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Bordetella pertussis variants lacking the vaccine antigen pertactin: first detection in the United States

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To the Editor

Global vaccination of children has dramatically reduced the incidence of illness and deaths from *Bordetella pertussis*, the causative agent of whooping cough. However, increased cases of whooping cough have recently been reported in several countries including the US. While there has been much attention given to waning immunity associated with the introduction of acellular vaccines[1], another factor contributing to the outbreaks may be adaptation of *B. pertussis* to vaccine selection pressure. Pertactin (prn) is a component of acellular vaccines. Pertactin-negative variants of *B. pertussis* have recently been reported in clinical isolates from Japan, France and Finland. The variants from Japan and Finland had deletions or insertion sequences in the *prn1* allele; the French isolates had deletions or truncations in the *prn2* allele.[2,3] Pertactin mutants retain lethality in mouse models of infection and are transmissible in humans.[2]

We analyzed the pertactin genes from twelve isolates of *B. pertussis* cultured from children hospitalized in Philadelphia during 2011–12 (Table 1). The entire coding region for pertactin was amplified and sequenced.[3,4] PFGE was performed with *Xba*I as the restriction enzyme.[4] The PFGE profiles were determined using the CDC database for US isolates. For Western blots, pertactin was detected using anti-69K antiserum (NIBSC#97/558) with WHO strain 18323 serving as the pertactin-positive reference strain.

By Western blot, eleven of the twelve *B. pertussis* isolates were negative for pertactin. Sequencing revealed that four of these isolates had insertion sequence IS*481* disrupting the pertactin coding region and seven had a stop codon truncating the protein. By PFGE typing, three isolates with IS*481* inserted at nucleotide 1613 were identical. The seven isolates with the stop codon at amino acid position 425 were identical or >92% related. The pertactin allele in all 12 isolates was *prn2*; mutations were different from the pertactin-negative *prn2* isolates from France. In the US, *prn2* has been predominant pertactin allele since the 1990s. [5] However, multilocus sequence typing used to determine pertactin allele types would not have detected these variants, as the mutations were outside of the sequenced region.

To our knowledge, this represents the first reported occurrence of pertactin-negative variants of *B. pertussis* in the US. Isolates of *B. pertussis* from geographically-distinct regions in the US should be evaluated to determine if our finding is a local event or represents a more widespread shift in *B. pertussis* strains. Understanding of the epidemiology and virulence of pertactin-negative variants is crucial to developing optimized pertussis vaccines.

References

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Table 1

Characterization of *B. pertussis* isolates from Philadelphia, PA.

Isolate	Date of isolation	Patient age	pertactin allele	pertactin mutation (nucleotide)	pertactin western	PFGE type
19-76	Jan-2011	2 mo	*prn2*	none	+	E (CDC013)
19-77	Feb-2011	45 days	*prn2*	STOP (1273)	−	B (CDC334)
19-81	Mar-2011	9 years	*prn2*	IS (1613)	−	A (CDC237)
20-2	May-2011	16 days	*prn2*	IS (1613)	−	A (CDC237)
20-7	Jul-2011	40 days	*prn2*	STOP (1273)	−	D (CDC002)
20-8	Jul-2011	78 days	*prn2*	STOP (1273)	−	D (CDC002)
20-9	Jul-2011	83 days	*prn2*	STOP (1273)	−	D (CDC002)
20-16	Sep-2011	5 mo	*prn2*	STOP (1273)	−	B (CDC334)
20-24	Oct-2011	21 days	*prn2*	IS (1613)	−	A (CDC237)
20-29	Feb-2012	22 days	*prn2*	IS (245)	−	C (CDC010)
20-30	Feb-2012	11 days	*prn2*	STOP (1273)	−	D (CDC002)
20-39	Mar-2012	14 years	*prn2*	STOP (1273)	−	D (CDC002)