Evidence evolves over time and should be based on data not opinion

David Hawkes  

Since the introduction of vaccines against certain types of human papillomavirus (HPV), there have been concerns voiced by those critical of the use of these vaccines. These arguments often follow similar patterns and use similar discussion approaches such as raising unfounded questions about safety or using ‘scary’ terms without context (eg, toxins). A recent manuscript by Little and Ward 1 provided a representative example of the type of arguments made by vaccine critics that appear to have merit on first examination but which fail when more thoroughly investigated, 2 and especially over time as the evidence base demonstrating vaccine safety increases. 3

Little and Ward, like many other critics of the HPV vaccine, raise the issue of toxicity. In particular, they raise concerns about Polysorbate 80 and its relationship with infertility. They state that up to the age of 12, children receive a combined 0.8 mg of Polysorbate 80 administered through the Australian childhood vaccination schedule. This figure should not be considered a cause for concern, as 0.8 mg of Polysorbate 80 (the cumulative dose over 12 years) is >90 000 times lower than the acute exposure dose (based on rat intravenous LD50 of 1790 mg/kg) 4 for a 41 kg 12-year-old girl or >6700 times lower for a 3 kg infant. The animal study, 5 cited by Little and Ward, examining Polysorbate 80 toxicity on neonatal rats (over 4 days) gave doses equivalent to 550–5500 times higher than the entire exposure a human child gets by the age of 12.

Little and Ward raise questions about whether the vaccine is more likely to cause adverse events in HPV naïve girls, specifically stating ‘most adverse events occur in girls naïve to the four vaccine HPV types prior to vaccination’. This statement can be viewed as factually true based on the evidence cited simply because there are 2889 HPV naïve (PCR and seronegative) girls given the Gardasil vaccine but only 255 PCR positive/seronegative or 810 seropositive women given the vaccine.

Two of the references Little and Ward cite to demonstrate their claim that HPV vaccination is causally linked to primary ovarian insufficiency (POI) were case reports of a combined total of only six cases, including their own report of three cases. 6

The prevalence of POI is generally considered to be in the range of 1%–4% of the female population. 6–8 The issues surrounding these six cases have been addressed previously 9 and includes a lack of temporal association between vaccination and the onset of symptoms, possible conflict of interests where an author was an expert witness for two of the cases (undeclared), and a lack of epidemiological data indicating a rise in the prevalence of POI that correlates with its introduction.

Little and Ward do make a valid point that POI is not easy to diagnose. One of the key defining features of POI is a lack of fertility, although it is acknowledged that fertility can be affected by a wide range of factors other than POI. It could be expected that in countries that have introduced HPV vaccination and produced very high rates of vaccination in young females (eg, Australia), irrespective of issues with diagnosis, fertility may be a reasonable proxy for observing increases in POI. Data from the Australian Bureau of Statistics suggest that the introduction of a national HPV vaccination programme in April 2007 did not cause any major drops in fertility beyond the pattern of decreasing fertility established over several decades (figure 1). 12 13

There is no biologically plausible mechanism by which HPV vaccination causes POI consistent with the few described cases. While the study by Naleway and colleagues is far from conclusive, as they highlight themselves, it does provide a methodological approach to examining a possible relationship between HPV vaccination and POI. Little and Ward have a number of complaints about the methodology but further investigation suggests that these issues may not be materially important. Little and Ward highlight that inclusion for the study by Naleway and colleagues only required 1 month of follow-up and that this could bias the prevalence of POI; however, over 81% of the cohort was followed for more than 24 months with a mean follow-up time of 5.14 years. Little and Ward also have a range of concerns about the details of vaccination, but the study by Naleway and colleagues was looking at a cohort of 58 871 women who received at least one dose of a HPV vaccine, but only a single case of POI following (23 months after) HPV vaccination. Little and Ward also complained that there was no gynaecologist input, when Naleway and colleagues clearly acknowledged the input of two OB/GYN clinicians. Population-based studies rarely have access to all data for each participant but as long as the limitations are clearly stated, as they were by Naleway and colleagues, Little and Ward’s approach of refusing to accept the findings appears to be a case of throwing the baby out with the bathwater.

In summary, raising questions about vaccinations from small case studies is a viable and essential way to look for early indicators of possible vaccine associated adverse events. However, small numbers of cases where clinical symptoms (of relatively common pathologies) occur after HPV
vaccination, irrespective of temporal association, are not enough to demonstrate causation, especially when the number of people vaccinated is in the tens, if not hundreds, of millions. Vaccine critics who continue to raise the same small number of case studies, whose initial concerns have been addressed both with critical analysis and large-scale population-based studies, again and again run the risk of being labelled as ‘antivaccine’. The difference between a vaccine critic and an antivaccinationist is that a vaccine critic bases their concerns of the best available data whereas an antivaccinationist cherry picks whatever information suits their a priori belief.

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ORCID iD
David Hawkes http://orcid.org/0000-0002-3882-801X

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