HEALTH/BIOLOGICAL EFFECTS

Histopathological and biochemical changes in lung tissues of rats following administration of fluoride over several generations

The possible effects of multigenerational administration of sodium fluoride (NaF) via drinking water on lung tissue morphology and biochemistry and body and lung weight were investigated in second-generation adult male rats. For this purpose we selected 45 Albino adult Wistar rats in nine cages, each of which consisted of four females and one male. Twenty-eight pregnant rats were selected for the experiment, divided into four groups of seven rats and given 1 (control group), 10, 50, and 100 mg NaF/L in drinking water during the gestation period.

After gestation the rats had a total of 165 pups. The mothers received fluoridated water during the lactation period and the offspring of the first generation had access to fluoridated water during the suckling period (21 days) and after the weaning period (30 days) until they became mature and at the start of the second part of the experiment. During this time 23 pups died and 79 female and 63 male first-generation rats survived. These first-generation rats were then used to obtain the second-generation offspring in the same manner as before, which were subjected to the same treatments.

At the end of 6 months the rats were sacrificed and autopsied. Serum fluoride levels and the activities of principal antioxidant enzymes were detected in lung tissue samples taken from all groups. In addition, the lung tissues were submitted for histopathological examination. Histological findings showed alveolar congestion, alveolar cell hyperplasia and necrosis, prominent alveolar septal vessels, epithelial desquamation, and macrophages in the alveolar spaces in the experimental groups. Additionally, there were inflammatory infiltrations in peribronchial, perivascular, intraparenchymal, and respiratory tract lumen; intraparenchymal hyperemic vessels; respiratory epithelial desquamation and proliferation; intraparenchymal thick walled vessels; parenchymal fibrosis; bronchiolitis; and pneumonic and focal emphysematous areas. Furthermore, the lung parenchyma was observed to have a distorted appearance with loss of alveolar architecture. These histopathological findings were more pronounced in the rats consuming 50 and 100 mg NaF/L. No significant histopathological changes were observed in the rats of the control group.

The increased activities of superoxide dismutase (SOD) and reduced glutathione peroxidase (GSH-Px) and the decreased activity of catalase (CAT) in the lung tissues with 10 mg NaF/L might indicate activation of the antioxidant
defense mechanism. The decrease in SOD, GSH-Px, and CAT activities with 50 and 100 mg NaF/L and the increase in thiobarbituric acid-reactive substance levels might be related to oxidative damage that occurred in the lung. This multigenerational evaluation of the long-term effect of different doses of fluoride intake through drinking water on lung damage shows that the lung tissues were damaged, there was emphysema and inflammation of lung parenchyma associated with loss of alveolar architecture, and the degree of lung damage seemed to correlate with the increased dosage of fluoride. A similar relationship was observed between the degree of lung damage, body and lung weight, and serum fluoride levels according to the fluoride dose. Therefore, these results contribute to a better understanding of chronic fluoride toxicity in lung tissue of second-generation rats, especially via drinking water, and the biochemical findings were in agreement with histological observations. In addition, increased fluoride concentration did not affect reproduction or the number of pups dying, but the body weight and lung weight ratios were affected by the high dose of fluoride in a dose-related pattern.

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Keywords: Alveolar effects; Biochemistry; Catalase; Fluoride toxicity; Glutathione peroxidase; Histopathology; Inflammatory effects; Lung damage; Rats; Multigenerational fluoride effects; Serum fluoride; Sodium fluoride; Superoxide dismutase,

Effects of fluoride and mercury on human cytokine response in vitro

RATIONALE: Over the past 50 years individuals in westernized societies have been increasingly exposed to mercury (e.g. through contaminated fish and dental amalgam) and fluoride (e.g. through drinking water, toothpaste and gels). Given the increasing incidence of allergic diseases and the known immunomodulatory effects of these agents, we investigated their potential allergy-promoting activity. METHODS: Peripheral blood mononuclear cells (PBMC) from 4 individuals were cultured up to seven days in culture medium or in culture media containing Con A in the presence or absence of mercuric chloride (HgCl) or sodium fluoride (NaF). Supernatants were harvested on days 2, 4 and 6 and IL-4 and gamma-IFN concentrations were measured by ELISA. RESULTS: HgCl and NaF significantly suppressed Con A-induced gamma-IFN production. Maximum suppression of gamma-IFN production by HgCl occurred on day 6 (10.4% ± 9.4% of the Con A response) and by NaF on day 4 (8.3% ± 7.2%). In contrast, HgCl and NaF significantly increased
Con A-induced IL-4 production, with a maximum on day 4 (362.9% ± 365%) and day 2 (660.8% ± 894.72%), respectively. Neither NaF nor HgCl significantly altered cytokine production in unstimulated lymphocytes. CONCLUSIONS: HgCl and NaF seem to selectively suppress Th1 activity and stimulate Th2 cytokine production in vitro. Although preliminary, these findings suggest that human exposure to mercury or fluoride may be playing a role in the observed increased incidence of allergic diseases in the industrialized world.

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Keywords: Allergic diseases; Allergy-promoting activity of fluoride; Cytokine response; Human cytokine response, Mercury.

Fluoride content in bones of Adelie penguins and environmental media in Antarctica

Fluoride (F) distribution and its effects (fluorosis) were investigated in Antarctica. Droppings (L) excreta selected of aquatic birds, lake water, soil and moss (Polytrichum alpinum) showed a high F concentration. Although bones of Adelie penguin (Pygiscelis adeliae) and skua (Catharacta maccormicki) showed exceptionally very high F concentration in the range of 832 to 7187 mg/kg, their radiographs did not show any evidence of skeletal fluorosis. The possible reason and geochemical aspects of F in Antarctica region are discussed.

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Keywords: Adelie penguins; Antarctica; Excreta; Fluoride; Geochemistry; Skeletal fluorosis; Skua.

DENTAL EFFECTS

Effect of drinking water changes upon dental fluorosis

OBJECTIVE: To assess changes in prevalence and degree of dental fluorosis in individuals born before and after the introduction of water with 1.2 mg/L fluoride instead of water with 2.0 – 10.0 mg/L fluoride previously used in Da Li County in China. METHODS: The students (n = 291) were divided into 2
groups. Dental fluorosis was scored according to Dean's classification. The statistical analysis was performed by t-test and chi² tests. RESULTS: The prevalence of dental fluorosis was significantly lower in the group of the students drinking water from the new well (group 1) as compared to the group of the students drinking the old water (group 2), \( i.e., 48.8\% \) versus \( 87.2\% \) (\( p < 0.01 \)). The percentage of moderate to very severe fluorosis was \( 13.9\% \) and \( 0\% \) in group 1 as compared to \( 32.0\% \) and \( 8.8\% \) in group 2. The fluorosis community index (FCI), defined by Dean, in group 1 and 2 was medium (1.01) and marked (2.12), respectively. CONCLUSIONS: The results showed that: (1) The prevalence of dental fluorosis was significantly lowered by the new source of drinking water. (2) Drinking water, even with 1.2 mg/L fluoride, may cause dental fluorosis during the period of tooth mineralization.

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Keywords: China; Dental fluorosis; Fluoride water.

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**FIRST ANNOUNCEMENT: XXVITH CONFERENCE OF THE INTERNATIONAL SOCIETY FOR FLUORIDE RESEARCH**

The XXVIth Conference of the International Society for Fluoride Research will be held at the Dorint Sofitel Pallas Wiesbaden hotel in Wiesbaden, Germany, September 26–29, 2005. The meeting will be hosted by Professor Jörg Spitz, Department of Nuclear Medicine, Wiesbaden, Germany.

Wiesbaden, population 270 000 and capital of the German Federal State of Hesse, is situated in the geographical centre of Germany on the Rhine river about 30 km from Frankfurt. The journey from Frankfurt Airport, with two international terminals, to Wiesbaden takes 35 minutes by commuter train.

Hildebrand Diehl, the Lord Mayor of Wiesbaden extends a welcome, in English, to visitors to his city at http://english.wiesbaden.de/index.php. The website has sections on the city, living in Wiesbaden, the market place, congresses and tourism, business, and services. The numerous photographs enable one, with the help of the appropriate plug-in, to go on a virtual tour of the city.

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