

Safety in numbers: anaphylaxis risk in childhood immunisation

Andrew Collinson

The history of immunisation can be traced through two major narratives. The first is a story of profound benefit to global health, the other a complex tale of risk and uncertainty versus safety and public confidence. These narratives are forever intertwined, not least because as successful immunisation programmes lead to progressive reductions in disease risk, so the prospect of adverse vaccine-related events becomes a dominant public concern.

Anaphylaxis has long been recognised as a rare but serious complication of vaccination, but despite millions of infants and children receiving vaccine doses every year, data describing the incidence of anaphylaxis as an adverse event following immunisation (AEFI) are surprisingly sparse. Erlewyn-Lajeunesse *et al*'s prospective survey of anaphylaxis as an AEFI, published in this issue, provides a valuable addition to the existing evidence concerning vaccination safety.¹

Serious allergic reaction in childhood sits alongside meningitis in the public consciousness as a seemingly random, rapidly progressive and life-threatening event. Anaphylaxis as an AEFI is feared by health professionals for the same reasons, and because it follows an active health intervention administered to healthy children. Exaggerated fears of provoking anaphylaxis by giving combined measles, mumps and rubella (MMR) vaccine to children with egg allergy have taken a long time to dispel, with many paediatricians receiving referrals for in-hospital MMR immunisation long after the publication of evidence providing strong reassurance that this is largely (and perhaps entirely) unnecessary.² In deciding how to manage very small risks of major complications, health professionals can find it difficult to determine the right balance between precaution and practicality, and to communicate this with confidence to parents and children.

Erlewyn-Lajeunesse *et al* present data describing the incidence and risk factors for anaphylaxis as an AEFI in the UK and Ireland between September 2008 and October 2009. The study was supported by the British Paediatric Surveillance Unit (BPSU), employing its "Orange Card" prospective active surveillance methodology.

The investigators used an accepted standardised case definition for anaphylaxis as an AEFI, which classifies cases according to diagnostic certainty, recognising that anaphylaxis is a clinical diagnosis based on composite clinical features with differing levels of sensitivity and specificity.

The investigators found no cases of anaphylaxis following immunisation with any of the vaccines in the UK infant and pre-school primary schedule, over a period in which more than five million infant vaccine doses were administered. This suggests an even lower risk than the one per million incidence of anaphylaxis as an AEFI cited in the current Department of Health (DH) "Green Book" immunisation guidance.³ This estimate was derived from the total number of anaphylactic and anaphylactic-type vaccine reactions reported to the Medicines and Healthcare products Regulatory Agency (MHRA) between 1997 and 2003, and therefore relates to all vaccines and age groups during a period when some vaccine products that have now been superseded were in use. The absence of reported anaphylaxis episodes related to MMR vaccination is particularly striking, because approximately 20 cases might have been expected from an earlier prospective population-based observational study, based on the UK General Practice Research Database.⁴ These data provide important reassurance for health professionals and families alike.

Among the seven cases identified in this study, two were associated with single-component measles vaccine, and three with bivalent human papilloma virus vaccine. The authors' estimate of anaphylaxis as an AEFI following single-component measles vaccine is 100-fold higher than the usually quoted overall incidence of vaccine-associated anaphylaxis. Interpretation of this finding is limited by the very small number of cases combined with ethical constraints precluding detailed case descriptions. Caution also needs to be exercised in drawing comparisons between rates of adverse reaction to vaccines used selectively and vaccines in the universal schedule, since there may be differences in population susceptibility and the exposure. For example, human papilloma virus vaccines are given to teenage girls, in whom incidence of anaphylaxis post-puberty is known to be higher than in boys.⁵ However, it is hard to conceive that recipients of single-component measles vaccine should have a higher prevalence of susceptibility to anaphylaxis.

More plausible, and of greater concern, is the possibility that the vaccines themselves are more allergenic as a result of poor manufacturing or quality control standards. Use of unlicensed single-component vaccines increased substantially in the UK in the years following 1998, as an expression of diminished public confidence in the combined MMR vaccine. Although the DH advice has articulated the compelling basis upon which MMR vaccine should be recommended and use of single-component vaccines discouraged, differences in risk of vaccine-related anaphylaxis have not formed part of that advice because the data, until now, have not been available.

Concerns regarding vaccine safety have ebbed and flowed in the public and professional consciousness with the introduction of new vaccines and the emergence of new concerns over vaccines in established use. Although such concerns naturally arise from evidence or assertions that a vaccine may cause harm, harm can also result from withholding vaccination on the basis of unfounded safety concerns. In the UK, vaccine safety is monitored primarily through the voluntary MHRA Yellow Card reporting scheme, a passive surveillance system that encourages health professionals to report suspected adverse reactions. A tendency to under-reporting, inherent in passive systems of this kind, may yield underestimates of true adverse reaction incidences. Importantly, this limitation also diminishes the extent to which such systems can confirm the true rarity of an adverse event.

The methodology employed in surveys supported by the BPSU provides a more effective mechanism for determining the true incidence of discrete rare conditions. Paediatricians are asked to report any cases seen in the preceding month, and also to submit a nil return if there were no cases seen. This system was originally inspired by the methodology of the National Childhood Encephalopathy Study conducted in the context of concerns over the safety of the whole-cell pertussis vaccine in the late 1970s. The greater than 90% response rate during the period of Erlewyn-Lajeunesse *et al*'s survey exemplifies the continuing high level of clinician engagement with this simple but effective system. Sadly, this latest BPSU-related publication coincides with the imminent termination of the grant that the BPSU currently receives from the DH Policy Research Programme, and thus, an uncertainty over the future of the BPSU in its current form.

Erlewyn-Lajeunesse *et al* point out that their calculation of anaphylaxis risk following single-component measles immunisation may underestimate the true likelihood, because standards of vaccine reporting expected of National Health Service providers are not required of the private clinics in which most single-antigen vaccine doses are administered. The Health and

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Social Care Bill 2010–2012, soon to become law, will pave the way for increased competition and a greater diversity of health service providers. The many professional bodies that have voiced opposition to the legislation have received assurances that increased competition will not put cost before quality. It is essential that the new regulatory framework and commissioning processes do not overlook the importance of obliging health service providers to engage with effective surveillance mechanisms. This is important in the context of childhood immunisation, so that uncommon or unexpected vaccine complications can be reliably detected and quantified, and to provide confirmatory evidence of vaccine

safety with which to confidently reassure families and health service providers.

Competing interests The author has acted as principal investigator for clinical vaccine trials conducted on behalf of his employing NHS Trust, sponsored by vaccine manufacturers, but has received no personal payments from them. The author will this year receive financial assistance from a vaccine manufacturer to attend a conference.

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REFERENCES

1. **Erlewyn-Lajeunesse M**, Hunt LP, Heath PT, *et al*. Anaphylaxis as an adverse event following

immunisation in the UK and Ireland. *Arch Dis Child* 2012;**97**:487–90.

2. **Ainsworth E**, Debenham P, Carrol ED, *et al*. Referrals for MMR immunisation in hospital. *Arch Dis Child* 2010;**95**:639–41.
3. **Department of Health**. *Vaccine Safety and the Management of Adverse Events Following Immunisation*. Immunisation against Infectious Disease. Department of Health 2006:53–64.
4. **Peng MM**, Jick H. A population-based study of the incidence, cause, and severity of anaphylaxis in the United Kingdom. *Arch Intern Med* 2004;**164**:317–19.
5. **Sheikh A**, Hippisley-Cox J, Newton J, *et al*. Trends in national incidence, lifetime prevalence and adrenaline prescribing for anaphylaxis in England. *J R Soc Med* 2008;**101**:139–43.



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