : Males

Age : C = 38 years; E1 = 36 years; E2 = 37 years

Exposure

Route : Inhalation

Duration : NR

C/D reported : E1 = 58.6 mg/m³; E2 = 12.8 mg/m³; C = 1.7 mg/m³ (geometric mean over 8 h)

CSU/DSU :

Ratio : 0 - 0.28

ASM : Personal air sampling pump during 1 shift

BM :

NSM : Personal noise dosimeter during 1 shift

NL : C = 80 dB(A) ; E1 = 88 dB(A) ; E2 = 89 dB(A)

Remarks : Cumulative styrene lifetime exposure ranged from 0 to 53275 mg/m³ months

Tests

Conclusions of the study might be biased because of the limitations of the method used for hearing evaluation

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	Pure tones at 3, 4, 6 and 8 kHz
• Cumulative lifetime styrene exposure or time weight average exposure were not a significant factors for hearing loss	• Audiometry tests performed at the beginning and at the end of the workshift

Mechanism of action

Authors' conclusion

No conclusive evidence for a chronic styrene-induced effect on hearing acuity

Our conclusion

No conclusive evidence for a chronic styrene-induced effect on hearing acuity

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 43; E1 = 170; E2 = 86 Sex : Males

Age : C = 38 years; E1 = 36 years; E2 = 37 years

Exposure

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Duration : NR

C/D reported : E1 = 58.6 mg/m³; E2 = 12.8 mg/m³; C = 1.7 mg/m³ (geometric mean over 8 h)

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NL : C = 80 dB(A); E1 = 88 dB(A); E2 = 89 dB(A)

Remarks : Cumulative styrene lifetime exposure ranged from 0 to 53275 mg/m³ months
The effect of noise exposure was not considered in this study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 3, 4, 6 and 8 kHz
• Cumulative lifetime styrene exposure or time weight average exposure were not a significant factors for hearing loss	• Audiometry tests performed at the beginning and at the end of the workshift

Mechanism of action

Authors' conclusion

No conclusive evidence for a chronic styrene-induced effect on hearing acuity

Our conclusion

No conclusive evidence for a chronic styrene-induced effect on hearing acuity

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : C = 65; E1 = 82; E2 = 72 Sex : Males

Age : C : 35.3 ; E1 : 34.0 ; E2 : 35.3 years

Exposure

Route : Inhalation

Duration : E1 = 9.6; E2 = 4.8(0.5-24.5) years

C/D reported : C and E1 = 0 : E2 = NR

CSU/DSU :

Ratio : NR

ASM : NR

BM :

NSM :

NL : C = 0 ; E1 = twice the levels of E2 (E1 = 96 dB) ; E2 = NR
Noise exposure E2 = 7.8 ±4.1 ans (0.5 - 28.0)

Remarks : Only the abstract was available in English

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry • - Significantly increased average hearing loss in styrene group as compared to both control groups at all frequencies (1-8 kHz) - Risk of hearing loss in styrene + noise group was 7 times higher than that of the non-exposed group and 4 times higher than in workers exposed only to noise - No relationship could be found between the amount of styrene exposure and hearing impairment, taking account of the confounding effets of age and noise	at 1, 1.5, 2, 3, 4, 6 and 8 kHz

Mechanism of action

Authors' conclusion

The results suggest that exposure to solvent mixtures with styrene as a basic component may exert, additional to noise, adverse effects on the auditory organ

Our conclusion

Co-exposition to styrene and noise may exert adverse effects on the auditory organ

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : E = 194; C = 157 Sex : Males and females

Age : C = 39.6 years; E = 33.8 years

Exposure

Route : Inhalation

Duration : At less 6 months

C/D reported : 60 ± 39.6 mg/m³

CSU/DSU :

Ratio : 0.3

ASM : Sampling pumps with glass tubes; during > 80 % of an 8 hour working shift

BM :

NSM : Sound level meter : Bruël and Kjaer type 2231 during 8 hours

NL : C = 73.2 dB(A) ; E = 80.3 dB(A)

Remarks : - Styrene concentration is a mean value of individual worklife averaged concentration. Exposure varied between 3.6 and 308 mg/m³
- Averaged noise exposure level over total time of employment
- Exposed workers employed for a minimum of 6 months

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 1, 2, 3, 4, 6 and 8 kHz
• - 56.2 and 33.8 % of abnormal audiograms in styrene exposed and control group, respectively. - The odds ratio of hearing loss was 5.2- fold greater in exposed group - Significant increase in hearing threshold within the frequency range 2 to 8 kHz	

Mechanism of action

Authors' conclusion

Occupational exposure to styrene leads to a significant increase in the chance of developing sensorineural hearing loss

Our conclusion

No convincing ototoxic effect of styrene because the workers exposed to styrene were more exposed to the noise than the controls

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker

: C = 157; E1 (styrène) = 194; E2 (bruit) = 66; E3 (styrène + bruit) = 56

Sex : Males and females

Age : C = 39.6 years; E1 = 33.8; E2 = 41; E3 = 36 years

Exposure

Route : Inhalation

Duration : At less 6 months

C/D reported : E1 = 60 ± 39.6 mg/m³ ; E3 = 34.4 ± 25.9 mg/m³

CSU/DSU :

Ratio : 0.3

ASM : Sampling pumps with glass tubes ; during > 80 % of an 8 hour working shift

BM :

NSM : Sound level meter : Bruël and Kjaer type 2231 during 8 hours

NL : C = 73.2 dB(A) ; E1 = 80.3 dB(A) ; E2 = 89.2 dB(A) ; E3 = 88.6 dB(A)

Remarks : - Styrene concentration is a mean value of individual worklife averaged concentration. Exposure varied between 3.6 and 308 mg/m³
- Averaged noise exposure level over total time of employment
- Exposure to styrene in styrene group was nearly twice higher than that in styrene + noise group. Exposed workers employed for a minimum of 6 months

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	Pure tones at 1, 1.5, 2, 3, 4, 6 and 8 kHz
• - Noise + styrene : odds ratios of developing hearing loss were two and three times higher than the respective values for styrene-only or noise-only exposed subjects - Abnormal audiograms in control, styrene-only, noise-only and styrene+noise exposed group (33.8 %, 56.2 %, 63.3 % and 76.8 %)	

Mechanism of action

Authors' conclusion

Combined exposures to noise and styrene seems to be more ototoxic than exposure to noise alone

Our conclusion

Combined exposure to noise and styrene seems to be more ototoxic than exposure to noise or styrene alone

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : E = 290; C = 223 Sex : Males and females

Age : C = 40 years; E = 35 years

Exposure

Route : Inhalation

Duration : At less 6 months

C/D reported : 61.8 ± 51.9 mg/m³

CSU/DSU :

Ratio : 0.35

ASM : Sampling pumps with glass tubes; during > 80 % of an 8 hour working shift

BM :

NSM : Sound level meter : Bruël and Kjaer type 2231 during 8 hours

NL : C = 77.9 dB(A) ; E = 82.1 dB(A)

Remarks : - Styrene concentration is a mean value of individual worklife averaged concentration. Exposure varied between 3.6 and 309 mg/m³
- Averaged noise exposure level over total time of employment
- Exposed workers employed for a minimum of 6 month
E = styrene exposed workers ; C = solvent non-exposed workers (including 66 workers exposed to noise only)

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 1, 1.5, 2, 3, 4, 6 and 8 kHz Examination performed at least 16 h after last exposure to noise

• - Group exposed to styrene or noise only : the odds ratio of hearing loss was 5.3 and 3.9 –fold greater than in control group (without exposure to noise or styrene)
- Combined exposure to noise and styrene : the odds ratio was increased 10.9 fold, compared to control group
- Significant increase in hearing threshold was found within the frequency range 1 to 8 kHz
- No dose-effect relationship between solvent exposure and hearing thresholds

Mechanism of action

Authors' conclusion

Additive effect of the co-exposure to styrene and noise

Our conclusion

Additive effect of the co-exposure to styrene and noise

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker # : E = 290; C = 223 Sex : Males and females

Age : C = 40 years; E = 35 years

Exposure

Route : Inhalation

Duration : At least 6 months

C/D reported : 61.8 ± 51.9 mg/m³

CSU/DSU :

Ratio : 0.35

ASM : Sampling pumps with glass tubes; during > 80 % of an 8 hour working shift

BM :

NSM : Sound level meter : Bruël and Kjaer type 2231 during 8 hours

NL : C = 77.9 dB(A); E = 82.1 dB(A)

Remarks : - Styrene concentration is a mean value of individual worklife averaged concentration. Exposure varied between 3.6 and 309 mg/m³.
- Averaged noise exposure level over total time of employment.
- Exposed workers employed for a minimum of 6 month.
E = styrene exposed workers; C = solvent non-exposed workers (including 66 workers exposed to noise only)
The effect of noise exposure was not considered in this study

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	at 1, 2, 3, 4, 6 and 8 kHz Examination performed at least 16 h after last exposure to noise

- - Group exposed to styrene only : the odds ratio of hearing loss was 3.9 fold greater than in control group
  - Significant increase in hearing threshold was found within the frequency range 1 to 8 kHz
  - No dose-effect relationship between solvent exposure and hearing thresholds

Mechanism of action

Authors' conclusion

Exposure to styrene in humans is associated with a increased risk hearing loss

Our conclusion

Exposure to styrene in humans is associated with a increased risk hearing loss

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Worker

: C = 127; E1 = 99; E2 = 118; E3 = 31; E4 = 17; E5 = 34

Sex : Males

Age : 40 years (mean)

Exposure

Route : Inhalation

Duration : At least 6 months

C/D reported : 1.7 à 48.5 ppm

CSU/DSU :

Ratio : 0.1-1.0

ASM :

BM : Mandelic + phenylglyoxylic acids : E1 = 50.8 ± 27.1 ; E2 = 229 ± 103 ; E3 = 970 ± 410 ; E4 = 196 ± 282 ; E5 = 319 ± 423 mg/g creatinine

NSM : NR

NL : 70-85 dB(A) (mean) ; Individual noise levels not measured

Remarks : Air styrene concentrations calculated from results of biological monitoring
Workers exposed to more than 85 dB were excluded
The effect of noise exposure was not considered in this study
Information concerning acoustic pause unclear

Tests

Test type • Effects reported	Details on test • Remarks
Pure tone audiometry	Pure tones low frequencies 125-1500 Hz, medium frequencies 2000-8000 Hz, high frequencies 9000-16000 Hz and at 8000-12500 Hz
• - Weak evidence for worsening of hearing thresholds in the range between 8000 and 12500 Hz among the high exposed group compared to the lower exposed groups. However, thresholds were always better in high frequencies for the medium group for the medium group. Therefore, a dose-response relationship was not evident - Lack of association between hearing threshold data and exposure - During work holidays, improvments in thresholds (125-1500 Hz) were observed but independent of styrene exposure - At frequencies up to 1500 Hz, statistically significant higher threshold were exhibited in the subgroup of high-long exposed workers compared to the low-short group. The difference disappears at higher frequencies	• - The evaluations refer to the frenquency-related hearing level for each ear without age correction. - Test performed during normal workdays and also during the company holiday
Transient evoked otoacoustic emissions (TEOAE)	Signal to noise ratio TEOAE1 at 1, 2, 3 and 4 kHz and amplidtudes of TEOAE2 at 1.4, 2, 2.8, 4, 5.7 and 8 kHz. At 80 dB SPL (Click)
• No correlation with the exposure data	

Mechanism of action

Authors' conclusion

Worse hearing thresholds for 1000-1500 and 8000-12500 Hz in long-term exposed workers with high styrene levels of 30-50 ppm and higher concentrations above 50 ppm in the past. No dose-responsa relationship could be proven except for 1000 and 1500 Hz with chronic exposure. Hearing function improved during holidays and improvement was related with exposure

Our conclusion

High-level long-term styrene exposure causes hearing impairment that can improve after exposition stops

Styrene

Styrene (monomer)
• TWAEV : 50 ppm | 213 mg/m³ D-TWAEV : 30 mg/kg/d

Population

Species : Rat Fisher 344 # : 8 - 12 Sex : Males

Age :

Exposure

Route : Inhalation

Duration : 14 h/d; 5 d/w; 3 w

C/D reported : 800 ppm

CSU/DSU :

Ratio : 16

ASM :

BM :

NSM :

NL :

Remarks :

Tests

Test type • Effects reported	Details on test • Remarks
Auditory brainstem responses • ABR were minimally affected at 4 kHz and moderately to severely affected at 8, 16 and 30 kHz	Tone pips of 75 dB at 4, 8, 16, and 30 kHz • Test performed 3 days after the end of exposure
Light and electron microscopy • - Outer hair cell loss observed in the upper basal and lower middle regions of the cochlea - Outer hair cells loss was least in the first row and greatest in the second and third rows	Cochleogram • Histology performed 3 days after the end of exposure

Mechanism of action

Mechanism of styrene induced hair cell loss was not determined

Authors' conclusion

Ototoxic effect at 800 ppm in rats. Data document mid-frequency auditory dysfunction in rats with significant damage to the organ of Corti

Our conclusion

Ototoxic effect at 800 ppm in rats. Data document mid-frequency auditory dysfunction in rats with significant damage to the organ of Corti

BIBLIOGRAPHY

Calabrese 1996 Calabrese, G., et al. (1996) Otoneurological study in workers exposed to styrene in the fiberglass industry. Int Arch Occup Environ Health. 68(4): 219-23.

Campo 2001 Campo, P., et al. (2001) Styrene-induced hearing loss: a membrane insult. Hear Res. 154(1-2): 170-80.

Campo 2003 Campo, P., et al. (2003) Is the aged rat ear more susceptible to noise or styrene damage than the young ear? Noise & Health. 5(19): 1-18.

Chen 2007 Chen, G.-D., et al. (2007). Styrene induced alterations in biomarkers of exposure and effects in the cochlea: mechanisms of hearing loss. Toxicol Sci, 98(1), 167-177.

Crofton 1994 Crofton, K.M., et al. (1994) Solvent-induced ototoxicity in rats: an atypical selective mid-frequency hearing deficit. Hear Res. 80(1): 25-30.

Fechter 1993 Fechter, L.D. (1993) Effects of acute styrene and simultaneous noise exposure on auditory function in the guinea pig. Neurotoxicol Teratol. 15(3): 151-5.

Gagnaire 2005 Gagnaire, F., et al. (2005) Relative ototoxicity of 21 aromatic solvents. Arch Toxicol. 79(6): 346-54.

Hoffmann 2006 Hoffmann, J., et al. (2006). Field study to explore possible effects of styrene on auditory function in exposed workers. Ind Health, 44(2), 283-286.

Johnson 2006 Johnson, A.C. et al. (2006). Audiological findings in workers exposed to styrene alone or in concert with noise. Noise & Health 8(30): 45-57.

Lataye 2000 Lataye, R., et al. (2000) Combined effects of noise and styrene exposure on hearing function in the rat. Hear Res. 139(1-2): 86-96.

Lataye 2001 Lataye, R., et al. (2001) Cochlear pathology induced by styrene. Neurotoxicol Teratol. 23(1): 71-9.

Lataye 2003 Lataye, R., et al. (2003) Solvent ototoxicity in the rat and guinea pig. Neurotoxicol Teratol. 25(1): 39-50.

Lataye 2004 Lataye, R., et al. (2004) Critical period for styrene ototoxicity in the rat. Noise & Health. 7(25): 1-10.

Lataye 2005 Lataye, R., et al. (2005) Combined effects of noise and styrene on hearing: comparison between active and sedentary rats. Noise & Health. 7(27): 49-64.

Lawton 2006 Lawton, B. W., J. Hoffmann, et al. (2006). The ototoxicity of styrene: a review of occupational investigations. Int Arch Occup Environ Health: 79(2): 93-102.

Loquet 1999 Loquet, G., et al. (1999) Comparison of toluene-induced and styrene-induced hearing losses. Neurotoxicol Teratol. 21(6): 689-97.

Loquet 2000 Loquet, G., et al. (2000) Combined effects of exposure to styrene and ethanol on the auditory function in the rat. Hear Res. 148(1-2): 173-80.

Mäkitie 2002 Makitie, A., et al. (2002) Functional and morphological effects of styrene on the auditory system of the rat. Arch Toxicol. 76(1): 40-7.

Mäkitie 2003 Makitie, A.A., et al. (2003) The ototoxic interaction of styrene and noise. Hear Res. 179(1-2): 9-20.

Mascagni 2007 Mascagni, P., et al. (2007). [Hearing function and solvent exposure: study of a worker population exposed to styrene] Udito ed esposizioni a solventi: studio di una popolazione di lavoratori esposti a stirene. G Ital Med Lav Ergon, 29(3 Suppl), 277-279.

Möller 1990 Moller, C., et al. (1990) Otoneurological findings in workers exposed to styrene. Scand J Work Environ Health. 16(3): 189-94.

Morata 2002 Morata, T.C., et al. (2002) Audiometric findings in workers exposed to low levels of styrene and noise. J Occup Environ Med. 44(9): 806-14.

Morioka 1999 Morioka, I., M. Kuroda, et al. (1999). Evaluation of organic solvent ototoxicity by the upper limit of hearing. Arch Environ Health 54(5): 341-6.

Muijser 1988 Muijser, H., et al. (1988) The effects of occupational exposure to styrene on high-frequency hearing thresholds. Toxicology. 49(2-3): 331-40.

Pouyatos 2002 Pouyatos, B., et al. (2002) Use of DPOAEs for assessing hearing loss caused by styrene in the rat. Hear Res. 165(1-2): 156-64.

Pouyatos 2004 Pouyatos, B., et al. (2004) Consequences of noise- or styrene-induced cochlear damages on glutamate decarboxylase levels in the rat inferior colliculus. Hear Res. 189(1-2): 83-91.

Pryor 1987 Pryor, G.T., et al. (1987) Hearing loss in rats caused by inhalation of mixed xylenes and styrene. J Appl Toxicol. 7(1): 55-61.

Rebert 1993 Rebert, C.S., et al. (1993) Combined effects of solvents on the rat's auditory system: styrene and trichloroethylene. Int J Psychophysiol. 14(1): 49-59.

Sass-Kortsak 1995 Sass-Kortsak, A.M., et al. (1995) An investigation of the association between exposure to styrene and hearing loss. Ann Epidemiol. 5(1): 15-24.

Sliwinska-Kowalska 2001 Sliwinska-Kowalska, M., et al. (2001). [Hearing impairment in the plastics industry workers exposed to styrene and noise]. Med Pr, 52(5), 297-303.

Sliwinska-Kowalska 2003 Sliwinska-Kowalska, M., et al. (2003) Ototoxic effects of occupational exposure to styrene and co-exposure to styrene and noise. J Occup Environ Med. 45(1): 15-24.

Sliwinska-Kowalska 2005 Sliwinska-Kowalska, M., et al. (2005) Exacerbation of noise-induced hearing loss by co-exposure to workplace chemicals. Environ Toxicol Pharmacol. 19: 547-553.

Triebig 2008 Triebig, G., et al. (2009). Occupational styrene exposure and hearing loss: a cohort study with repeated measurements. Int Arch Occup Environ Health, 82(4), 463-480.

Yano 1992 Yano, B.L., et al. (1992) Abnormal auditory brainstem responses and cochlear pathology in rats induced by an exaggerated styrene exposure regimen. Toxicol Pathol. 20(1): 1-6.