ABSTRACTS

BIOLOGICAL EFFECTS IN ANIMALS
DECREASED IN VITRO FERTILITY IN MALE RATS EXPOSED TO FLUORIDE-INDUCED OXIDATIVE STRESS DAMAGE AND MITOCHONDRIAL TRANSMEMBRANE POTENTIAL LOSS

Fluorosis, which often caused by contamination of drinking water with inorganic fluoride, is a public health problem in many areas around the world. The aim of this study was to evaluate the effect of environmentally relevant dosages of fluoride on the in vitro fertilization (IVF) capacity of spermatozoa, and its relationship to spermatozoa mitochondrial transmembrane potential (ΔΨm). Male Wistar rats were exposed to fluoride-containing water providing 5 mg fluoride ion/kg body mass/24 hr or to deionized water (control group) orally for 8 weeks. Several spermatozoa parameters in treated and untreated rats were evaluated: i) standard quality analysis; ii) superoxide dismutase (SOD) activity; iii) generation of superoxide anion (O₂⁻); iv) extent of lipid peroxidation; v) ultrastructure of spermatozoa using transmission electron microscopy; vi) mitochondrial transmembrane potential (ΔΨm); vii) acrosome reaction; and viii) IVF capability. Spermatozoa from fluoride-treated rats exhibited a significant 33% decrease in SOD activity, accompanied by a significant 40% increase in the generation of O₂⁻, a significant 33% decrease in ΔΨm, and a significant 50% increase in lipid peroxidation relative to spermatozoa from the control group. Consistent with these findings were alterations of the plasma membrane of spermatozoa from fluoride-treated rats. In addition, the percentage of fluoride-treated spermatozoa capable of undergoing the acrosome reaction was decreased relative to control spermatozoa (34 vs. 55%), while the percentage of fluoride-treated spermatozoa capable of oocyte fertilization was also significantly lower than in the control group (13 vs. 71%). These observations suggest that subchronic exposure to fluoride causes oxidative stress damage and loss of mitochondrial transmembrane potential, resulting in reduced fertility.

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NEUROTOXIC EFFECTS
IN UTERO METHANESULFONYL FLUORIDE DIFFERENTIALLY AFFECTS LEARNING AND MAZE PERFORMANCE IN THE ABSENCE OF LONG-LASTING CHOLINERGIC CHANGES IN THE ADULT RAT

There is increasing evidence that acetylcholinesterase (AChE) may have various specific developmental roles in brain development. Nevertheless, specific effects of AChE inhibition during early brain development have not been adequately investigated. Therefore, methanesulfonyl fluoride (MSF), an irreversible AChE inhibitor that shows high selectivity for the central nervous system (CNS) was used to produce AChE inhibition in utero to study subsequent adult behaviors, sleep, and cholinergic markers. Rats exposed to MSF in utero showed a deficit in spatial learning tasks using appetitive motivation but, surprisingly, they performed equally well or better than controls when aversive motivation was used. One hypothesis was that MSF treatment in utero affected the response to stress. Tests of anxiety, however, showed no differences in basal levels of anxiety. On the other hand, studies of sleep behavior indicated a higher level of REM sleep which is only seen during the light phase of male rats exposed to MSF in utero as compared to controls. No differences in cholinergic markers in the brains of adults were found except that females exposed to MSF in utero had a higher level of ChAT (choline acetyltransferase) activity in the synaptosomal fraction of the hippocampus. Even so, whether cholinergic alterations accompany the in utero MSF exposure remains to be detailed. The failure to find widespread changes in cholinergic markers in the adult brains suggests changes in behaviors should be further investigated by testing the participation of postsynaptic mechanisms, measuring of cholinergic markers during earlier development periods and the possible participation of other neurotransmitter systems to reveal more clearly the role of the cholinergic system following in utero MSF exposure.

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OXIDATIVE STRESS MIGHT BE A MECHANISM CONNECTED WITH THE DECREASED
α7 NICOTINIC RECEPTOR INFLUENCED BY HIGH CONCENTRATION OF
FLUORIDE IN SH-SY5Y NEUROBLASTOMA CELLS

The possible mechanism concerning decreased α7 nicotinic acetylcholine receptor (α7 nAChR) influenced by fluorosis was investigated. SH-SY5Y cells were exposed to fluoride in the range of 0.05–5 mM [0.95–95 mg/L], or ferrous iron (1–100 µM) [0.056–5.6 mg/L], a free radical inducer. The levels of α7 nAChR expression, lipid peroxidation, and protein oxidation were determined. The results showed that high concentrations of both fluoride and ferrous iron induced increased levels of lipid peroxidation and protein oxidation in SH-SY5Y cells in a concentration-dependent manner. In addition, inhibition of α7 nAChR at protein level was observed in the cells exposed to the higher concentrations of fluoride or ferrous iron. Furthermore, a lower B_max value in [125I]α-bungarotoxin binding sites was found in the cells treated with the high concentration of fluoride. Interestingly, antioxidants (vitamin E and glutathione) were observed to attenuate the inhibition of the receptor induced by fluoride. These findings suggest that oxidative stress resulting from fluorosis might directly induce a deficit of α7 nAChR.

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[Editor’s note: The units for the fluoride concentrations in the above report have been corrected from µM, as originally published, to mM after correspondence with ZZ Guan. See also Abstract 25 by these authors for their presentation of the related features of this work at the XXVIIth Conference of the ISFR published in Fluoride 2007;40(4):269.]

CORRECTION

The volume number in the headers on pages 10–96 of Fluoride 2008;41(1) should be 41(1) rather than 40(1). My apologies for the error and I will endeavour to check more carefully in future issues.

Bruce Spittle
Managing Editor, Fluoride