Febrile convulsions after 2010 seasonal trivalent influenza vaccine: implications for vaccine safety surveillance in Australia

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Passive surveillance cannot be relied on as the sole means of surveillance

On 22 April 2010, use of seasonal trivalent influenza vaccine in children aged 5 years and under was suspended across Australia, pending an investigation into an apparent increase in reports of adverse events following immunisation (AEFI).[1] This unprecedented halt to a national immunisation initiative followed Western Australia's decision to place a moratorium on the use of this vaccine in young children after observing a spike in emergency department presentations for high fever and febrile convulsions after vaccination.[2] A subsequent investigation by the Therapeutic Goods Administration indicated that febrile convulsions related to the vaccine were reported from all jurisdictions except the Northern Territory.[2] The apparent rate of febrile convulsions following vaccination was 5–9 per 1000 doses administered, about 50 times higher than that reported following measles–mumps–rubella vaccination.[2,3] A recent review, requested by the Minister for Health in WA, has highlighted significant deficiencies in AEFI surveillance.[4]

In Australia, the current mechanism for identifying AEFI nationally is passive surveillance. Passive surveillance relies on health providers and the public recognising and reporting suspected AEFI to state or federal health authorities. The constraints that are inherent to passive surveillance, including under-reporting and biased reporting, are compounded by the diverse approaches to surveillance that are employed throughout Australia, as illustrated by a fourfold difference in AEFI reporting rates per 100 000 population between jurisdictions.[5,6] Adding to concerns about variable sensitivity across the state systems is the inevitable delay in collection, aggregation and analysis of AEFI reports forwarded to the national authority.

A number of the issues evident during the response to the vaccine-associated reactions were recognised 5 years earlier during the National Vaccine Safety Workshop.[7] A clear set of recommendations for improving adverse event surveillance was identified at the time, but many of the recommendations have not been adequately addressed.

Robust postmarketing surveillance is vital for influenza vaccines because seasonal trivalent influenza vaccine does not require clinical trial data to demonstrate safety before release — it is assumed that safety is not altered by the annual change in the combination of vaccine strains. While past experience suggests that this is true, history also indicates that future vaccine scares are inevitable and we should plan accordingly.[8] Trivalent influenza vaccine, in particular, highlights the need for postmarketing surveillance to be linked with the capacity for rapid review and response, because a large proportion of the vaccine is administered over a short period before the onset of the influenza season each year.

The way forward is to establish a coordinated, uniform approach to AEFI reporting, coding, collation and analysis. A standing vaccine safety monitoring group which includes key stakeholders — representing the regulators, state and national immunisation programs and vaccine safety and epidemiology experts — needs to be urgently established.

The inability of the existing surveillance systems to detect the early signal of an increased incidence of febrile convulsions, within 24 hours of receiving 2010 seasonal trivalent influenza vaccine, demonstrates that passive surveillance cannot be relied on as the sole means of surveillance. Complementary active surveillance systems which can methodically detect potential AEFI signals, quickly establish rates and establish causality should be developed. The Australian Childhood Immunisation Register is uniquely placed to contribute to vaccine safety surveillance through data linkage with hospital morbidity and emergency department datasets, as demonstrated by a recent study from South Australia.[3] Sentinel surveillance in four tertiary care Australian paediatric hospitals has been shown to be an effective mechanism of surveillance for specific AEFI.[9] Implementing active AEFI surveillance systems will require sustainable funding, but this will be a small fraction of the cost expended on vaccines and vaccine delivery and could be resourced by levying a surcharge per vaccine dose sold, similar to methods adopted elsewhere to support compensation for vaccine-associated injuries.[10]

Central to any system of vaccine safety monitoring are issues of governance; specifically, transparency in decision making. Other countries currently provide full disclosure and web access to de-identified AEFI reports and open access to the deliberations of expert committees.[11,12] This engenders public trust in immunisation programs, and similar strategies should be considered in Australia.

The vast majority of Australian parents, vaccine recipients and health care providers trust public health authorities to assess and monitor vaccine safety. This is critical to ensure that the benefits of vaccination outweigh any potential risks. In the aftermath of the 2010 seasonal trivalent influenza vaccine experience, maintaining the public's trust requires that we get started on building the fully functional, standard-of-care AEFI surveillance system that Australia deserves. Vaccine safety should be an integral component of the National Immunisation Strategy, which should include strategies for comprehensive and complementary passive and active systems of surveillance.

Competing interests

Michael Gold was a member of the Therapeutic Goods Administration Adverse Drug Reactions Advisory Committee from 2006 until 2009. Peter Richmond has received grants from GlaxoSmithKline for otitis media epidemiological research; grants from CSL for pneumonia research; payment from CSL for sitting on a scientific advisory board for adjuvanted influenza vaccine in 2007; and honoraria from Baxter for chairing and speaking at a meningococcal vaccine workshop in 2008 and speaking at an international scientific meeting in Thailand in 2007. He was also an unpaid member of a Wyeth advisory board on pneumococcal conjugate vaccine in 2008. Murdoch Childrens Research Institute has received payment from CSL for Jim Buttery participating in data safety monitoring boards for influenza vaccine studies and trials, and a grant from CSL for a Guillain–Barré syndrome surveillance study.

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