ADDRESS LETTERS TO
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HPV vaccination reactions

Dear Editor

We agree with Dr Douglas (*AFP* March 2009) that, to date, quadrivalent HPV vaccine appears both effective and safe.[1] However, it is important to understand that surveillance after registration of vaccines is designed to detect rare events and this can be difficult when using only voluntary (passive) reporting, as we do nationally to the Australian Adverse Drug Reactions Advisory Committee (ADRAC).

Both HPV vaccines were extensively investigated before registration. In fact, these vaccine trials were large enough to detect adverse reactions occurring with a frequency up to one in several thousand. So we can certainly feel reassured that problems more common than this that occur due to vaccination should have been detected. The role of post licensure surveillance is thus to detect events rarer than this and events occurring when the vaccine is in use in the general population rather than in the selected trial population. Unfortunately this is not easy, despite the large number of people being vaccinated, because of incomplete notification of events (due to the largely passive nature of reporting) and because, in any given population, numerous health events occur in any given timeframe with or without vaccination episodes.

Anaphylaxis is a typical example of a potentially serious complication of vaccination that is too rare to ascertain even in a very large trial but the occurrence of which is potentially very important. We reject Dr Douglas' suggestion that we used the incorrect denominator for estimating rates of anaphylaxis following HPV vaccination in the New South Wales school based vaccination program[2] and that the appropriate denominator was the number of doses distributed nationally. This would be like conducting a detailed audit of side effects due to a medication in a hospital setting and then using the doses of that medication sold nationally during that period as the denominator for calculating the incidence of side effects, rather than the doses used in the hospital. In NSW we were fortunate enough to have daily faxed reports from every team of school vaccinators reporting all vaccine doses administered that day and all adverse events that occurred at the schools. Thus our surveillance data and denominator data were much more complete for surveillance of events occurring shortly after vaccination than any comparable national data available. Even still, national adverse events following immunisation data also document a higher number of anaphylaxis notifications (n=11) after HPV vaccination than after any other vaccine in the past 5 years of reporting.[3] This remains true even if all the cases reported from NSW and classified as anaphylaxis by ADRAC (n=7) are excluded.

We would like to encourage practitioners to report serious or unusual events that they observe after vaccination. All adverse event reports following immunisation are important and it is only with detailed and timely reporting that we can be truly reassured that rare but potentially serious adverse events due to a vaccine do not go undetected.

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Andrew Kemp, Margaret Burgess, Sydney, NSW
Mike Gold, Adelaide, SA

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Pelvic examination of asymptomatic women

Dear Editor

We would like to reply to the comment made by Dr Gary Fisher (*AFP* March 2009).

Dr Fisher stressed the importance of examining the relevant body part with each examination. The relevant body part can only be identified after taking a thorough history, such as a gynaecological history, for example, when a woman presents for a Pap test. If the woman is asymptomatic when a thorough gynaecological history is taken, then there is no indication or evidence to conduct an examination as intimate as a pelvic examination. The examples offered by Dr Fisher would likely have been identified via history taking, and if truly asymptomatic, it could be argued that management would remain unaltered anyway. Take for instance the case of the undiagnosed prolapse, if the woman was asymptomatic, surely prophylactic repair surgery is not warranted. With regards to fibroids, if the woman has no menstrual complaints then why treat them? Again, with vaginal infections and pregnancy, thorough history would diagnose most cases, and we are certainly not advocating that swabs for STI screening (eg. chlamydia) should not be done at the time of a smear in at risk groups. The discovery of a melanoma and sarcoma of the perineal area by Dr Fisher is to be congratulated and general inspection of the perineum before doing a Pap smear is worthwhile, but certainly not as invasive as a pelvic examination. In any case, it can be argued that routine skin checks advocated as preventive care in general practice, (or done opportunistically as part of a 'well woman check') would have identified the skin lesions.

After extensive review of the literature we argue that if a thorough history is taken and a woman is truly asymptomatic with regards to gynaecological symptoms, then there is no place for an invasive examination such as that of the pelvis as a screening tool.

Rebecca Stewart, Townsville, Qld
Jill Thistlethwaite, Sydney, NSW

Vitamin D deficiency

Dear Editor

Thank you for presenting the interesting review article by Stroud et al[1] highlighting vitamin D deficiency. There are several points on which I would like to comment.

It is now widely accepted that vitamin D deficiency is diagnosed by serum 25-hydroxy vitamin D levels, with deficiency currently defined as <50 nmol/L,[2] though as the authors indicate, this threshold is open to debate. The additional presence of pathological abnormalities corrected by physiological doses of vitamin D is not considered necessary for deficiency to be diagnosed.

There is an error in Table 1: Australian adequate intake (AI) of vitamin D is 200 IU/day for ages 1–18 years.[3] The AI for pregnant and lactating women is 200 IU as given, but with scope for supplementing further with up to 400 IU in those with limited sun exposure.[3]

From the statement that regular sunlight is sufficient to maintain adequate vitamin D levels in children, it might be construed by the reader that vitamin D deficiency is not a significant problem in children. There are Australian data showing that in 16 year old boys the prevalence of deficiency may be as high as 68% in winter in northern Tasmania,[4] and New Zealand data show that in 15–18 year olds, 39% of girls and 55% of boys have levels <50 nmol/L.[5] In my opinion, this brings the assumption that regular sun exposure will be sufficient in older teenagers into question and raises the issue of whether older teenagers are likely to safely achieve sufficient sun exposure to maintain adequate vitamin D levels.

Tania Winzenberg
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Reply

Dear Editor

We thank Dr Winzenberg for her comments which highlight the tension between what is known and yet to be known regarding vitamin D.

Regarding deficiency of vitamin D, it is known that the best biochemical measure of vitamin D status is the serum 25(OH) vitamin D level. Different methods of assay influence the result, particularly for higher levels, but this is more relevant to research than to clinical practice.

Defining deficiency is more problematic, and both target levels and the classification system will need to change as the nonmusculoskeletal actions of 25(OH) vitamin D become further defined. There will always be pathological abnormalities at some level associated with deficiency, and the contrasts in the article are between disease treatment versus potential disease prevention, and between physiological dose vitamin D replacement therapy versus pharmacological dose therapy to treat the rarer conditions mentioned. It is also known that the two main forms of vitamin D are not similar with cholecalciferol (vitamin D3) being preferred to, and more potent[1] than, ergocalciferol (vitamin D2) in treatment. The two forms have different metabolites and pharmacokinetics. In Australia, the available form was recently changed to cholecalciferol and care is needed in applying vitamin D2 based regimens.

Dr Winzenberg highlights the controversies of adequate intake of vitamin D for children aged 1–18 years. The NHMRC recommendation is 200 IU/day, regardless of sunlight, and notes that for certain groups regular sun exposure might not be enough to meet the body's requirements and dietary vitamin D is needed.[2] The 2006 consensus statement however, recommends that for children with these and other at risk factors, 400 IU/day is recommended.[3] It is known that rapid bone growth, especially with marginal calcium intake, consumes more vitamin D and depletes body stores faster. Children aged 6 months to 3 years are thought to be particularly vulnerable.[4] Given that the level defining deficiency was 25[OH] vitamin D <27.5 nmol/L and the absence of data on how much vitamin D is required to prevent deficiency in 1–8 year olds, the 400 IU level was used.

The third point regarding pregnant and lactating women shows that we can measure different endpoints and raises the question of whether it is better to set a lower adequate intake level for a lactating mother and recommend supplementing the infant with vitamin D, or recommend a higher adequate intake for the lactating mother and not need to supplement the breastfed child. It is our hypothesis that it is possible to do the latter through sun exposure/diet and not only with the use of supplements. Optimal vitamin D requirements for pregnant and lactating women are not known but are likely to be higher than current recommendations.[5]

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