

Protecting infants from pertussis

Meghan Gilley MD Ran D. Goldman MD FRCPC

Abstract

Question With the increased rate of pertussis in children, several families have asked me about ways to protect their young infants from pertussis infection. What should I recommend to these families?

Answer Pertussis is a preventable disease that is endemic worldwide. In adults pertussis causes a mild coldlike illness followed by a persistent cough. In young infants it can cause apnea, seizures, encephalopathy, bronchopneumonia, and death. Infants younger than 4 months of age account for 86% of all deaths due to pertussis. Cocooning, the vaccination of adults in close contact with infants, is recommended by numerous global and national agencies but is likely to prevent only 20% of cases of pertussis in infants. Vaccination during pregnancy is more effective but not yet approved in Canada. Vaccination at birth has not been shown to be consistently effective and therefore is not recommended at this time.



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Pertussis (whooping cough) is a respiratory infection caused by *Bordetella pertussis* that occurs in 3 stages: catarrhal, paroxysmal, and convalescence. The catarrhal stage consists of mild respiratory symptoms that are indistinguishable from a cold. The paroxysmal stage is the most recognizable, consisting of coughing fits followed by an inspiratory whoop and posttussive emesis. This stage can last from 2 to 6 weeks, making pertussis widely known as the 100-day cough. Finally, the convalescence stage is characterized by gradual improvement over several weeks.^{1,2}

Epidemiology

The World Health Organization estimated that in 2008, 16 million people worldwide (95% of whom were in developing countries) had pertussis, causing the death of 195 000 children.¹ In 1943, the pertussis vaccine became available in Canada and it was integrated into the vaccination schedule in 1949, resulting in a considerable reduction in the incidence of pertussis.²

Almost half a century later a Canadian resurgence of pertussis began, likely secondary to a less effective vaccine, increased physician awareness, and waning immunity in adolescents and adults. Waning immunity against pertussis is caused by the bacterium's complex combination of virulence factors and toxins.^{2,3} With the introduction of a more effective vaccine and adolescent boosters, pertussis rates dropped to their lowest rate, with less than 5000 cases reported every year in Canada.²

Morbidity and mortality

Infants experience the highest incidence of morbidity and mortality from pertussis. Between 1990 and 2004, infants in the United States younger than 4 months of age accounted for 86% of all cases resulting in death.⁴ In Canada, between 2005 and 2009, the incidence of pertussis in infants younger than 1 year of age was 86 cases per 100 000 infants, with 1 to 3 deaths each year, largely in infants too young to be vaccinated.^{2,5}

Mortality is thought to be secondary to refractory pulmonary hypertension, exacerbating hypoxemia leading to shock and cardiac failure. With histopathologic examination of samples, Paddock et al found that pertussis caused occlusion of small bronchioles with necrotic debris and inflammatory leukocytes.⁵ Infants younger than 3 months of age are also more prone to apneic spells, seizures, encephalopathy, and bronchopneumonia secondary to *B pertussis*.^{2,5}

Current schedule and protection

The current North American immunization schedule recommends the acellular pertussis vaccine (diphtheria and tetanus toxoids and acellular pertussis [DTaP] vaccine) be administered to infants at 2, 4, and 6 months of age, and booster doses be administered at 18 months of age and between 4 and 6 years of age. In addition, adolescents between 14 and 16 years of age should be administered a dose of the tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine. The DTaP vaccine has full amounts of diphtheria toxoid and

acellular pertussis in addition to tetanus toxoid, whereas the Tdap vaccine contains tetanus toxoid and reduced amounts of diphtheria toxoid and acellular pertussis.² The acellular pertussis was incorporated into the tetanus booster for those 14 to 16 years of age because of waning pertussis immunity in adolescents and in order to increase herd immunity.^{2,3,6-9} Given this schedule, infants aged 0 to 3 months—the most vulnerable population—have little to no direct immunity against pertussis.⁴⁻⁷

Early infancy protection

The lack of protection for young infants, who are at the highest risk of substantial morbidity and mortality, has led to identification of strategies for earlier pertussis protection: cocooning, vaccination during pregnancy, and earlier infant vaccination.

Cocooning. Cocooning indirectly protects susceptible infants by immunizing adults who surround them.^{4,6,7} The World Health Organization, the Centers for Disease Control and Prevention (CDC), the Global Pertussis Initiative, and the Public Health Agency of Canada recommend immunizing adults who are in close contact with infants and who have not recently received a booster dose of Tdap.^{1,2,8,9}

For cocooning to be applicable, 2 assumptions must be made: 1) infants are infected with pertussis from close contacts and 2) vaccination of close contacts will prevent their infection.³ Close contacts account for 35% to 68% of pertussis infections in infants, with mothers being the most common source.^{6,7,10-12} The effectiveness of multicomponent acellular pertussis vaccines has been reported to be 85%, based on review of 6 randomized controlled trials in a systematic Cochrane review.⁶ In 2005, Ward et al examined the effectiveness of a trivalent acellular pertussis vaccine in adults and adolescents via a national US double-blind randomized controlled trial with a 2.5-year follow-up. This vaccine was found to be 92% protective when compared with controls (with a wide 95% CI of 33% to 99%).¹³

In a computer simulation study funded by Sanofi Pasteur, Coudeville et al projected which of 4 strategies for adult and adolescent immunization (not including vaccination during pregnancy) would best curb rates of pertussis infection. Cocooning with an adolescent and adult booster was found to be the best strategy to control pertussis infection, as it provided herd immunity in the pertussis reservoir.¹⁴

Two studies from Canada⁴ and Italy¹⁵ examined local retrospective epidemiologic pertussis data to calculate the number needed to vaccinate (NNV) to prevent hospital and intensive care unit admissions and deaths related to pertussis infection in infants. Infants younger than 3 months⁴ and younger than 12 months¹⁵ of age were examined. In both studies, the NNV was greater

than 10 000 to prevent 1 hospitalization (assuming close-contact transmission accounted for 35% of infant illness) and greater than 1 million to prevent 1 death.^{4,15} Assuming close-contact transmission accounted for 55% of infant illness, the NNV to prevent 1 hospitalization was greater than 5000.^{4,15} Given the high NNV, cocooning might not be an effective method in areas with a low incidence of pertussis.^{4,15}

Pertussis vaccination during pregnancy. Direct protection of infants with antibodies against pertussis via either a Tdap booster during pregnancy, causing placental transfer of maternal antibodies, or earlier administration of DTaP to neonates would protect infants not only from close contacts but also from casual contacts infected with pertussis.^{6,7} This is important because “casual contacts” (ie, people not in the home or regularly around the infant) are believed to cause 34% of infant infections.¹⁶

Using a cohort model, Terranella et al studied the cost and number of pertussis cases prevented with vaccination during pregnancy versus the cocoon method. Vaccination during pregnancy prevented more cases of infant pertussis and deaths than cocooning did (33% vs 20% and 49% vs 16%, respectively), and had a lower cost per quality-adjusted life-year.¹⁷

Although data on the safety of Tdap during pregnancy are limited, reports from the CDC, the US Food and Drug Administration, and pharmaceutical pregnancy registries indicate no safety concerns.^{6,18,19} Moreover, the Advisory Committee on Immunization Practices, part of the CDC, has recently published a statement that supports vaccination of pregnant mothers in their third trimester of pregnancy as a preventive strategy for infant pertussis.¹⁸ In Canada, routine immunization of women during their second or third trimesters with Tdap is currently under review by the National Advisory Committee on Immunization.³

Earlier infant vaccination. The immunization of newborns might prevent infant pertussis with direct antibody protection. The strategy involves either DTaP or acellular pertussis immunization at birth, followed by the regularly scheduled immunizations at 2, 4, and 6 months of age.⁶ Halasa et al found evidence of decreased mean antibody levels against pertussis toxin, as well as virulence factors pertactin and fimbriae, later in infancy when newborns were vaccinated with DTaP at birth.²⁰ Two other studies that reviewed the strategy of acellular pertussis immunization at birth followed by the regular schedule found enhanced pertussis antibodies but decreased *Haemophilus influenzae* B and hepatitis B antibodies later in infancy.⁷ Ultimately, this strategy has not garnered support because there is insufficient literature to support its effectiveness.⁷

Conclusion

Currently, the National Advisory Committee on Immunization is reviewing vaccination during pregnancy with Tdap as an indication for prevention of pertussis infection in infants. The literature indicates that this is a more effective strategy than cocooning or vaccination at birth. Until vaccination during pregnancy is approved, the recommended method of protection is cocooning, vaccination with a Tdap booster of adults living with young infants. 🌸

Competing interests

None declared

Correspondence

Dr Ran D. Goldman, BC Children's Hospital, Department of Pediatrics, Room K4-226, Ambulatory Care Bldg, 4480 Oak St, Vancouver, BC V6H 3V4; telephone 604 875-2345, extension 7333; fax 604 875-2414; e-mail rgoldman@cw.bc.ca

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Dr Gilley is a member and Dr Goldman is Director of the PRETx program. The mission of the PRETx program is to promote child health through evidence-based research in therapeutics in pediatric emergency medicine.

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