

**“Ototoxicity – a new challenge in the prevention of hearing damage?”****4 - 5 July 2006, BGA Hennef**

The term “ototoxicity” refers to the damaging effect of certain substances on the hearing, vestibular organ but also the seventh cranial nerve. In the clinical field, there are a number of drugs that have ototoxic side-effects – certain antibiotics (aminoglycoside), cytostatic agents (cis-platinum), loop diuretics but also salicylates (aspirin) and quinine. To a large extent, their mechanisms of action within the inner ear are known. The main area to come under attack is the organ of Corti with its hair cells and the adjacent tissue. The ototoxic side-effects of such drugs can be avoided by means of targeted dosage, coupled with monitoring of the inner-ear function.

Some hazardous substances are also known to have ototoxic effects though only a fraction of the knowledge required for a toxicological risk assessment is available. The following list shows substances with ototoxic potential that play an important role in the world of work:

Arsenic	Cadmium	Carbon disulphide
Carbon monoxide	Cyanide	Ethyl benzene
Lead	Mercury	n-heptane
n-hexane	n-propylbenzene	Styrene
Toluene	Trichloroethylene	Xylene

Although there are noisy workplaces in the chemical-manufacturing industry, relevant exposure to potentially ototoxic hazardous substances is not likely as a rule. To date, the regular hearing tests have not identified any ototoxic effects without their having been exposure to noise.

In the metal industry, where there are a considerable number of workplaces in noise zones, a wide range of ototoxic industrial chemicals are used. A preliminary risk analysis in work areas with this type of combined exposure identified the activities in which the occupational exposure limits for specific substances were adhered or, in some cases, exceeded. This information can be used to derive risk groups and to develop targeted protection measures.

The construction industry also uses potentially ototoxic substances and is no stranger to noisy workplaces. However, the data on audiometric findings and health screenings for persons exposed to specific hazardous substances do not give any clear indication of the way in which ototoxic industrial chemicals influence the hearing.

In the period from 1993 to 2002, the Berufsgenossenschaft (“BG”) institution for statutory accident insurance and prevention in the printing and paper-processing industry conducted a field study on the subject of toluene in gravure printing works. The study specifically examined the issue of ototoxic effects combined with noise and also recorded exposure levels extremely meticulously. It did not find any toluene-induced reduction of the hearing threshold, nor was there any evidence of hearing damage being intensified due to interaction between noise and toluene. It can be assumed that there is no ototoxic effect if the limit value of 50 ppm is adhered to.

In addition to measurement data for sound pressure levels and concentrations of airborne substances, the MEGA exposure database (for hazardous substances) and the OMEGA exposure database (for noise), located centrally at the BG Institute for Occupational Safety and Health (BGIA), provide breakdowns of data for specific sectors, areas of work and jobs. By pooling the data, it is possible to determine which groups might face a higher risk due to combined exposure.

The effects of occupational exposure to noise and industrial chemicals was the topic of the multinational EU research project “NoiseChem”. Based on animal experiments and epidemiological studies, it concluded that occupational exposure to organic solvents meant a higher probability of hearing loss developing. The risk posed by combined exposure is

significantly higher than exposure to noise or ototoxic industrial chemicals alone. Furthermore, the current limit values might not provide adequate protection. There is evidence that ototoxic effects on balance could be early indicators of neurotoxicity.

The Federal Institute for Occupational Safety and Health (BAuA) examined the literature on ototoxicity of solvents to check it for meaningfulness and comparability. The results showed that the findings of the epidemiological studies were inconsistent. There are however a great many indications that low concentrations of solvents can be ototoxic. Knowledge of this area is extremely scant due to numerous problems and weaknesses in the published studies.

With regard to the ototoxicity of styrene, the data available from animal experiments shows that damage to the hair cells is irreversible. It can be caused by relatively short, high levels of exposure. The mechanisms of action for noise and styrene are different. Below styrene's effect level, the effect of the noise does not increase. The level of styrene in the blood is the crucial internal dose. A limit value with an adequate safety factor has been derived as 50 ppm (current occupational exposure limit = 20). Uncontrolled exposure at laminating workstations can result in a risk of hearing damage.

A critical analysis of the results of major international working groups, particularly in relation to current conditions at workplaces, indicates significant weaknesses in the way that exposure is handled. For instance, the dose/response relationships have not yet been determined, nor has there been any discussion of effect levels. The effects of occupational exposure, some of which are considerable, relate to cohorts that were exposed both to noise and hazardous substances above the limit values. If the current limit values are adhered to, hearing losses of >25 dB are not very probable.

Concluding remarks

Ototoxic industrial chemicals comprise a variety of chemicals with different properties, of which the toxicology and potential risk for the hearing are not adequately known. In particular, there has not been much investigation of pathomechanisms, dose/response relationships or effect levels .

With regard to scientific findings relating to human beings, a point worthy of criticism is that a precise recording of exposure is problematic and there is hardly any knowledge about ototoxic effects in the lower exposure conditions at today's workplaces. There is also no reliable data on the possible combined effects of noise and ototoxic industrial chemicals.

The knowledge presently available is so incomplete that it is currently not possible to determine with the necessary accuracy whether the chemicals suspected of posing a risk do constitute substantial risks in the world of work and, if so, which chemicals cause the risks and under which working conditions risks might occur.

During the panel discussion, the participants agreed the following conclusions regarding the current workplace situation:

- 1) If the current limit values are adhered to, the probability of significant hearing loss is low.
- 2) There can be a higher risk in activities involving ototoxic industrial chemicals if the limit values are exceeded.
- 3) Noise is the highest risk factor for hearing damage. Ototoxic effects are of a similar proportion to those caused by other confounders, such as cigarette smoke or a genetically determined heightened sensitivity. Measures to combat noise-induced hearing loss continue to have top priority.

A position paper by the Committee for Occupational Medicine of the DGUV (German Statutory Accident Insurance) sets out recommendations for future practice on the basis of these conclusions.