EFFECTS OF COMBINED EXPOSURE TO NOISE AND TOXIC SUBSTANCES: A CRITICAL REVIEW OF THE LITERATURE

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Abstract—A number of studies have been conducted in recent years investigating the potential effects on various health endpoints of the combination of noise and a variety of different industrial substances. This review indicates that the information available in both animals and humans on this subject is limited particularly with respect to assessing occupational risk. Most studies have focused on auditory effects in animals, although investigations have been performed for other toxicological endpoints. For some substances, notably toluene, the information from animals studies does suggest an interaction but these were performed only at exposure levels to both noise and chemicals which were each individually ototoxic. Single simultaneous exposure to noise and styrene did not result in any enhancement of auditory impairment above that produced by noise or styrene alone. Single simultaneous exposure to noise and carbon monoxide (CO), however, showed some evidence of enhancement of ototoxicity beyond that produced by noise or carbon monoxide alone, although only at high atmospheric concentrations of CO. When 1,3-dinitrobenzene was administered parenterally at neurotoxic dose levels with continuous noise exposure, there was an increased severity of effects in the brain stem. Combined exposure to noise and lead and/or cadmium resulted in histopathological heart lesions of undefined severity, a finding which was not observed for either of those agents in isolation. Dermal exposure to dimethylformamide and noise or inhalation exposure to xylene and noise resulted in some biochemical changes in cardiac muscle which were of doubtful toxicological significance. In developing mice, there was evidence that combined exposure to cadmium sulphate and noise caused an increased incidence of external and skeletal malformations but only at dose levels of cadmium which would have induced developmental effects. Combined exposure to noise and to solvents (implicated in these studies) and noise often occurs. Some reports (for example Morata et al., 1994) suggest that because of such interactions current workplace controls may not be adequate. Due to these concerns, we felt it necessary to evaluate the literature available and consider its relevance to the occupational setting. This review is not intended to appraise the independent

INTRODUCTION

Over the last decade a number of studies have investigated the effects of combined exposure to noise and industrial substances. The emerging findings have raised concern in some quarters, most notably the printing industry where combined exposure to solvents (implicated in these studies) and noise often occurs. Some reports (for example Morata et al., 1994) suggest that because of such interactions current workplace controls may not be adequate. Due to these concerns, we felt it necessary to evaluate the literature available and consider its relevance to the occupational setting. This review is not intended to appraise the independent

*This review does not necessarily reflect the views and policies of the Health and Safety Executive.
action of these agents. Furthermore, this review concentrates on the interaction of noise with industrial substances and does not cover those data derived from studies investigating therapeutic substances such as some antibiotics, loop diuretics and cis-platinum all of which are known to interact adversely with noise on hearing.

STUDIES IN ANIMALS

Most of the work performed has investigated auditory function although other reports are available covering investigations of effects on the heart, developmental toxicity and general toxicity.

Effects on auditory function

Reports are available of studies in which the combined effects of exposure to noise and toluene, styrene or carbon monoxide (CO) were investigated. These studies have been performed mainly in the rat, the auditory frequency range of which is from around 0.25 to 80 kHz, with a maximum sensitivity around 8 kHz (Kelly and Masterton, 1977). The auditory range for young adult humans is around 20 Hz to 20 kHz, with the greatest sensitivity around 1-4 kHz. Thus, although extended to the ultrasonic range, the rat auditory range overlaps that of the human.

Toluene. Toluene is known to produce ototoxicity in rats following exposure via the inhalation, oral and parenteral routes of exposure (Bell et al., 1989).

The exposure levels chosen for both toluene and noise in the following experiments are known to induce auditory impairment. In the first study, rats were exposed to toluene or noise alone or in a combination of toluene followed by noise (Johnson et al., 1988). Exposure to toluene was to a nominal concentration of 1000 ppm, 16 h day\(^{-1}\), 5 days week\(^{-1}\) for 2 weeks. Noise exposure was to a 2 kHz wide noise band continuously sweeping between 3 and 30 kHz, with a maximum sound intensity of approximately 105 dB sound pressure level (SPL) within the range 5-15 kHz (equivalent to a sound level of 100 dB across the frequency range). Noise exposures were for 10 h day\(^{-1}\), 7 days week\(^{-1}\) for 4 weeks with random noise-free pauses for a total of 2 h during the exposures, giving an overall exposure time of 12 h. Hearing impairment was assessed by auditory brainstem response (ABR) to the noise stimulus.

Toluene and noise alone were both found to increase the threshold for ABR indicating auditory impairment. The group exposed to toluene followed by noise showed the greatest increase in the threshold for ABR at 2-5 days post-exposure, with some rats showing no auditory response to the highest available intensity of stimuli at both 12.5 and 20 kHz although there was some recovery 6 months post-exposure. The loss of auditory function was greater than the summated loss caused by toluene and noise alone at 3.15 and 6.3 kHz.

In a further study, the order of exposures was reversed and the toluene exposures were for 7 instead of 5 days week\(^{-1}\) (Johnson et al., 1990). The effect of sequential exposure to noise and toluene was essentially the same in both the immediate and interrupted noise groups; in both cases the threshold sound intensity was increased at all tested frequencies and was greater than those of noise or toluene alone at 6.3,
12.5 and 20 kHz. The loss did not exceed the summated values for these insults alone (that is the effect was at most additive) and at 12.5 kHz was less than additive. The effects observed of this sequential exposure were therefore less marked than those seen when toluene was followed by noise.

The value of the results of these studies is limited with respect to the occupational setting. The daily exposures to both toluene and noise were long at 16 h day$^{-1}$ and 10 h day$^{-1}$ respectively but the overall exposure periods (2 and 4 weeks) were relatively short. Whether or not shorter daily exposure times would have resulted in auditory impairment either alone or in combination is not clear. Also, the insults employed in themselves induced auditory impairment and these data do not allow any assessment of whether non-ototoxic levels of exposure to toluene and/or noise would have produced any effects (for example, what might have been the effects seen if exposures were at say concentrations closer to the current U.K. OES of 50 ppm 8-h TWA for toluene or the first action level of 85 dB(A) for noise?). Furthermore, the insults were delivered sequentially rather than simultaneously which is less representative of the likely working environment and a clear difference was observed in terms of the severity of effect depending upon the sequence of delivery. Thus, overall, the only firm conclusion that can be drawn from these studies is that ototoxic levels of both toluene and noise delivered sequentially produced either synergistic or additive auditory impairment, depending upon the order of delivery of the insults.

Styrene. Styrene has been found to induce auditory impairment, as assessed by ABR, in rats (Yano et al., 1992). Fechter (1993) exposed guinea pigs to either noise or styrene alone or the two insults combined. Exposure to styrene was to a single 7-h exposure to either 500 or 1200 ppm; noise exposure was to 95 dB(A) white noise.

Groups of guinea pigs received either 500 ppm of styrene alone for 7 h, 95 dB(A) alone also for 7 h or both the styrene and noise for 7 h. In those animals which received noise alone or noise and styrene together, an increase was observed in the auditory threshold at 8, 12 and 16 kHz. This increase was of the same magnitude in both groups. Styrene exposure alone had no effect on auditory function in this experiment. Only a slight, non-statistically significant increase in cholear microphonic was observed in these groups at lower frequencies, the biological significance of which was considered to be doubtful since it may have been an artefact of the technique employed. Overall, since styrene alone did not produce any effects and the combined exposure did not result in any auditory impairment over and above that induced by noise alone this study provided no evidence for any interaction of the two agents.

Following on from this first experiment, groups received either 500 or 1200 ppm styrene with noise for 7 h, noise alone or no treatment; there was no styrene only group. Again, there was no indication that styrene combined with noise produced any enhancement of effects compared to noise alone.

Overall, this study provides limited evidence that styrene combined with noise during a simultaneous exposure does not result in any enhancement of auditory impairment compared to noise alone. Unfortunately, the study only employed single exposures and this limits the conclusions that can be drawn from this study with respect to repeated exposures and possible interactions.
**Carbon monoxide.** Carbon monoxide (CO) only appears to be ototoxic at high exposure concentrations. The rationale for the following investigations was that noise may induce cochlear damage by reducing the availability of O₂ in the tissue through increased metabolic demand and that a hypoxia-inducing agent, such as CO, may enhance any noise-induce damage.

In one study, groups of rats received single exposures of either CO (1200 ppm) or noise alone or the two combined (Young et al., 1987 and Fechter, 1988). White noise was generated for 120 min between ~0.5 and 35 kHz with a maximum intensity of ~105 dB SPL between 4 and 8 kHz, equivalent to 110 dB(A). The CO-alone rats received a 210 min single exposure to the gas. Rats which received the combined exposure were exposed to CO as for the CO-alone group but also received noise for the last 120 min of exposure. This 90 min CO pretreatment was designed to ensure that carboxyhaemoglobin levels had attained a state of equilibrium prior to noise exposure. Measurement of auditory impairment was then made at 1 and 3 weeks post-treatment. In a second study, groups were again exposed to noise and/or 250, 500 or 1200 ppm CO. Auditory function was assessed by determination of reflex responses to noise at 10 and 40 kHz. These reflex thresholds were only determined pre- and at 1 week post-exposure and only at 10 and 40 kHz.

The results of these studies showed that when rats were exposed to a combination of noise and CO at 500 ppm or more, auditory function was impaired more than if the rats had been exposed to noise alone. At the concentrations of CO used there was no effect of CO alone on auditory function hence the results of the study appear to provide some support for the hypothesis that reduced cochlear oxygenation is involved in noise-induced hearing damage and that this can be potentiated by hypoxia-inducing agents. The concentrations of CO used were high relative to current occupational exposure limits, however, (for example U.K. OES of 50 ppm 8-h TWA; 300 ppm 15-min STEL) and it is not possible to determine whether or not potentiation of the effects of noise would be seen at CO exposure levels closer to the U.K. OES; however, the absence of any observable effects for noise ± 250 ppm CO is reassuring. Also, the level of noise employed was again designed to induce auditory impairment and so it is not possible to draw any conclusions regarding lower noise levels. A further difficulty is that only a single (although at least concomitant) exposure was employed. Overall, therefore, although these results provide some evidence that at noise levels inducing auditory impairment, concomitant CO exposure can enhance this impairment, it is not possible to draw any conclusions regarding possible interactions at lower levels of exposure to both agents.

**Effects on brain**

The combined effect of noise and 1,3-dinitrobenzene (DNB) on those parts of the brain related to processing of auditory input was investigated (Ray et al., 1992). DNB has been found to induce symmetrical lesions in the brain stem of rats, including in those regions associated with auditory function. These lesions have been found to occur in areas of the brain stem which lie in the auditory pathways. The rationale for the study was that since the lesions occur in areas of the brain stem which have high resting metabolic states it may be possible that the processing of auditory information may be contributing to local increased metabolic activity.
which may increase local metabolism and hence toxicity of DNB. Thus if functional activity could be modulated (by altered auditory input for example) then it might alter the expression of DNB toxicity at these sites.

When rats were partially deafened in one ear, the rate of glucose utilisation was altered in some areas of the brain stem associated with hearing. In the next phase of the study, rats that had been unilaterally partially deafened by left tympanic membrane rupture received $4 \times 10 \text{ mg kg}^{-1}$ of DNB by the intraperitoneal (i.p.) route over 28 h, with or without noise. Noise exposure began at the time of the first dose of DNB and was continuous for the following 48 h.

The results of this study demonstrated an association between the severity of neurotoxic effects in the brain stem in those regions where glucose utilisation was altered by modulation of auditory input. When this was reduced by unilateral deafening, local brainstem lesions were reduced in severity. With respect to the occupational environment, however, it is difficult to draw more meaningful conclusions. The dose of DNB was chosen to be toxic to those areas of the brainstem being investigated and thus it is not possible to draw any conclusions regarding any potential interactions at lower, non-toxic doses of DNB. Furthermore, the noise exposure was continuous and it is not possible to determine whether or not the enhancements seen would have occurred under a discontinuous exposure regimen. Another difficulty was that the DNB was administered via the i.p. route, which may or may not be more effective in inducing the types of lesions seen compared to other more realistic routes of occupational exposure. Thus, although this report presents some interesting observations few firm conclusions can be drawn from it with respect to the occupational setting other than that it demonstrates an interaction between noise and DNB exposure at neurotoxic doses of DNB.

**Studies on the heart**

Two studies have investigated the interaction of noise and hazardous substances on the heart: in the more recent study, rats received exposure to noise, cadmium or lead alone and also combinations of two or all three agents (Conetta, 1993). Lead was administered as 14 daily oral gavage doses of lead acetate at $\sim 100 \text{ mg kg}^{-1} \text{ day}^{-1}$. Cadmium sulphate was administered at a dose of $\sim 2.5 \text{ mg kg}^{-1} \text{ day}^{-1}$. The noise exposure employed was white noise in the frequency range 0.2–1 kHz at 68–72 dB(A) for 15 min day$^{-1}$ for 28 days. Combined groups received sequential exposures to Pb and/or Cd for the 14 days prior to noise.

General clinical signs of toxicity were observed during the study in the Pb and/or Cd + noise groups and in some of the combined groups (mainly Pb + noise).

Histopathological examination of the heart muscle revealed early necrotic changes (severity unclear) in all treated groups but none in controls, and complete necrotic lesions in all groups except the noise only and untreated control groups but again the severity and extent is unclear although none of the lesions resulted in mortality. There appeared to be no interaction between noise and chemical exposure with respect to either their incidence or severity. Lymphocytic infiltration (severity unclear) was observed in all groups with the numbers of affected animals similar in the untreated control, Pb + noise and Pb + Cd + noise groups but elevated in the other groups.
The main observation of an interaction between noise and Pb and/or Cd was in the incidence of muscle cell hypertrophy, muscle fibre fragmentation and sarcolysis (severity unclear). In all three cases the numbers of rats affected in the Pb + noise, Cd + noise and Pb + Cd + noise groups was greater than in all the other single or combined treatment groups (and untreated controls), in which generally these effects were not observed. Nevertheless, the overall perception is that in the noise + - substance groups these effects were either enhanced or observed where they were not seen following individual insults.

Overall, therefore, although there are some limitations to the reporting of this study, the results appear to indicate that combined exposure to noise and Pb and/or Cd can result in an increase in histopathological changes in the heart of rats. The results are of some interest as they suggest that certain specific lesions of heart tissue developed following the combined exposure to substances and noise which in themselves did not induce such changes. The conclusions that can be drawn in relation to occupational exposure, however, are limited by the fact that the insults were sequential rather than concomitant and animals were dosed by the oral route of exposure.

In another study, groups of rats were exposed to noise and dimethyl formamide (DMF) or xylene either alone or with noise and substance exposure combined (Ivanovich et al., 1983, 1985). DMF was administered as a dermal application at daily doses of ~95, 190 or 945 mg kg\(^{-1}\) for 5 days week\(^{-1}\) for a total of 6 weeks. Rats were exposed by inhalation to xylene at 300 mg m\(^{-3}\) for 4 h day\(^{-1}\), 5 days week\(^{-1}\) for 6 weeks. Noise exposure (white noise at 46, 85 or 95 dB) was for 2 h day\(^{-1}\) for DMF and 4 h day\(^{-1}\) for xylene for a total of 30 exposures.

With respect to noise alone no changes in a range of biochemical measures were seen at either 46 or 85 dB. Although some changes were observed at 95 dB alone these appeared to be inconsistent between the studies. Although combined exposures were concomitant for DMF/xylene and noise the general lack of consistency of the changes in the parameters measured makes it difficult to draw any conclusions about their biological or toxicological significance.

Studies on developmental effects

Groups of pregnant mice received either Cd or noise alone or combined. Cd was administered as a single i.p. dose of 1 or 2 mg kg\(^{-1}\) of Cd sulphate on day 7 of gestation (Murata et al., 1993). Noise exposure was to 100 dB(C) white noise on day 7 of gestation for either 3 or 6 h continuously or intermittently for 6 h. Groups received these treatments either alone or in the combined groups the noise immediately after the Cd sulphate treatment.

Cadmium sulphate treatment alone resulted in an expected dose-dependent increase in the total percentage of malformed fetuses with increases in the percentages with external and/or skeletal malformations. In general these increases were only statistically significant at 2 mg kg\(^{-1}\) apart from the total percentage of malformed fetuses and the percentage with skeletal malformations at 1 mg kg\(^{-1}\). Following noise alone, the only effects were seen after 6 h continuously and with 15 min on/off for 6 h. Three hours continuous noise and 5 min on/off for 6 h was without effect.
Effects of combined exposure to noise and toxic substances

Combined exposure to both insults increased the percentage of fetuses affected. This was greatest in the groups which received 2 mg kg$^{-1}$ Cd sulphate and noise. In these groups as noise exposure ‘increased’ from intermittent to continuous, a clear increase in the total percentage of fetuses malformed was observed but this increase was not statistically significantly different from the group given the same dose of Cd alone and overall looked at most to be additive of the Cd and noise exposures.

There was some evidence from this study that combined Cd and noise exposure could increase the incidence of external and skeletal malformations. The doses of Cd used were chosen to induce developmental toxicity, however, and thus it is difficult to draw any meaningful conclusions about whether or not the interactions seen would have been observed at lower doses not toxic to development. Furthermore, the use of the i.p. route for this type of study, particularly within the context of occupational exposure, is of very limited value and there was no convincing evidence of a greater than additive effect. Overall, therefore, although some possible additive effects were seen in this study no useful conclusions regarding their significance for the occupational setting can be drawn.

HUMAN STUDIES

The human studies reviewed below relate to effects on auditory function of noise in combination with chemical exposures. The studies are broadly categorised into those providing information on interactive effects with solvents and other agents, which may also include some solvent exposures. Many of the studies are insufficient for determining any interactive effect between noise and chemical agents on hearing, although as relevant human studies are limited they have been included for completeness.

Solvents and noise

An investigation of four cases where sensinoneural hearing loss (SNHL) was greater than predicted from past noise exposure identified paint-related solvent exposure in all cases, three of whom where shipyard paint sprayers (Barregård and Axelsson, 1984). A follow-on investigation of audiological data from 30 shipyard paint sprayers aged 22–64 years (mean age 42 years) found no cases of SNHL that could not be adequately explained by noise exposure alone. The lack of reference population data, small case numbers and crude exposure measurement mean that this study is of little use in determining the combined effects of noise and solvent exposure on hearing.

Workers simultaneously exposed to noise and carbon disulphide were investigated in a study of 205 workers from a Brazilian viscose rayon factory (Morata, 1989). Continuous noise levels in the factory were in the range 86–89 dB(A) and atmospheric carbon disulphide concentration was measured at 90 mg m$^{-3}$. The workers were male, aged 18–60 years and reported no previous exposure to noise or carbon disulphide prior to work in the factory. Hearing loss within the cohort was classified into grades of severity using pure tone audiometry (PTA) (Table 1).

The study reported a strong association between duration of combined exposure and hearing loss (grades I–IV) that was not related to presbyacusis. Comparison
Table 1. Classification of hearing loss in a Brazilian viscose rayon factory (Morata, 1989)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Average threshold at 0.5, 1, 2 kHz (dB)</th>
<th>Pure-tone threshold of better ear in 3-8 kHz range (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0-25</td>
<td>0-25</td>
</tr>
<tr>
<td>I</td>
<td>0-25</td>
<td>30-40</td>
</tr>
<tr>
<td>II</td>
<td>0-25</td>
<td>45-55</td>
</tr>
<tr>
<td>III</td>
<td>0-25</td>
<td>60-</td>
</tr>
<tr>
<td>IV</td>
<td>&gt;25</td>
<td>—</td>
</tr>
<tr>
<td>NOHL*</td>
<td>Those without characteristic audiogram of NIHL*</td>
<td></td>
</tr>
</tbody>
</table>

*NOHL, non-occupational hearing loss; NIHL, noise-induced hearing loss.

with results from a noise-only exposed foundry population indicated that the overall prevalence of hearing loss was greater (60.1% vs 53.1%) as was the prevalence of the most severe grade (grade IV) of hearing loss (12.7% vs 3.5%) but no information indicating the similarity of these workers with regard to noise exposure, employment duration, age range or other important variables was provided. Overall therefore, no meaningful conclusions regarding an interaction between noise and carbon disulphide can be drawn from this study.

An audiological study of 190 workers from a Brazilian printing and paint manufacturing factory provides the best-designed study of those reviewed (Morata et al., 1993). Questionnaire responses on duration of employment, medical history and relevant past exposures were elicited and workers categorised into, unexposed, noise-only exposed, noise and toluene exposed, and solvent-only exposed groups (Table 2). Pure tone and immittance audiometry was performed on all subjects and

Table 2. Exposure groups from study of Morata et al. (1993)

<table>
<thead>
<tr>
<th>Exposure group</th>
<th>Number and employment location</th>
<th>Noise exposure</th>
<th>Solvent exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexposed workers</td>
<td>50 workers from the preparation division of a printing plant</td>
<td>Below 85 dB(A)</td>
<td>No solvent exposure</td>
</tr>
<tr>
<td>Noise only exposed workers</td>
<td>50 workers from the finishing and binding division of a printing plant</td>
<td>Historical and current levels in the range 88-97 dB(A)</td>
<td>No solvent exposure</td>
</tr>
<tr>
<td>Noise and toluene exposed workers</td>
<td>51 workers from the rotogravure printing division of a printing plant</td>
<td>Historical and current levels in the range 88-98 dB(A)</td>
<td>Historical TWA of toluene in air, 600 ppm in 1978 to 75 ppm in 1990. The peak level was 1860 ppm recorded in 1978</td>
</tr>
<tr>
<td>Solvent only exposed workers</td>
<td>39 workers from a paint manufacturing plant</td>
<td>Below 85 dB(A)</td>
<td>Current maximum exposure measurements in the paint filling division; toluene 70 ppm, xylene 40 ppm, benzene 2 ppm, methyl ethyl ketone 20 ppm, ethanol 16 ppm*</td>
</tr>
</tbody>
</table>

*Authors acknowledged that the reported measurements were insufficient due to restricted plant access and lack of historical data.
PTA results were classified according to the criteria previously outlined in Morata (1989) but replacing the NOHL with categories V-C, and V-U, representing conductive and unilateral hearing losses respectively. Analysis of variance indicated that the noise plus toluene exposed workers had significantly ($P < 0.001$) more grade I hearing loss than all the other groups. No significant differences were observed between groups for grades II, III, IV, V-C and V-U. In a logistic regression analysis utilising hearing loss (I–IV) as a dichotomous variable, employment duration and exposure group were the only two variables found significant enough to include in the model. Age was excluded because of its strong correlation with duration of employment and categories V-C and V-U were considered as normal hearing subjects for purposes of analysis. Estimates of relative risk from the model were 4.1 (95% CI = 1.4–12.2) for the noise-only group, 10.9 (95% CI = 4.1–28.9) for the noise and toluene group, and 5.0 (95% CI = 1.5–17.5) for the solvent-only group. Although the authors acknowledge that conductive and unilateral hearing losses (V-C and V-U groups) are probably not work-related, the assumption that they are normal hearing within the statistical model could have biased results. Grades V-C and V-U constituted 20, 22, 9.8 and 10.25% of the exposure groups, unexposed, noise-only, noise and toluene, and solvent-only, respectively, hence their inclusion in the regression analysis will have resulted in slightly increased relative risks for the noise and toluene, and solvent only groups. Despite this caveat it is still evident that the noise and toluene group represents the greatest risk for hearing loss. Little can be deduced concerning the interactions of these agents on hearing loss, however, because the chemical exposures between the noise and toluene, and solvent-only group are not comparable. Indeed the data suggest that the toluene exposures within the noise and toluene group were far in excess of those in the solvent-only group (see Table 2). Consequently the excess of hearing loss observed within the noise and toluene group may simply represent a dose–response effect related to increased toluene exposure. The study also reports that the noise plus toluene group had a significantly greater percentage of cases with abnormally rapid acoustic reflex decay, indicative of retrocochlear damage not normally associated with NIHL. It is plausible, however, that retrocochlear damage could reduce the effectiveness of the acoustic reflex and hence expose the cochlea to greater noise energy. Overall therefore no useful conclusions can be drawn from this study either.

Other chemical agents and noise

Two further cohort studies investigated hearing loss among workers exposed to noise and chemical agents. Berström and Nyström (1986) analysed audiograms from 319 employees of a Swedish timber processing firm. The results indicated a greater percentage of those employed in the chemicals division ($N = 47$) were classified as 10% or greater hearing disabled (23%) than in the sawmill ($N = 41$, hearing disabled = 5%), paper pulp production ($N = 123$, hearing disabled = 8%), maintenance ($N = 84$, hearing disabled = 6%), or other divisions ($N = 24$, hearing disabled = 13%). Ten per cent or greater hearing disablement in Sweden is designated if mean tone thresholds at 0.5, 1 and 2 kHz are 35 dB or more and thresholds at 3, 4 and 6 kHz are 50 dB or more. The criteria are also met if the mean threshold at 2 kHz is 40 dB or more and the previous stated criteria at 3, 4 and 6 kHz are met. Noise exposure within the firms was predominantly continuous and
reported to be lower in the chemicals division [mean 85 dB(A)] than either the paper pulp [mean 94 dB(A)] or sawmill [mean 99 dB(A)] divisions. The proportion of workers with initial hearing problems was similar in all divisions and the use of PPE was similar between the chemical and the paper and pulp divisions. Mobility between divisions within the company was reported to be low but no information on chemical exposures was reported and therefore no useful conclusions can be drawn from this study regarding possible interactive effects of noise and chemicals on hearing.

A study of 1020 male power plant workers showed a small non-significant increase in hearing loss among those exposed to noise and ototoxic agents \( N = 145 \), mean age = 44.1 years) compared to noise-only exposed workers \( N = 609 \), mean age = 43.5 years). Both groups were reported as having comparable noise exposures, although no specific details of the chemical exposures were reported (Irion and Lazarus, 1988). Again this lack of exposure information precludes drawing conclusions regarding the interactive effects of noise and chemicals on hearing.

**DISCUSSION**

The studies which have investigated the potential for noise and chemical interactions are very limited. There are only a few human studies investigating auditory function and because of various deficiencies, not least of which is the lack of comparative exposures between groups, no meaningful conclusions can be drawn from them.

In animals, the most useful information is from those studies of effects on auditory function. Data from such studies suggest that at relatively high ototoxic levels of toluene and noise, an interaction can be seen which can be at least additive and, depending upon the sequence of delivery, possibly greater in terms of impairment of auditory function. Unfortunately, there is no indication of whether or not such effects might occur at lower levels of exposure to both agents and no information on concomitant exposures. Consequently, it is not clear whether or not exposure–response relationships might vary at such lower exposure levels, which are of most relevance for the occupational setting.

Other endpoints have been studied in animals. Although there have been some suggestions of possible interactions between noise and some substances on the heart and development, the data available must be treated as of limited value and at best only suggestive of an effect. By contrast, the study by Ray et al. (1992) did provide some interesting results and some indications for an interaction between noise and 1,3-DNB. Unfortunately, this study suffers from some of the drawbacks of those performed on auditory impairment, not least of which is the use of toxic doses by parenteral routes of exposure. Consequently, it is again not possible to draw any conclusions regarding the effects that might or might not be observed at lower, nontoxic levels.

Overall, therefore, it is concluded that the data currently available indicate that at high levels of exposure, which in themselves are capable of tissue insult, interactions between noise and hazardous substances may occur. The information currently available, however, does not allow any conclusions to be drawn with respect to lower, more occupationally relevant, levels of exposure.
REFERENCES


