

# Recombination/re-assortment events with live human vaccines

## FactSheet For Health Professionals



Scientists at the Asia-Pacific Centre for Animal Health in Melbourne recently published study data suggesting that recombination of live attenuated herpes-viruses from different veterinary vaccines has occurred and generated a more virulent virus in chickens housed in close quarters.<sup>1</sup> The vaccines are used to control infectious laryngotracheitis in poultry.

## Discussion Points

### Use of live vaccines for humans

We do **NOT** recommend immunising with more than one of the same live vaccine type in the same person at the same time. Furthermore none of the vaccines on the current National Immunisation Schedule contain more than one strain of the same live virus.

### The distinction between the live human vaccine viruses is important

- Varicella and herpes zoster - double stranded DNA viruses
- Rotavirus - double stranded RNA virus
- Polio - single stranded RNA virus
- Measles, mumps and rubella - single stranded RNA viruses

The live human vaccines closest to the veterinary vaccines in the reported study are the varicella and herpes zoster vaccines. Both these vaccines are derived from the same strain of virus so there is no potential for recombination. A frame shift of latent varicella virus DNA from the initial varicella infection can manifest as herpes zoster in later years.

### Attention has focused on vaccines containing RNA viruses, particularly the rotavirus vaccines

We often refer to RNA viruses as quasi-species as it is well documented that they can recombine to generate new RNA viruses (Professor Vernon Ward, emailed personal communication 2012 July 18). The RNA polymerases do not have a proof reading mechanism so there is a wide diversity of sequences about the core genetic type.

Rotavirus, a double stranded RNA virus, also has segmented genomes and can re-assort to new rotavirus strains, somewhat analogous to the influenza virus. The influenza virus undergoes genetic shift through whole segment changes and drift through accumulated mutations. This is why we are required to change the influenza vaccine antigens most years.

The pandemic noroviruses that can affect rest homes and other care facilities are largely recombinant strains.<sup>2</sup>

Massive diversity and change occurs all the time in viruses. While no vaccine is completely risk free, the risk-benefit analysis is overwhelmingly in favour of using live attenuated vaccines to control disease.

### What is the risk of live human vaccine virus recombination or re-assortment?

Recombination and re-assortment events are occurring all the time in wild type viruses (Professor Vernon Ward, emailed personal communication 2012 July 18). There is a theoretical risk of recombination or re-assortment of live human vaccine viruses.

MacDonald et al.<sup>3</sup> showed for the first time that genetically distinct rotavirus with the same G/P-type can co-circulate and cause disease. They also suggested that, although gene segment exchange occurs, most re-assortment strains are replaced over time by lineages with preferred 'genome constellations'. So the wild type is the 'fittest' strain and the selection pressure is to revert.

In the case of the rotavirus vaccine (Rotarix<sup>®</sup>), the two genes that determine G-types and P-types (vaccine specificity G1P[8]) can be passed on separately to progeny viruses so different combinations are possible.

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### Data from the U.S. Rotarix® data sheet<sup>4</sup>

Vaccine virus transmission has been observed in twin studies during a median period of 10 days but there was no clinical disease.

In one hundred pairs of healthy twins 6-14 weeks of age randomized to receive Rotarix (N = 100) or placebo (N = 100), transmitted vaccine virus was identified in 15 of 80 twins receiving placebo (18.8% [95% CI: 10.9, 29.0]). Median duration of the rotavirus shedding was 10 days in twins who received Rotarix as compared to four days in twins who received placebo in whom the vaccine virus was transmitted.

Rotavirus vaccine strain has been documented to re-assort to virulent forms in immunodeficient patients however these patients remain contra-indicated for the vaccine.

### Could rotavirus vaccination exacerbate the risk of re-assortment?

The only difference between vaccination and the wild type situation is attenuation of the vaccine viruses and subsequent clinical disease. It is easy to suggest vaccination might lead to a problem however, given the very high incidence of wild type rotavirus it would be hard to see much difference. A move towards a more immune population through high vaccination coverage might eventually have effects and this is being monitored.<sup>5</sup>

### Oral polio vaccine and re-assortment

The live oral polio vaccine is a combination of three attenuated virus serotypes administered simultaneously which creates ideal conditions for intertypic recombination. Oral polio vaccine was administered to billions of people through the course of the polio eradication campaign. Recombinant strains were noted soon after vaccination began and comprised up to 36% of the excreted viruses. The recombination of the three strains gradually resulted in loss of attenuation and restoration of 'fitness' in a small percentage of excreted viruses however the individual was immune to polio before they could develop any clinical disease.<sup>6</sup>

### Do recombination and re-assortment events require surveillance in New Zealand?

It is unlikely that monitoring for these events will be useful (Professor Vernon Ward, emailed personal communication 2012 July 18).

The questions being asked need careful thought, specifically *how is the vaccine materially different to the wild type situation and is there any evidence overseas from issues around the rotavirus vaccines?*

Such surveillance would need to monitor:

- Viral transmission from vaccinees
- The possibility that vaccine virus may re-assort with co-circulating wild type strains
- Animal rotavirus strains, particularly among animals in close contact with humans e.g. house animals/pets

### References:

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