

Maternal immunisation in third trimester of pregnancy – evidence review



KEY POINTS:

1. Pertussis vaccination during pregnancy has been shown to be safe during pregnancy in studies involving over 40,000 women.
2. Vaccination during pregnancy has been shown to be the most effective way to protect infants from pertussis until they are old enough to receive their own immunisation.
3. Maternal antibodies in response to vaccination are transferred in utero to the foetus providing protection from birth.

BACKGROUND

The current NSW pertussis vaccination schedule [1] is based on national guidelines [2]. Vaccination is recommended for children at 6-8 weeks, 4 and 6 months of age, with a booster at 3½ -4 years and in the first year of high school. Vaccination is also recommended for women planning pregnancy or in their third trimester of pregnancy, individuals living with or caring for infants (parents, siblings, grandparents, childcare workers), as well as for all health care workers.

Current strategies to protect infants before they commence their primary vaccination schedule such as cocooning have been difficult to implement, and have limited evidence of effectiveness [3], with a recent study finding a 51% (95% CI, 10-73%) reduction in infant pertussis cases when both parents were vaccinated at least 4 weeks before onset [4].

Recent evidence suggests that infants (who are at the greatest risk for pertussis associated morbidity and mortality [5, 6]) will receive greater protection through maternal vaccination in the third trimester of pregnancy. The greater protection of infants is likely due to the combination of direct in utero transfer of antibodies to the infant and indirectly through reducing the likelihood of the mother acquiring and transmitting pertussis [3, 5]. Third trimester vaccination of pregnant women is likely the most effective strategy to protect infants against pertussis disease until their pertussis vaccination schedule begins at six weeks of age.

Recent cost analysis from the US has also found that pertussis vaccination during pregnancy would avert more infant cases and deaths at a lower cost than vaccination of the mother after birth even when combined with cocooning strategies [7].

EFFECTIVENESS

Vaccination of women during pregnancy has been shown to be highly effective at preventing disease in new born infants.

The UK, in response to a nationwide pertussis epidemic, implemented a pertussis vaccination program for pregnant women [3]. Two subsequent evaluations of the program have both found vaccine effectiveness for preventing infant pertussis to exceed 90%, providing the first strong evidence of the effectiveness of maternal vaccination to protect infants [3, 5].

In an observational study conducted in England, vaccination of pregnant women in the third trimester was found to have vaccine effectiveness for preventing pertussis in children aged less than three months of 91% (95% CI, 84-95%) compared to 38% (95% CI -95-80%) for those vaccinated between six days before birth and up to 13 days after birth. The study also found that in the year prior to the program there were 14 deaths in infants with confirmed pertussis. Post implementation there were three deaths all of whom were infants whose mothers were not vaccinated during pregnancy. The study was based on 26,684 live births collected from 520

GPs which were representative of the English population [3].

A similar result was found in a case control study conducted over the same period in England and Wales with a vaccine effectiveness for preventing pertussis of 93% (95% CI, 81-97%) in infants aged less than eight weeks [5].

SAFETY

Although inactivated vaccines such as the diphtheria, tetanus and pertussis vaccine (dTpa) are viewed as safe for use during pregnancy by the World Health Organization (WHO) Global Advisory Committee on Vaccine Safety [8], it is only recently that studies directly assessing the safety of pertussis vaccination during pregnancy have been published [9-13].

Current evidence (from studies involving more than 40,000 participants) suggests that vaccination during pregnancy is safe for both the mother and baby. Studies, including a large observational study and a randomised clinical trial, have found no increased risk of adverse events or adverse pregnancy outcomes such as stillbirth, hypertensive disorder of pregnancy, preterm birth or small for gestational age birth [9, 10, 12, 13].

IMMUNE RESPONSE

Placental transfer of pertussis antibodies has been shown after recent maternal immunisation with acellular vaccine [14]. In a randomised



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clinical trial higher antibody levels were observed at birth and at two months in infants whose mother had been vaccinated during pregnancy compared to those whose mothers were vaccinated after birth (Table 1) [11]. Maternal antenatal vaccination also had no significant impact on infant antibody levels after their primary course with no evidence of immune “blunting” in the infants [11].

Table 1. geometric mean concentrations of antibodies to dTpa pertussis antigens in sera from infants whose mothers were vaccinated antepartum or postpartum [11]. Antibodies are measured in EU/ml and 95% CI of geometric mean concentrations is shown.

Antigen/Study Group	At birth (cord blood)	Months		
		2	7	13
Pertussis toxin				
Antepartum	68.8 (52.1-90.8)	20.6 (14.4-29.6)	64.9 (53.8-78.3)	80.1 (57.3-112.1)
Postpartum	14.0 (7.3-26.9)	5.3 (3.0-9.4)	96.6 (56.7-164.6)	83.9 (50.0-140.8)
Filamentous hemagglutinin				
Antepartum	234.2 (184.6-297.3)	99.1 (75.8-129.6)	40.6 (30.6-54.0)	69.9 (49.5-98.7)
Postpartum	25.1 (10.6-60.3)	6.6 (2.8-15.5)	78.6 (52.9-116.7)	108.9 (78.3-151.5)
Pertactin				
Antepartum	219.0 (134.4-357.0)	71.1 (42.4-119.1)	72.3 (48.7-107.4)	203.3 (121.5-340.1)
Postpartum	14.4 (5.4-38.4)	5.2 (2.4-11.5)	77.9 (38.9-152.6)	115.2 (54.8-242.1)

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