The immunobiology of aluminium adjuvants: how do they really work?

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Aluminium adjuvants potentiate the immune response, thereby ensuring the potency and efficacy of typically sparingly available antigen. Their concomitant critical importance in mass vaccination programmes may have prompted recent intense interest in understanding how they work and their safety. Progress in these areas is stymied, however, by a lack of accessible knowledge pertaining to the bioinorganic chemistry of aluminium adjuvants, and, consequently, the inappropriate application and interpretation of experimental models of their mode of action. The objective herein is, therefore, to identify the many ways that aluminium chemistry contributes to the wide and versatile armoury of its adjuvants, such that future research might be guided towards a fuller understanding of their role in human vaccinations.

Background

A recent spate of exciting and insightful research papers have, at long last, purported to explain the modus operandi of aluminium adjuvants (AlADJ) [1–7]. Unfortunately, the flurry of review papers that followed the new research have not reached consensus upon the aetiology of the biological activities of AlADJ [8–10]. Indeed close scrutiny of the new research suggests that an all too liberal application of Occam’s razor by scientists and journalists alike was pervasive in them reaching their conclusion that the immunologists’ ‘dirty little secret’ [11] had been revealed. Actually, the recent research, rather than explaining how AlADJ work, has opened the lid on a Pandora’s Box associated directly with the adjuvant [14–16], and some of this ‘free’ antigen may also be in a complex with aluminium. Injection of this vaccine ‘soup’ usually involves the dilution of ca 0.5 mg of total aluminium into the interstitial fluid at the injection site. The interstitial fluid composition similar to plasma, and to be rich in nutrients and metabolites related to tissue growth and function. In short, its composition is very different than that of a vaccine preparation away from the injection site it will be significantly influenced by its mixing with the vaccine. There will also be ingress of plasma and infiltration of blood cells from the disruption of capillaries as the direct result of the physical consequences of an injection. While there will be an immediate limited migration of some of the smaller or non-particulate forms of the vaccine preparation away from the injection site the