Monitoring vaccine safety: a critical component of every immunisation program

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Postmarketing surveillance of vaccine safety requires active input from vaccine providers and health care professionals

Human papillomavirus (HPV) vaccines have now been licensed worldwide and at least 26 million doses have been distributed, including more than 3.7 million in Australia.[1] Australia was one of the first countries to implement a universal HPV immunisation program for females aged 12–26 years, commencing in April 2007.

Concerns over vaccine safety have the potential to derail immunisation programs. This may, in turn, cause considerable harm through resurgence of disease as vaccination coverage falls. For example, fears that the measles–mumps–rubella vaccine might cause autism resulted in a recent resurgence of measles in the United Kingdom.[2] Thus, monitoring and ensuring vaccine safety is critical to the success of any immunisation program.

When a new vaccine (such as the HPV vaccine) is first licensed, the majority of vaccine safety data are derived from Phase I, II and III clinical trials. Vaccine trials are powered to detect adverse reactions occurring at rates of up to 1 in 10 000, but cannot reliably detect rarer reactions. Australia monitors for such events using passive surveillance, whereby health care providers, parents or vaccinees are requested to report any adverse events following immunisation (AEFI) that they regard as serious and/or unexpected. In Australia, AEFI are reported to the Adverse Drug Reactions Unit of the Therapeutic Goods Administration (TGA), either directly (https://www.tgasime.health.gov.au/SIME/ADRS/ADRSRepo.nsf?OpenDatabase) or through state vaccine units.

AEFI fall into a number of categories, including events that are causally related to the vaccine (caused by the vaccine antigen or excipients), coincidental (unrelated to the vaccine), the result of injection reactions (related to the process of vaccination and not to the vaccine itself), or the result of program errors (eg, errors in the vaccination schedule or route of administration). It is the role of public health authorities to collect all reports of AEFI, classify them according to these categories and then initiate appropriate action.

In this issue of the Journal, Buttery et al (*page 261*)[3] report on a cluster of events described as a "mass psychogenic response" to HPV vaccination in the context of a school-based program. They identify the layout of the school as a possible precipitant. The key message for the public, vaccinators and parents is that the reported cluster of AEFI related to the process of vaccination rather than the vaccine itself. Despite the rapid public health response and reassuring outcome, the propensity for rapid dissemination of both information and misinformation about vaccination by the media and vaccine opponents/sceptics is clearly highlighted by this incident. Loss of parental confidence in the safety of HPV vaccination could undermine the impact of the entire program, given that achieving high vaccination coverage in adolescent girls is the most significant factor in reducing population rates of HPV infection, with very little population benefit to be gained by vaccinating women who are already sexually active.[4]

In a recent letter to the Journal, Das et al reported a case of acute pancreatitis following HPV vaccination.[5] A 26-year-old woman presented 4 days after receiving the first dose of HPV vaccine. No other potential cause for the pancreatitis was identified, and it is unclear whether the "prodromal illness" between vaccination and the onset of pancreatitis was related to vaccination or coincidental. Every year in Australia about 180 women aged 25–29 years are hospitalised with a principal diagnosis of acute pancreatitis (ICD-10-AM code K85), with an average annual incidence of 25 per 100 000 from 1998–99 to 2004–05.[6] In up to 90% of these cases, a cause is identified (chiefly gallstones or alcohol), but this still leaves 10% of cases with an undetermined cause. When a three-dose vaccination schedule is superimposed at the population level, incidents of pancreatitis shortly after HPV vaccination will inevitably occur.

How then does one disentangle coincidence from causality? Differentiating these two categories of AEFI is beyond the capability of a passive AEFI system. Further epidemiological investigations, using large population-based health datasets such as hospitalisations or health insurance records, are required to determine the rates at which a reported event occurs in vaccinated and unvaccinated individuals, in order to determine relative risk. For example, using such methods, researchers were able to confirm an increased rate of intussusception following rotavirus vaccination in the United States.[7,8]

Data linkage is a promising tool for such investigations where vaccination registers or records exist, and an investigation into the use of data linkage for AEFI surveillance in Australia is underway. At this stage, it is impossible to draw any conclusions about whether the case of pancreatitis reported by Das et al[5] was causally related to the HPV vaccine or was coincidental. In the US, where over 16 million doses of HPV vaccine have been distributed since 2006, only one case of acute pancreatitis in the age group 18–29 years had been reported to the Vaccine Adverse Event Reporting System as at July 2008.[9] In Australia, two cases of pancreatitis, including the case described by Das et al, have been notified. These data are insufficient to warrant further investigation into a possible association between the vaccine and acute pancreatitis at present.

In Australia, the ability to monitor the safety of a newly licensed vaccine is critically dependent on vaccine providers and health professionals reporting to the TGA any AEFI that they regard as serious and/or unexpected. Understanding that there are different types of AEFI is helpful in the interpretation of surveillance reports and in explanations to parents and vaccinees. When faced with media-driven public concerns about vaccine safety, the principles of risk communication may provide guidance. These include adequate preparation, establishment of communication networks for sharing information before an event receives media attention, and being responsive and open to the media once public attention is drawn to the possible adverse effects of a vaccine.[10]

The TGA provides updated information about HPV vaccine adverse event reports (http://www.tga.gov.au/alerts/medicines/gardasil.htm), and the National Centre for Immunisation Research and Surveillance has information to help immunisation providers address common HPV vaccine questions and "rumours" (http://www.ncirs.usyd.edu.au/facts/hpv_faq.pdf).

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