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Thimerosal Induces Toxic Reaction in Non-Sensitized Animals

Abstract

The effects of injection of thimerosal solution on nonsensitized animals was investigated. Intrafootpad injection of thimerosal solution in nonsensitized mice resulted in a swelling response which peaked 1 h after injection and lasted for more than 24 h. Histopathological examination showed that there were severe edema and infiltration of polymorphonuclear neutrophils at the site of injection. An increased vascular permeability was observed after cutaneous injection of thimerosal solution on the back of nonsensitized rats. Since mercuric chloride and methyl mercury induced severer reactions, and thiosalicylic acid had no effect, mercury contained in thimerosal would have caused the reactions observed in this study. These results suggest that part of these hypersensitivity reactions against thimerosal observed among patients were possibly induced by the toxic effect of thimerosal. Therefore, thimerosal contained as a preservative in vaccine may augment the side-effects of the vaccination.

Key Words

Footpad swelling
Histamine release
Mast cells
Thimerosal, vascular permeability

Introduction

Thimerosal (merthiolate, mercurothiolate), a compound of organic mercury and thiosalicylic acid, has been widely used as a preservative in vaccine, eye drops, and contact lens care solutions. Recently, many investigators [1–4] have reported that thimerosal participates in the allergic reactions such as local swelling, and that immediate-type reactions occur after vaccination. Most of these authors have postulated that thimerosal might act as an allergen after repeated sensitization. A variety of immunopathological effects by mercury compounds are also reported, such as autoantibody formation [5], allergic contact dermatitis [6], alterations of serum immunoglobulin concentrations [7], and autoimmune glomerulonephritis [8], in both animal models [5–7] and in man [8].

In our study, thimerosal elicited an immediate reaction at the site of injection in nonsensitized animals. The reaction is commonly observed after injection of thimerosal and two other mercury compounds, mercuric chloride and methyl mercury, in naive mice and rats with different genetic background. In this report, the toxic reactions observed in nonsensitized animals after injection of thimerosal are demonstrated and the possible mechanism of the induction of toxic reactions after injection with thimerosal is discussed.

Materials and Methods

Animals

Female BALB/c CrSlc, C57BL/6 CrSlc, and C3H/He Slc mice (6 weeks of age) and female Sprague-Dawley (Slc:SD) rats (8 weeks of age) were purchased from the Shizuoka Laboratory Animals Center, Shizuoka, Japan.