

*Preliminary Communication*

## Mercury exposure in protein A immunoadsorption

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### Abstract

**Background.** Immunoadsorption is increasingly used to treat antibody-mediated autoimmune diseases. To prevent microbial growth during storage, reusable protein A-Sepharose gel columns are primed with ethyl mercury thiosalicylate (thiomersal, 0.1% solution) and rinsed with phosphate buffer before use. In this study, we tested the hypothesis of systemic mercury exposure in protein A immunoadsorption.

**Methods.** Whole blood mercury levels were measured by atomic absorption spectroscopy before and after protein A immunoadsorption (11 patients, 26 treatments), anti-IgG immunoadsorption (eight patients, 13 treatments) and LDL apheresis (DALI and Therasorb systems; nine patients, 14 treatments).

**Results.** Patients treated with protein A immunoadsorption had significantly elevated baseline mercury levels compared with the other groups, which were not different from healthy controls. Following protein A immunoadsorption, mercury levels increased from  $5.9 \pm 1.4 \mu\text{g/l}$  (mean  $\pm$  SEM, normal,  $< 5 \mu\text{g/l}$ ) to  $32.3 \pm 5.7 \mu\text{g/l}$ ,  $P < 0.001$ ). In one intensively treated patient, acute neurological toxicity developed at a mercury level of  $107 \mu\text{g/l}$ . Symptoms abated slowly and did not recur after switching to a thiomersal-free system and chelation therapy. No mercury release to patients occurred in anti-IgG immunoadsorption or LDL apheresis treatments.

**Conclusion.** This preliminary report suggests that protein A immunoadsorption columns primed with thiomersal during storage may cause a sustained increase of systemic mercury concentrations, which exceed current safety recommendations in a proportion of patients. Considering the potential for mercury-induced toxicity, every effort should be undertaken to reduce systemic mercury exposure, either by adding chelators to the rinsing solution or ideally by replacement of thiomersal.

**Keywords:** immunoadsorption; mercury; thiomersal; toxicity; tremor

### Introduction

Immunoadsorption is a novel adsorption technique for semi-selective extracorporeal removal of circulating autoantibodies in disorders such as recurrent kidney graft rejection due to HLA hypersensitization [1], renal autoimmune disorders [2], haemophilia with inhibitors to factor VIII or IX [3], congestive heart failure [4] and neurological autoimmune diseases including myasthenia gravis and Guillain-Barre syndrome [5]. Current apheresis systems employ reusable columns designed for long-term storage (20–50 treatment sessions). To prevent microbial growth, staphylococcal protein A-Sepharose (PA) columns are primed with ethyl mercury thiosalicylic acid (buffered thiomersal 0.1% solution) during storage and rinsed with phosphate buffer before use [6]. In contrast, anti-IgG immunoadsorbents are stored after priming with phosphate-buffered saline (PBS)–sodium azide [7].

The long half-life of ethylmercury could theoretically result in accumulation and toxicity during chronic application, as discussed in the context of thiomersal-containing vaccines [8]. Following recommendations from the US Public Health Service and the American Academy of Pediatrics, thiomersal has been largely replaced in infant vaccines, although no clear evidence of potential health and development problems has been demonstrated so far [8]. Organic mercury toxicity affects mainly the central nervous system (CNS), with symptoms such as lethargy, loss of appetite, weight loss, tremor, memory loss, sleep disturbance, emotional lability and confusion [9]. Furthermore, mercury may cause significant damage to the haematopoietic and renal system [9]. Since PA immunoadsorption has been used successfully for several years at our department, the lack of long-term safety data led us to investigate the hypothesis of a thiomersal-related mercury release during apheresis.

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