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Reply to Pawaskar et al.

To the Editor—The commentary by Pawaskar et al. focused on the vaccine efficacy (VE) of the monovalent OKA/Merck vaccine. In our study, the 10-year GSK OKA/recombinant-immunotoxin (OKA/RIT) VE of 67.2% [1] was used, compared to Chan et al.'s 78.0% estimate [2] for the OKA/Merck vaccine. We wish to clarify why the 10-year OKA/Merck VE of 94.4% [3] was considered inappropriate, with emphasis on vaccination age, dose level (plaque-forming units [PFU]) and effectiveness studies.

The Kuter et al. [3] study was a 10-year follow-up of Weibel et al. [4], in which subjects aged 1–12 years (mean age, 4.43 years) received a 17,430 PFU-containing formulation. In the study by Povey et al. [1], children aged 12–22 months (mean age, 14.2 months) received the OKA/RIT vaccine with a potency of 1,995 PFU.

Studies by GSK and MSD suggest that older age at vaccination leads to a lower risk of varicella and a higher VE. Varis and Vesikari [5] demonstrated a lower VE with OKA/RIT vaccinees aged 10–18 months (64%) versus vaccinees aged 19–24 months (82%). Chan et al. [2] showed that at 5gp enzyme-linked immunosorbent assay, the risk of varicella infection decreased by ~ 80% in children aged 5.5 years versus children aged 1.5 years. Comparisons at equivalent titers indicated that the varicella infection risk decreased by ~ 73% in children aged 4.43 years versus children aged 14 months.

VE differences resulting from varying dose levels need to be highlighted as higher doses (10,000–17,000 PFU) are associated with better protection than lower doses (1,000 PFU) [5, 6]. This is illustrated by a crude comparison of the 100% OKA/Merck VE after 9 months of follow-up in Weibel et al. [4] with the 86% VE at 1 year in White et al. [7], in which the OKA/Merck dose ranged between 1,000 and 1,625 PFU among enrollees with a mean age of 3.98 years. Similarly, Kuter et al. [8], in a 7-year follow-up of Weibel et al. [4], with enrollees aged 4.7 years on average reported that 95% of vaccinees remained varicella-free following household exposure. This VE rate could be compared with Vessey et al.'s VE of 88.5% [9] over a 7-year period in enrollees with a median age of 3.6 years, with vaccine doses of 2,900–9,000 PFU and household exposure. The currently licensed monovalent OKA/Merck vaccine contains at least 1,350 PFU, which limits comparisons with prelicensure VE studies.

Overall, the bias risk with Kuter et al.'s VE in a comparative analysis with the OKA/RIT vaccine can be limited with Chan et al.'s VE estimate of 78.0% [2], for the reason previously reported, acknowledging limitations inherent to the absence of head-to-head efficacy studies across similar age groups and dose levels. A meta-analysis of observational studies by Marin et al. [10] reported a pooled 1-dose VE of 81% (95% confidence interval, 78%–84%) against any varicella with no differences by vaccine, in agreement with our conclusion on predicted similar effectiveness between GSK and MSD varicella-containing vaccines.

Conclusively, we believe that the most accurate VE estimate was used for the OKA/Merck vaccine. Importantly, both vaccines effectively reduce the varicella burden, with GSK varicella-containing vaccines potentially being more cost-effective.

Notes

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Applying Clinical and Laboratory Features Associated With *Mycoplasma pneumoniae* (*Mp*) Infection With the New Diagnostic Test of *Mp*-Specific Immunoglobulin M (IgM) Antibody–Secreting Cells to *Mp*-IgM Seroconversion in *Mp*-Positive Children With Community-Acquired Pneumonia

To the Editor—We read with interest the recent publication by Meyer Sauteur et al [1] with regard to identifying clinical and laboratory features associated with *Mycoplasma pneumoniae* (*Mp*) infection with the new diagnostic test of *Mp*-specific immunoglobulin M (IgM) antibody–secreting cells (ASCs). The study concluded that *Mp* positivity was statistically associated with older age, no underlying disease, family with respiratory symptoms, prior antibiotic treatment, prolonged prodromal respiratory symptoms and fever, and extrapulmonary skin manifestations. In addition, lower levels of C-reactive protein (CRP), white blood cell count, absolute neutrophil count, and procalcitonin (PCT) were statistically associated with *Mp* infection.

In the current primary care setting, serologic tests remain a preferable choice in the diagnosis of *Mp* infection in children with community-acquired pneumonia (CAP), while polymerase chain reaction–based assays are considerably more expensive and require specialized expertise and equipment. Nevertheless, a major disadvantage of IgM-based diagnosis is its high false-negative rate, measuring 32.5% in a previous study [2]. Therefore, a definite diagnosis is often delayed until the appearance of *Mp*-IgM seroconversion, defined as a change from a negative acute serum sample to a positive convalescent serum sample, resulting in inaccurate treatment by pediatricians and progressing to severe CAP or extrapulmonary manifestation, which protracts and complicates the clinical course [3, 4].

We applied the clinical features and biomarkers in the above-mentioned study to 5 pediatric patients with confirmed diagnosis of *Mp* pneumonia, who were initially *Mp*-IgM negative but showed seroconversion of *Mp*-IgM 1 week after admission. All of the patients met the features of age older than 5 years, white blood cell count less than 18 000 (cells/μL), and absolute neutrophil count less than 8000 (cells/μL). CRP less than 50 mg/L, prodromal respiratory tract infection (RTI) greater than 6 days, and combinations of the clinical features "age >5 years + prodromal fever + RTI >6 days" were found in 80% of patients. Sixty percent of those enrolled were noted to have fever for more than 6 days, no underlying disease, and have had prior antibiotic treatment (Table 1).

Clinical applications of *Mp*-IgM-ASC detection as a diagnostic test may need further standardization, optimization, and reproducibility. Nonetheless, the impressive discriminative potential of this technique among other diagnostic methods used currently [5], and the clinical features and biomarkers associated with *Mp* CAP identified by the dataset of this new diagnostic test, may aid in the prediction of *Mp* infection in children with CAP, especially those who initially presented as *Mp*-IgM negative but were clinically symptomatic at an early stage, to avoid ineffective first-line empirical β-lactam antibiotics but allow targeted treatment against *Mp* in severe cases, even though the *Mp*-IgM-ASC assay is not routinely applied in clinical care.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that

Table 1. Applying Clinical and Laboratory Features Associated With Mp Infection With *Mp*-IgM-ASC Assay to *Mp*-IgM Seroconversion in *Mp*-Positive Children With CAP

	Mp-IgM Seroconversion in *Mp*-Positive Community-Acquired Pneumonia (N = 5), n (%)
Age >5 years	5 (100)
No underlying disease	3 (60)
Prior antibiotic treatment	3 (60)
Fever >6 days	3 (60)
RTI >6 days	4 (80)
Age >5 years + prodromal fever + RTI >6 days	4 (80)
WBC <18 000 (cells/μL)	5 (100)
ANC <8000 (cells/μL)	5 (100)
CRP <50 (mg/L)	4 (80)

Abbreviations: ANC, absolute neutrophil count; CRP, C-reactive protein; IgM, immunoglobulin M; *Mp*, *Mycoplasma pneumoniae*; RTI, respiratory tract infection; WBC, white blood cell count.