Vaccination against influenza in pregnant women

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Pregnancy places otherwise healthy women at an increased risk of complications arising from an influenza infection. It is suggested that physiological changes such as immunological changes, increased cardiac output and oxygen consumption, as well as lung tidal volume might increase the susceptibility to influenza complications if infection occurs during pregnancy. Immunization of pregnant women against influenza is currently recommended in many countries and has been proven to be safe and effective in reducing rates and severity of the disease in vaccinated mothers and their children. Influenza vaccination is also cost-effective. Nevertheless, influenza vaccine coverage remains low in pregnant women. This might stem from the lack of healthcare workers' education, a feeling among the general public that influenza is not a serious disease and a failure of prenatal care providers to offer the vaccine. In order to protect pregnant women and infants from influenza related morbidity and mortality an educational programme targeting healthcare workers in charge of pregnant women should be implemented.

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INFLUENZA IN PREGNANT WOMEN AND THEIR INFANTS

Pregnant women form a special group of patients that, although infected with influenza with similar frequency as general population, display complications more frequently. Pregnant women are more often admitted to hospitals with cardiac complications in the course of influenza than women in the postpartum period. The risk of complications depends on the pregnancy stage and is higher at 37–42 weeks of gestation compared with 21–26 weeks of gestation (Neuzil et al., 1998). Interesting data come from observations made during the last influenza pandemic: 32% of pregnant women suffering from the flu required hospitalization, whereas the appropriate rate in the general population was 8% (Jameson et al., 2009). Furthermore, 9% of pregnant women hospitalized due to influenza required treatment in the intensive care unit (ICU), 20% of whom were diagnosed with pneumonia that in some patients led to the development of acute respiratory distress syndrome (Jameson et al., 2009).

Pregnant women were over 7 times more often hospitalized, and 4.3 times more likely required treatment in the ICU when compared with the general population (Creanga et al., 2010). It was also calculated that among all deaths from influenza in 2009–2010, 4–13% of them concerned pregnant women (Creanga et al., 2010; WHO, 2010). Factors increasing the risk of severe course of influenza in pregnant women are associated with physiological changes occurring mainly in the third trimester of pregnancy, including debilitating changes in the immune system, increased cardiac ejection fraction, increased oxygen consumption and reduced lung volume (Puck et al., 1980; Creanga et al., 2010; Steinhoff et al., 2010).

The effect of influenza virus infection on the fetus is not fully understood. Fetus viremia in the course of infection with influenza virus is rarely ascertainment, but transplacental transmission of influenza viruses is possible, as evidenced by descriptions of the disease in newborns (Fisher et al., 2012). It is known that infection during pregnancy increases the risk of miscarriage and premature births and stillbirths. This also applies to infections caused by the influenza virus (Stanwell-Smith et al., 1994; Louie et al., 2009; Leick-Courtois et al., 2011). Some researchers have suggested there is a relationship between mother’s influenza virus infection and the incidence of fetal birth defects such as a cleft palate, neural tube development disorders or congenital heart defects (Stanwell-Smith et al., 1994). However, it seems that the influenza virus has no direct teratogenic effect and damage to the fetus may be caused by a fever. Indeed, it has been shown that if fever occurs in women in the third trimester of pregnancy, it is associated with the occurrence of neural tube defects of the fetus and seizures in the neonatal period (Nishiura et al., 2009).

It should be emphasized that currently registered and available influenza vaccines are meant for individuals over 6 months of age and when outbreaks of influenza occur in younger infants they carry a high risk of complications, hospitalization and death. Indeed, outbreaks of infections caused by influenza virus have been described in neonates (Pierce et al., 2011). Data from the season 2003/2004 in the United States indicate that the death rate from influenza in infants aged 0–6 months was 88/100,000, with only one third of deaths that could be attributed to chronic diseases such as bronchial asthma, chronic lung disease or cardiovascular conditions (Glass et al., 2009). The question is “How can we protect newborns and young infants from influenza virus infections?” Undoubtedly, a protective role is played by maternal antibodies transferred transplacentally (IgG antibodies) and during lactation (IgA antibodies) to the...
child (Englund et al., 1993). Duration of passive protec-
tion seems to depend on the concentration of the an-
tibody in the cord blood and is believed to operate up
to 6 months of age (Englund et al., 1993). Accord-
ingly, children with higher levels of antibodies in the cord
blood had flu occurring at a later age, and less severe
than in children with lower levels of antibodies derived
from the mother (Puck et al., 1980).

INFLUENZA VACCINATION IN PREGNANT WOMEN,
PROOFS OF SAFETY AND IMMUNOGENICITY, EFFECT
ON INFANTS

Influenza vaccines (inactivated split virion vaccine
or subunit vaccine) were given to millions of pregnant
women in the world with no harmful effects on either
the mother or the child. During the 2000–2003 season,
an estimated 2 million pregnant women were immunized
and only 20 adverse events among women who received
TIV were reported to Vaccine Adverse Event Reporting
System (VAERS), including nine injection-site reactions
and eight systemic reactions (e.g., fever, headache and
myalgia). In addition, three miscarriages, not known to
be causally related to the vaccination, were reported (Is-
cander et al., 2006). The incidence of adverse reactions
was similar among vaccinated and unvaccinated women
(Munoz et al., 2005), and there was no increased risk of
obstetric complications during pregnancy (Sumaya et al.,
1979; Sheffield et al., 2011) or more cesarean deliveries
in vaccinated women, including the risk of the preterm
delivery (Black et al., 2004; Englund et al., 1993; Zaman
et al., 2008). Importantly, the efficacy of pregnant wom-
en vaccination in reducing the number of respiratory
infections with fever and reducing the number of cases
of influenza and hospitalization due to influenza in chil-
dren born to mothers vaccinated against influenza during
pregnancy has been extensively demonstrated.

One of the first published papers aimed to determine
the effectiveness of influenza vaccination in pregnant
women was a randomized controlled study conducted by
Zaman and coworkers (2008), which involved more than
300 patients in Bangladesh in the season 2004/2005.
The authors proved a reduction in the number of infec-
tions with influenza-like symptoms and fever in mothers
by 36% and demonstrated that 88% of vaccinated wom-
en produced protective levels of antibodies after vaccina-
tion (Zaman et al., 2008). Later study by Thompson and
coworkers (2014) provided further substantial evidence
on the effectiveness of the vaccination against influenza
in pregnant women demonstrating that influenza vac-
cination of pregnant women reduced the risk of getting
the flu by 50%.

Vaccination of pregnant women against influenza pro-
tects their infants. Benowitz and coworkers (2010) indi-
cated 92% effectiveness of vaccination during pregnancy
in preventing hospitalization due to influenza in chil-
dren 12 months after delivery. Poehling and coworkers
(2011) demonstrated that infants of mothers vaccinated
during pregnancy had a reduced risk of hospitalization
due to flu by 45–48%. Eick and coworkers (2011) also
showed that children born by vaccinated mothers had
the risk of influenza reduced by 41% and the risk of
hospitalization arising from infection with influenza-like
symptoms reduced by 39%.

Influenza vaccines administered during pregnancy did
not show any harmful effects on fetuses, newborns and
infants. No differences have been observed in the de-
velopment of infants during their first 6 months of age
(Munoz et al., 2005; Sheffield et al., 2011). No differences
in the incidence of preterm births, incidence of low birth
weight among two groups have been revealed (Zaman
et al., 2008). Omer and coworkers (2011) showed a lower
risk of intrauterine immaturity and hypotrophy among
infants of vaccinated women.

RECOMMENDATIONS FOR INFLUENZA VACCINATION
OF PREGNANT WOMEN

Recommendations for influenza vaccination of
pregnant women in the second and third trimester of
pregnancy using inactivated virus have been imple-
mented in the United States and Canada for over 10
years. They were first published by the U.S. Adviso-
ry Committee on Immunization Practices (ACIP) in
1997; in 2004 these recommendations were expand-
ed, recommending influenza vaccination not only in
the second and third trimesters, but also in the first
trimester of pregnancy (in both healthy women and
those affected by chronic diseases, which might con-
stitute a risk factor for severe and complicated course
of the flu) (ACIP, 2005). The WHO in 2005 recom-
manded vaccination for all pregnant women during an
epidemic season (WHO, 2005). Vaccination against
influenza in pregnant women has also been recom-
mented by the American College of Obstetricians
and Gynecologists (ACOG, 2004). Despite the official
recommendations of experts, the level of vaccinations
against influenza in the population of pregnant wom-
en is very low and varies from of 2 to 20% (CDC,
2010). The reasons of low influenza vaccination rates
among pregnant women can be such as: lack of physi-
cians’ recommendation, difficulties with access to vac-
cinations in obstetric and gynecological wards, insuffi-
cient knowledge about influenza and its complications
in pregnant women and medical professionals, scarce
knowledge concerning safety and efficacy of influen-
za vaccination both in pregnant women and medical
staff, the common belief expressed by patients that the
flu is not a serious disease, lack of reimbursement
of vaccination, or even the misconception that vac-
cination against influenza can cause flu (Panda et al.,
2010; Tong et al., 2010; Yudin et al., 2011). Indeed,
some studies indicate insufficient medical knowledge
concerning influenza vaccination in pregnancy: 40%
of surveyed doctors and nurses did not know that
pregnant women were in the high risk group for com-
plicated and severe course of influenza and only 65%
were aware of recommendations for influenza vacci-
nations for this group of patients (Panda et al., 2010;
Tong et al., 2010; Yudin et al., 2011). All this shows
that intensive educational efforts should be directed
toward medical staff, especially those taking care of
women of childbearing age, in order to improve the
influenza immunization status among this patient pop-
ulation. Vaccines-related topics, including vaccination
against influenza among pregnant women, should be
implemented into the national courses for medical
and nursing students (pre-graduate educational level)
and also should be a part of postgraduate continu-
ous medical education. Researchers need to monitor
vaccination-related intentions, attitudes, and behaviors
among patients. Psychometrically validated tools also
must be developed and implemented in longitudinal
studies in order to capture and measure baseline atti-
dutes to vaccination and then track their evolution in
near real time (Thompson et al., 2012).