Correspondence

Ambient Temperature and the Rates of Adverse Reactions of Pertussis Vaccines

To the Editor—Diphtheria-tetanus-pertussis whole-cell (DTwP) and acellular (DTaP) vaccines are the 2 main pertussis-contained vaccines. DTwP, developed in the 1930s, has contributed to the reduction of pertussis, but has often been associated with vaccine-related adverse reactions (ARs) [1]. This had severely affected the public confidence in immunization programs, followed by decreased vaccine coverage and pertussis outbreaks in many industrialized countries in the 1970s [2]. DTaP, which was developed in the 1980s and replaced DTwP in developed countries in the 1990s, has been associated with fewer ARs due to removal/reduction of endotoxin [1]. China began replacing DTwP with DTaP in its national immunization programs in December 2007, and its passive Adverse Events Following Immunization (AEFI) surveillance system was established in 2005 [3]. The Intergovernmental Panel on Climate Change Fifth Assessment Report indicates that the planet is warming at an unprecedented pace, and global average surface temperatures will continue to rise over the coming decades [4]. The pertussis vaccines are unstable at high and low temperature, which may affect not only potency but also the safety of these vaccines [5, 6]. However, the association between temperature and ARs remains largely unknown.

The data in Duanzhou in Guangdong province, China, located in a subtropical zone and which established an enhanced AEFI surveillance system for DTwP and DTaP, were used to examine the association of ARs with climate factors in children aged <7 years. We performed a series of negative binomial generalized linear regression analyses to assess the associations of maximum/minimum temperature and sun exposure with the rates of ARs for DTaP and DTwP in children. The models were adjusted for monthly vaccination doses included as an offset term and a first-order autoregression term to control autocorrelation. There appeared to be a positive association between ambient temperature and the rates of ARs for DTaP and DTwP (Figure 1). Our results indicate that increases in both maximum temperature (model I:

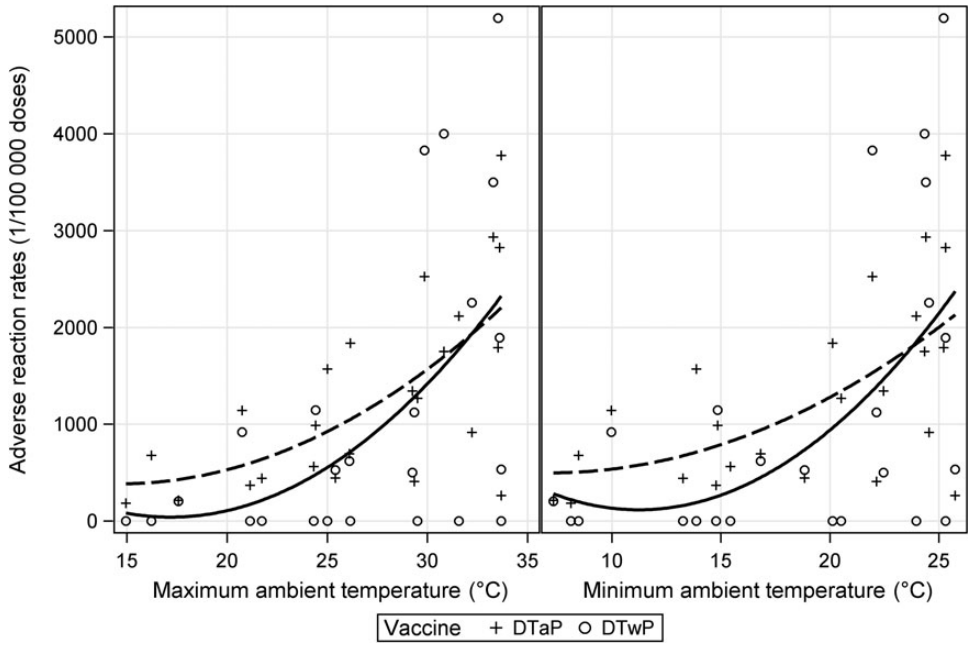

Figure 1. Associations between maximum and minimum temperatures and adverse reactions of 2 pertussis vaccines**.** Scatterplot with regression fitting. The dashed line stands for diphtheria-tetanus-pertussis acellular vaccine (DTaP), and the solid line for diphtheria-tetanus-pertussis whole-cell vaccine (DTwP).

Table 1. Relative Risk for Adverse Reactions of Pertussis Vaccines

Model	DTwP Relative Risk (95% CI)	DTaP Relative Risk (95% CI)
Model I		
Maximum temperature	1.15 (1.06–1.25)	1.07 (1.02–1.12)
Sun exposure duration, h	0.92 (.65–1.29)	0.99 (.85–1.16)
Model II		
Minimum temperature	1.12 (1.05–1.20)	1.05 (1.01–1.10)
Sun exposure duration, h	1.04 (.74–1.47)	1.05 (.89–1.23)

Abbreviations: CI, confidence interval; DTaP, diphtheria-tetanus-pertussis acellular vaccine; DTwP, diphtheria-tetanus-pertussis whole-cell vaccine.

relative risk $[RR]_{DTwP}$: 1.15; 95% confidence interval [CI], 1.06–1.25; and RR_{DTaP}: 1.07; 95% CI, 1.02–1.12) and minimum temperature (model II: RR_{DTwP}: 1.12; 95% CI, 1.05–1.20; and RR_{DTaP}: 1.05; 95% CI, 1.01–1.10) were statistically significantly associated with the occurrence of ARs (Table 1).

Vaccines are sensitive to temperature variation [7]. Either direct exposure to heat when handling vaccination outside the cold chain, or inappropriate exposure to excessive freezing temperature within the cold chain in hot weather, may influence the quality of vaccine and increase ARs.

Failure to follow the temperature requirement of vaccines may lead to more ARs. The agglutination of aluminium-based excipients under the exposure may result in more systematic or local reactions for pertussis vaccines [5]. Although ARs often occur as part of the immune response, a quality and safe vaccine usually reduces ARs to a minimum while eliciting the maximum immunity [5]. The recent resurgence of pertussis outbreaks in many countries raises concerns about the potency of DTaP, the effectiveness of the switch from DTwP to DTaP, and the complementary "cocooning strategy" dealing with the waning immunity of DTaP [1]. It is important to maintain safety of DTaP and DTwP and to develop a more stable and effective pertussis-contained vaccine within the context of climate change.

Notes

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References

1. Cherry JD. Epidemic pertussis in 2012—the resurgence of a vaccine-preventable disease. N Engl J Med **2012**; 367:785–7.
2. Chen RT, DeStefano F. Vaccine safety. Lancet **1998**; 352:63–4.
3. Liang X-F, Li L, Liu D-W, et al. Safety of influenza A (H1N1) vaccine in postmarketing surveillance in China. N Engl J Med **2011**; 364:638–47.
4. Intergovernmental Panel on Climate Change. Working Group I contribution to the Fifth assessment report of the Intergovernmental Panel on Climate Change. Available at: http://www.ipcc.ch/report/ar5/wg1/. Accessed 25 January 2014.
5. World Health Organization, Regional Office for the Western Pacific Region. Immunization safety surveillance: guidelines for immunization programme managers on surveillance of adverse events following immunization. 2nd ed. Manila, Philippines: WHO Press, **2013**:112.
6. US Agency for International Development. Immunization essentials: a practical field guide. Washington, DC: USAID, **2003**.
7. World Health Organization, Department of Immunization and Biologicals. Immunization in practice: a practical guide for health staff. Geneva, Switzerland: WHO, **2004**.

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