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 ScienceDirect

Experimental and Toxicologic Pathology 61 (2009) 133–136

EXPERIMENTAL
AND
TOXICOLOGIC
PATHOLOGY

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SHORT COMMUNICATION

Gender-selective toxicity of thimerosal[☆]

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Received 20 March 2008; accepted 22 July 2008

Abstract

A recent report shows a correlation of the historical use of thimerosal in therapeutic immunizations with the subsequent development of autism; however, this association remains controversial. Autism occurs approximately four times more frequently in males compared to females; thus, studies of thimerosal toxicity should take into consideration gender-selective effects. The present study was originally undertaken to determine the maximum tolerated dose (MTD) of thimerosal in male and female CD1 mice. However, during the limited MTD studies, it became apparent that thimerosal has a differential MTD that depends on whether the mouse is male or female. At doses of 38.4–76.8 mg/kg using 10% DMSO as diluent, seven of seven male mice compared to zero of seven female mice tested succumbed to thimerosal. Although the thimerosal levels used were very high, as we were originally only trying to determine MTD, it was completely unexpected to observe a difference of the MTD between male and female mice. Thus, our studies, although not directly addressing the controversy surrounding thimerosal and autism, and still preliminary due to small numbers of mice examined, provide, nevertheless, the first report of gender-selective toxicity of thimerosal and indicate that any future studies of thimerosal toxicity should take into consideration gender-specific differences.

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Keywords: Thimerosal; Thimerosal toxicity; Gender-selective toxicity; Maximum tolerated dose; Autism

Introduction

Thimerosal is an organic compound that contains mercury and has been used historically as a preservative in vaccines and pharmaceutical products. The breakdown product, ethylmercury, in thimerosal-preserved childhood vaccines has been suggested to be neurotoxic and to contribute to the etiology of neurodevelopmental disorders, including autism; however, this supposition is highly controversial (Mutter et al., 2005; Geier et al., 2007; Ng et al., 2007; Zareba et al., 2007; Thompson et al., 2007; Schechter and Grether, 2008). It has, however, been shown that mercury and thimerosal administration results in the decreased production of

[☆]*Ethical Statement:* All animal studies were performed under an approved animal use protocol (AUP) for the care and use of animals (mice) by Nuero-Technics, 2000 Ellesmere Road, Scarborough, Ontario, Canada. Nuero-Technics is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International and the Canadian Council on Animal Care. The study was conducted under the direction of Dr. Albert Licollari, DVM, Ph.D.

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