

## Two studies on influenza immunization of mothers and its protective effect for their children

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### Influenza Vaccine Given to Pregnant Women Reduces Hospitalization Due to Influenza in Their Infants

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This hypothesis for this study is that vaccination of women during pregnancy may protect the infant through transfer of antibodies from the mother. To conduct the study the authors undertook a matched case-control study from 2000 to 2009, where case patients were infants aged <12 months admitted to a large urban hospital in the North East of the United States diagnosed with laboratory-confirmed influenza. The matching was used 1 or 2 controls per case who were infants matched for date of birth and date of hospitalization (within 4 weeks) with the cases but who tested negative for influenza. Confounding adjusted vaccine effectiveness was calculated using matched odds ratios.

Information about vaccinations and co-morbidities of the infants was obtained by reviewing records of all providers of medical care. The mothers' medical records from primary medical providers, obstetricians, pharmacies, and anywhere else the mother stated that she had received influenza vaccine were reviewed. This information was then used to ascertain whether a woman had received influenza vaccine during pregnancy, whether she had received the vaccine at any time prior to that pregnancy, and whether she had received the vaccine during the same influenza season as the infant's hospital admission. To include a case or control written documentation of receipt of influenza vaccine during her pregnancy, excluding vaccinations received within 14 days of delivery, had to be identified.

The authors presented the results for two age groups: infants aged less than 6 months and infants aged 6 months or over. Among the group of infants aged less than 6 months it was found that the mothers of 2 out of 91 (2.2%) cases and the mothers of 31 out of 156 (19.9%) controls were vaccinated against influenza during pregnancy. Similarly, among the group of infants aged 6 months or over the authors found that the mother of 1 out of 22 (4.6%) cases and the mothers of 2 out of 36 (5.6%) controls were vaccinated against influenza during pregnancy. The vaccine effectiveness was calculated with these data; in this way, the effectiveness of influenza vaccine given to mothers during pregnancy in preventing hospitalization among their infants, adjusted for potential confounders, was estimated to be 91.5% (95% confidence interval; 61.7% - 98.1%) among the group of infants aged <6 months, and -41.4% (95% confidence interval; -2257.3% - 91.5%) among the group of infants aged 6 months or over. Hence it was concluded that influenza vaccine given to pregnant women was 91.5% effective in preventing hospitalization of their infants for influenza in the first 6 months of life. In the contrary, influenza vaccine given to pregnant women was ineffective in preventing hospitalization of their babies because of influenza after the age of 6 months.

### Transplacental Antibody Transfer Following Maternal Immunization With a Pandemic 2009 Influenza A(H1N1) MF59-Adjuvanted Vaccine

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The aim of this study was to evaluate the antibody presence in women immunized with a pandemic influenza A(H1N1) MF59-adjuvanted vaccine during pregnancy and to assess the duration of passively acquired maternal antibodies in their infants. This study was conducted in Milan, Italy, over October and November 2009, when the pandemic influenza virus was transmitting vigorously. In the study women in their third trimester of pregnancy were offered a single dose of 0.5 ml of MF59-adjuvanted influenza A(H1N1) vaccine, which contained 7.5 µg of A/California/07/2009(H1N1)-haemagglutinin antigen. The exclusion criteria was influenza vaccination during the preceding year. If mothers consented maternal blood was collected at delivery and at 2 and 5 months after birth. Again with parental consent infant blood was obtained within 2 days of birth and 2 and 5 months of age. The antibody responses were determined by haemagglutination-inhibition (HI) assay, and for immunogenicity analyses the authors calculated the geometric mean antibody titres and the proportions of participants who achieved a titre of 1:40 or above (the level considered to be protective for seasonal vaccination). Sixty nine maternal-infant pairs completed the study.

All mothers had HI-antibody titres to the 2009 pandemic virus of 1:40 or above at the time of delivery and during the follow-up period. The proportion of infants with HI-antibody titres of 1:40 or above was 95.6% at birth, declining to 81.2% at around 5 months of age. Maternal geometric titres (GMTs) were similar among mothers, decreasing around 5 months later, however, in infants GMTs progressively decreased during the 5-month follow-up period. The trans-placental transfer of antibodies, defined as the GMT ratio of the HI-antibody titres in infants and mothers at time of delivery, was 0.55 (95% CI, 0.49-0.61). The estimated half-life of passively acquired maternal antibody against A/California/07/2009(H1N1) was 83.4 days. No serious adverse events were reported in mothers and infants and none of them developed influenza-like illness during the 5-month follow-up period. These findings suggest that passively acquired serum antibody levels following immunisation of infants resulting in protection can persist in most infants for at least 5 months.

### ECDC Comment (10<sup>th</sup> December 2010):

During the 2009 pandemic pregnant women were at increased risk of experiencing a severe clinical outcome if infected with the H1N1 virus [1-3]. An increased risk of influenza complications in pregnant women has been observed also during seasonal influenza epidemics, although the risk was lower than what usually seen in pandemics [4, 5]. Incidence of influenza is usually higher in children but those below 2 years of age are at increased risk of hospitalization if infected with an influenza virus [6-11]. The risk of severe influenza illness and complications in children increases with decreasing age and in those with pre-existing conditions. Six months old children - and younger - are not eligible for influenza vaccination due to limited data on vaccine safety and effectiveness in this age-group.

These two studies conducted in different settings and using different designs came up to the same conclusion that vaccination of pregnant women either with the trivalent seasonal influenza vaccine (TIV) or with the 2009 monovalent A (H1N1) pandemic vaccine confers protection against influenza infection to their newborn infants during the first 5-6 months of life. Results are consistent with an earlier study conducted in Bangladesh and coming up with a similar vaccine effectiveness estimate [12].

These findings are of public health relevance and indicate that influenza immunisation offered to all pregnant women on a routine basis can be a highly effective strategy. Both the trivalent and the 2009 monovalent influenza vaccines can be used safely during pregnancy and can be administered at any pregnancy trimester [13]. During pregnancy various contacts with the health services usually occur. These are opportunities for offering vaccination with the seasonal vaccine to all pregnant women for whom there is no contraindication to influenza vaccination thus also offering protection to their vulnerable offspring.

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