Lyme disease vaccination: safety first

In the Article by Nina Wressnigg and colleagues[1] and the related Comment by Paul Lantos[2] describing a novel Lyme vaccine, the authors attempt to avoid discussion of the side-effects of the previous Lyme vaccine, LYMErix (SmithKline Beecham, Pittsburgh, USA). This approach to safety issues bodes ill for the new Lyme vaccine candidate.

LYMErix was put on the market in 1998 and withdrawn by the manufacturer in 2002, ostensibly because of poor sales. However, the so-called poor sales were related to safety concerns raised in a class-action lawsuit by more than 400 patients who claimed that they developed Lyme-like symptoms after vaccination with LYMErix.[3,4] Subsequent studies showed that outer surface protein A (OspA), the antigenic component of *Borrelia burgdorferi* used to create both LYMErix and the new candidate vaccine, induced joint-reactive and nerve-reactive antibodies in animals and human beings vaccinated with the protein antigen.[3–6] Even more disturbing, other studies indicated that LYMErix induced reactivity against multiple target antigens that were never characterised, and these studies called into question the OspA specificity of the vaccine.[7,8] By withdrawing LYMErix when it did, the manufacturer avoided releasing phase 4 post-marketing data that probably would have shown increased side-effects related to the vaccine.[9] The data have never been disclosed, and this lack of disclosure has fostered persistent patient mistrust of Lyme vaccine manufacturers.

Wressnigg and colleagues provide minimum safety data about the new OspA-based Lyme vaccine, whereas Lantos glosses over the "largely unsubstantiated safety concerns" about LYMErix. Adoption of this view by Lyme vaccine manufacturers, regulators, and promoters has shaken patient confidence in Lyme vaccines despite the fact that this patient population is generally pro-vaccination.[10] Any new Lyme vaccine will need extensive safety testing, more transparency about side-effects, and improved patient communication on the part of the vaccine manufacturer to allay valid patient concerns about safety.[4,10] Let's hope that history does not repeat itself because Lyme vaccine manufacturers, regulators, and promoters once again underestimate or ignore justified patient concerns about Lyme vaccination risks.

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Authors' reply

We refute the assertion by Raphael Stricker and Lorraine Johnson that we avoided discussion of the side-effects of the previously licensed Lyme vaccine, LYMErix, in our report of a novel multivalent candidate vaccine against Lyme borreliosis.[1] In our introduction, we provide a full and balanced description of the hypothesised safety concerns associated with the monovalent outer surface protein A (OspA) vaccine LYMErix, and we present and discuss in detail the safety data generated in our phase 1/2 trial of the new multivalent vaccine.

Post-licensure investigations into the safety of LYMErix were undertaken by the Centers for Disease Control and Prevention and the US Food and Drug Administration, which took into account over 1·4 million distributed vaccine doses. These investigations did not detect any unexpected or unusual patterns of adverse events after administration of the monovalent OspA vaccine, other than hypersensitivity reactions, compared with adverse events seen in clinical trials.[2] A separate study concluded that treatment-resistant Lyme arthritis alleles were not found more commonly in people who developed arthritis after vaccination with LYMErix.[3]

The hypothesised relation between immunity to OspA and Lyme arthritis has been examined in detail, and a vaccine-induced immune response to OspA was not found to replicate the sequence of events needed in natural borrelia infection to induce antibiotic refractory Lyme arthritis.[4] Moreover, there are no data in Stricker and Johnson's cited publications that support the statement that "joint-reactive and nerve-reactive antibodies" are induced in human beings vaccinated