TOXICITY AND CARCINOGENIC RISK AFTER LONG-TERM INHALATION OF Cd-COMPOUNDS IN WISTAR-RATS.

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INTRODUCTION
Earlier studies showed, that inhaled CdCl₂ induced primary lung tumors in Wistar rats (1,2). Also an increased mortality from respiratory cancer in workers exposed to cadmium has recently been reported (3). Furthermore an overview was given concerning airborne cadmium and carcinogenesis of the respiratory tract (4).

MATERIALS AND METHODS
This long-term inhalation study with male and female Wistar rats was designed to describe the toxicity and the carcinogenicity from 4 different Cd-compounds, namely Cd-chloride, Cd-oxide in the two forms, dust and fume, Cd-sulfate, Cd-sulfide and a combination of Cd-oxide/Zn-oxide. The planned exposure time towards the different Cd-aerosols was either 22 hours per day for 7 days per week and 18 months or in single cases for 40 hours a week and 6 months. The animals were exposed in horizontal flow inhalation chambers of 225 l volume. The aerosol-flow was 80 liters per minute. Each chamber contained two stainless steel wire mesh cages with 10 rats. The Cd-aerosols were produced by a reliable technique from earlier and new experiments (5). The CdCl₂, CdSO₄ and CdS aerosols were generated by jet nebulizers. The CdO dust aerosol was produced from a Cd-acetate solution and pyrolysis at 750 °C in a tube furnace and the Cd-fume aerosol by an electric arc generator. The particle size distributions were measured with a spiral centrifuge and the Cd-concentrations were determined by AAS (6, 7). The particle sizes ranged between 0.2-0.5 μm mass median aerodynamic diameter and the particles were thus respirable for rats.

RESULTS
In the literature no results were available on a long-term inhalation toxicity of Cd-compounds other than our own two experiments with CdCl₂ on rats. Because of lower water solubilities and expected lower toxicities we chose relatively high aerosol concentration for CdSO₄, CdS and CdO (8, 9). In some cases the chosen aerosol concentrations were too toxic. For instance the inhalation period with CdSO₄ at a concentration of 90 μg Cd/m³ was finished for male rats after an exposure time of 13.5 months whereas the inhalation period for the female rats was 18 months. Thus, we found also a difference in the mortality between male and female animals (10). In case of CdS the aerosol concentrations of 270, 810 and 2430 μg Cd/m³ had toxic effects, too. The inhalation period was stopped for 270 μg/m³ Cd after 15.5 months, for 810 μg/m³ after 6.8 months for male rats and after 9.7 months for female rats. For the highest concentration the exposure period was only about 3.5 months till the mortality rate was more than 25%. Therefore we exposed 20 male and 20 female rats to the lower concentration of 270 μg Cd/m³ for only 40 hours a week and 6 months.
CdO exists in two different forms as dust and fume. In our study we included both forms. The surface area of Cd-fume particles is greater than those of Cd-dust.

Therefore we assumed that Cd-fume may have a higher bioavailability and also a higher toxicity, but the present results do not support such assumptions.

Zinc is known to protect against the effects of Cd (11, 12). In two groups the rats were fed with a low-zinc diet.

In comparison to other groups exposed to the same Cd concentrations of 30 μg/m³ but without zinc diet, the mortality appeared to be higher. The protective effect of zinc can be demonstrated from the exposure to combinations of Cd- and Zn-aerosols.

Remarkable results were found from the gross necropsy. In all groups, not in the controls, we found a lot of lung nodules macroscopically; these were confirmed by histopathological examinations.

CONCLUSION AND SUMMARY

Based on the fact that this study includes the inhalation of water soluble and insoluble Cd-compounds, the toxicity must be considered under the aspect of bioavailability which includes the concept of solubility. This concept also includes the importance of lung-clearance and phagocytic activity of the macrophages (13, 14). With regard to the carcinogenicity, we must conclude that all different compounds of Cd possess carcinogenic potencies.

In all Cd exposed groups the same kind of lung tumors were found namely adenomas, adenocarcinomas, squamous cell carcinomas and mixed forms (Tab. 1). Therefore the carcinogenicity of inhaled Cd-aerosols must be related to the Cd ion.

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