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Will dual Japanese encephalitis and measles-rubella vaccination hinder measles and rubella eradication?

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In *The Lancet Infectious Diseases*, Yan Li and colleagues[1] present a multicentre randomised controlled trial to assess whether live-attenuated Japanese encephalitis vaccine (LJEV) impairs measles and rubella antibody responses to coadministered measles-rubella vaccine. China's National Immunisation Programme has recommended dual LJEV and measles-rubella vaccination at 8 months of age since 2008 but there are no data on interference between these two vaccines. The major international effort to eliminate measles from all six WHO regions by 2020 requires high levels of vaccine coverage and herd immunity,[2] and thus interference with measles antibody responses would be problematic. The authors' demonstration of non-inferiority in prevalence of seroconversion for measles IgG antibodies (difference –0·8% [90% CI –2·6 to 1·1]) alleviates these concerns.

This finding is perhaps not surprising given that previous studies have shown that LJEV does not interfere with antibody responses to single measles vaccination.[3,4] One caveat is that many countries use the measles-mumps-rubella (MMR) vaccine rather than measles-rubella vaccine and indeed China's National Immunisation Advisory Committee has recently recommended using this vaccine rather than measles-rubella vaccine. A previous study confirmed absence of interference between the MMR vaccine and another Japanese encephalitis vaccine—the live-attenuated chimeric vaccine[5]—and one would predict that the MMR vaccine responses would be similarly unaffected by LJEV.

WHO recommends commencing measles vaccination at 9 months of age and considers additional doses before 9 months as supplementary.[6] The high measles seropositivity (almost 99%) achieved in both groups confirms that administering the first measles-containing vaccine (MCV) at 8 months of age is an acceptable strategy in this population, and can be considered the first dose of MCV rather than a supplementary dose.[6] Many countries have included rubella-containing vaccines in their childhood national immunisation programmes in an effort to eliminate the potentially devastating effects of rubella infection in pregnancy;[2] thus, non-interference with rubella antibody responses (difference 0·8% [90% CI –1·8 to 3·4]) is also an important finding in Li and colleagues' study.[1]

Japanese encephalitis is the leading cause of viral encephalitis in Asia, there is no effective treatment, and neurological sequelae and mortality are very high.[7] The widespread rollout of Japanese encephalitis vaccination in endemic countries is crucial for prevention. The effect of measles-rubella vaccine on LJEV antibody responses was not tested in this study; however, non-interference has been confirmed in previous studies.[8] This finding further supports administration of Japanese encephalitis vaccine and an MCV in a single visit, which offers the benefits of being more cost effective and likely to improve vaccination coverage against these important infections than if multiple visits are required. Reassuringly, in this study, active monitoring for adverse events following immunisation (AEFIs) did not detect any serious adverse events and there was no signal that the dual vaccinated infants had more AEFIs after being coadministered the two live vaccines than did infants who were administered measles-rubella vaccine alone.

The large cohort in Li and colleagues' study of 1093 infants from two provinces in China was well powered to assess their primary outcome. Cohort characteristics including infant gestational age, birth weight, infant sex, breastfeeding, maternal age, maternal measles and rubella infection, and vaccination history

were balanced between randomisation groups. Baseline prevalence of seropositivity for measles and rubella antibodies were less than 1·2% for measles and less than 1·6% for rubella, supporting waning of maternal antibody by 8 months of age. Although the authors report that six of the seven measles seropositive infants at baseline did not seroconvert according to their criteria, baseline and post-vaccination concentrations were above the seroprotective concentration of 200mIU/mL or more for all seven infants, which suggests that they would be protected. Likewise, while seven of the ten rubella seropositive cases also failed to seroconvert, all had protective concentration of 10 IU/mL or more before and after vaccination.

Overall, these new data provide reassurance for countries wishing to roll out LJEV vaccination at the same time as measles and rubella vaccination, while maintaining the high prevalence of measles and rubella seropositivity required for eradication. They also show that maternal antibody has generally waned by 8 months of age and thus MCV can be given at this early time point to improve herd immunity in this vulnerable age group.

Katie L Flanagan
Department of Immunology and Pathology, Monash University, Melbourne, VIC, Australia; School of Health and Biomedical Science, RMIT University, Melbourne VIC, Australia; and School of Medicine, Faculty of Health Sciences, University of Tasmania, Launceston, TAS 7250, Australia
katie.flanagan@ths.tas.gov.au

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Can cleaning REACH further in reducing hospital infections?

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Few well controlled studies have helped us to understand whether, when, and to what extent the contaminated health-care environment contributes to the transmission of pathogens that can cause health-care-associated infection.[1] Into this context lands the Researching Effective Approaches to Cleaning in Hospitals (REACH) study, by Brett Mitchell and colleagues published in *The Lancet Infectious Diseases*,[2] a multicentre stepped-wedge randomised controlled trial of enhanced environmental hygiene (used here to described cleaning or cleaning and disinfection) in reducing health-care-associated infection. Previous studies have shown that switching to more powerful disinfectants,[3,4] introducing automated room decontamiation,[5,6] or making changes to environmental hygiene protocols (eg, by increasing the frequency of cleaning or disinfection)[7] can reduce transmission or health-care-associated infection, or both. However, this is the first randomised controlled trial to investigate the effect of a systematic bundle of interventions to improve environmental hygiene, targeting both routine daily cleaning and cleaning and disinfection at patient discharge.

The study was done in 11 Australian hospitals between May, 2016, and July, 2017. The intervention involved a review of the environmental hygiene approach in each hospital and a structured, tailored set of recommendations to improve product choice, technique, audit, training, and communication of performance; a unique aspect was to raise the organisational profile of environmental hygiene. The primary outcomes were incidences of health-care-associated *Staphylococcus aureus* bacteraemia, *Clostridium difficile* infection, and vancomycin-resistant enterococci infection of usually sterile sites. Vancomycin-resistant enterococci infections reduced by 37% (from 0·35 to 0·22 per 10 000 occupied bed-days; relative risk 0·63, 95% CI 0·41–0·97, p=0·0340), but no significant changes were seen in the incidence of *S aureus* bacteraemia (0·97 to 0·80; 0·82, 0·60–1·12, p=0·2180) or *C difficile* infection (2·34 to 2·52; 1·07, 0·88–1·30,