

Correspondence and Replies

ASIA, chronic fatigue syndrome, and selective low dose neurotoxicity of aluminum adjuvants



To the Editor:

In their recent paper, Ameratunga et al¹ have considered the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA) to be inexistent. We have questioned long-term aluminum adjuvants safety since the understanding that some adult vaccine recipients cannot clear out aluminum hydroxide particles from their immune cells as assessed by very long persistence of a lesion called macrophagic myofasciitis (MMF) at the site of previous immunizations.² These patients typically present with diffuse myalgias, chronic fatigue, characteristic cognitive dysfunction, and positron emission tomography with fluorodesoxyglucose scanner abnormalities,³ forming a syndrome used as a paradigm of ASIA by Prof. Y. Shoenfeld.⁴ On the basis of a thorough investigation of 348 symptomatic patients with MMF and recent experimental findings from our lab, we would like to raise some important points.

- (1) According to Ameratunga et al,¹ diagnostic criteria for ASIA are too large and vague. This is not very surprising because delineation of ASIA primarily aimed to encompass and conceptually unify a wide spectrum of medical conditions observed in individuals exposed to immunologic adjuvants. These criteria now require validation/refinement by a panel of international experts. We emphasize that the subset of patients with MMF typically meet the validated Oxford 1991 and CDC 1994 international criteria for chronic fatigue syndrome.⁵
- (2) Much less convincing is what Ameratunga et al¹ present as “strong human data refuting the existence of ASIA caused by aluminum-containing vaccine adjuvants.” First, they report on a series of 28 patients with lupus who had no exacerbations after hepatitis B immunization. What can be concluded from this small series? None of the patients with MMF followed in our center or described in the literature had systemic lupus erythematosus, and the chronic fatigue syndrome they suffer from is not an autoimmune disease. Second, they refer to a Danish survey showing decreased, instead of increased, incidence of autoimmune disease in patients undergoing allergen-specific immunotherapy with aluminum-containing compounds. Again, chronic fatigue syndrome is not an autoimmune disease and, therefore, was not included in the list of 16 autoimmune diseases considered in the study they refer to. Moreover, Ameratunga et al pointed out that “100 times the dose of aluminum contained in 3 hepatitis vaccinations” was intradermally injected to the patients. This is the exact contrary of a massive argument against aluminum hydroxide toxicity because the dose-response curve of aluminum hydroxide neurotoxicity indicates that low doses of the adjuvant are selectively associated with aluminum translocation to brain and neurobehavioral changes 6 months after injections in mice.⁶ In contrast, the highest doses, forming large adjuvant aggregates remaining trapped at the periphery, were nontoxic. Thus the dose does not “make the poison” in case of aluminum adjuvants. In addition, whether or not systemic diffusion of

particles may be significantly influenced by the route of administration, for example, intramuscular versus intradermal injections, is currently unknown.

In conclusion, assertions based on indirect arguments cannot satisfactorily replace epidemiological studies specifically designed to assess aluminum-containing vaccines’ long-term safety that are notoriously lacking in both adults and children.⁷

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Refutation is a strong word for partial evidence in ASIA



To the Editor:

Refutation is a theoretical concept in Philosophy of Science that means rejection of a scientific hypothesis after negative evidence in a definitive test. In their article, Ameratunga et al¹ stated that evidence refutes the existence of autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA). However, their data are only useful against support of the causation of ASIA by vaccine adjuvants containing aluminum. Patients receiving aluminum-containing allergen preparations were shown to have a lower incidence of autoimmune disease. Those results contrast with the high incidence of autoimmune diseases reported in a cohort of sick building

syndrome (SBS) before the date when the authors supposed first description in 2011.² Clinical and statistical analysis showed a coincidental onset of autoimmune processes triggered by the sick building and a parallel absence of definitive score for SBS in people without immune problems.^{2,3} The discussion was raised to the arena in response to the statement that ASIA presents without autoantibodies,⁴ which had to be admitted. Although overlooked, evidence from those studies allows us to support that SBS, and possibly another ASIA, translates an immune susceptibility for autoimmune diseases or other immune phenomena⁵ triggered by adjuvants or environmental components. Problems with ASIA, as SBS, are the oddity of their presentation, which defies the medical explanation. For example, SBS investigations have focused on the effects of the buildings, but clinical individual assessment has been neglected and surveys are usually run by no experts. In conclusion, refutation of existence of ASIA is a strong statement without enough base.

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Reply to Crépeaux et al and Blasco



To the Editor:

We thank Crépeaux et al¹ and Blasco² for their responses to our article refuting the existence of the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA).³

The evidence for the existence of ASIA is based on the diagnostic criteria published by its creators (Fig 1).⁴ As shown in our review, the symptoms of ASIA such as pyrexia, arthralgias, and irritable bowel syndrome are nonspecific and are commonly experienced in the community. The criteria for ASIA could include the entire community. This alone refutes the existence of such a syndrome as a clinically useful diagnosis.

The second scientific question we addressed was whether aluminum salts cause autoimmunity. The causes of most

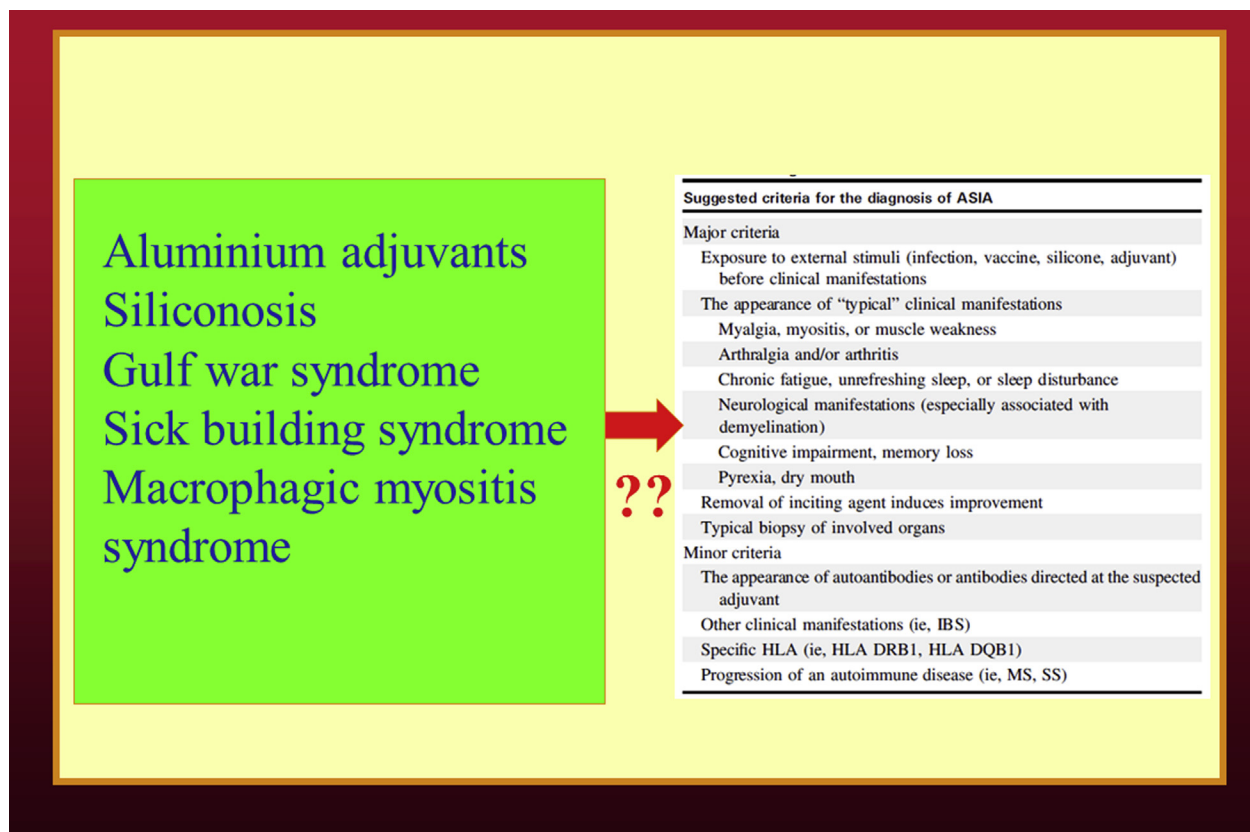


FIGURE 1. Causes and manifestations of the ASIA syndrome. A range of conditions are stated to cause a large number of nonspecific symptoms. The symbol ?? represents the unproven link between the exposure (vaccine adjuvants, silicone, etc.) and outcomes (ASIA).

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