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Vaccinations In Pregnancy

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ABSTRACT

This article gives a brief update of vaccinations in pregnancy.

INTRODUCTION

Pregnancy is a period of relative immunosuppression, making pregnant mothers at greater risk of infections, with associated increased morbidity and mortality rates. Also, during the period of early infancy, especially the first 6 months of life where the neonatal immune system is yet able to mount a good immune response, infants have a greater susceptibility to infections and its potentially devastating consequences. In fact, more than 2 million newborns and infants under the age of 6 months die each year worldwide from infection.[1-3] The rationale for antenatal vaccination thus works on a two-pronged approach - protection for the mother from diseases which could potentially have an impact on her health, as well as providing passive protection to the neonate or infant via trans-placental transmission of maternal antibodies to the fetus.

Having recognised the clinical benefits and large reaching impact of antenatal vaccination, the Ministry of Health (Singapore) recently extended the use of Medisave for Vaccines under the National Adult Immunisation Schedule (NAIS) as one of the measures to improve vaccination uptake rates. From 1st November 2017, Singaporeans have been able to use their Medisave for NAIS vaccinations at Medisave-accredited healthcare institutions, such as hospitals, polyclinics, and CHAS GP clinics, and this includes both the influenza inactivated vaccine as well as the tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine.

This article discusses the above-mentioned two vaccines specifically recommended during the antenatal period of pregnancy with regards to the benefits and rationale for vaccination, contraindications and side effects of these vaccines as well as current recommendations from local and international guidelines.

INFLUENZA AND INFLUENZA VACCINATION IN PREGNANCY

Influenza infection

Influenza is a highly infectious respiratory viral illness that is transmitted person to person through respiratory droplets propelled by coughing and sneezing or via contact with contaminated surfaces. The contagious period is from 1 day before onset of symptoms till 5 to 7 days after onset. Common symptoms include fever, headache, chills, cough, sore throat, muscle aches and generalized malaise and fatigue.

Burden of disease

Locally in Singapore, influenza is commonly seen, with between 1500 and 3500 people experiencing influenza-like illness every week. Most infected people have mild illnesses and will recover within 1 to 2 weeks, but certain populations (e.g. pregnant women, children under 59 months, the elderly, individuals with chronic medical conditions, individuals with immunosuppressive conditions) are at higher risk of morbidity such as the

development of severe illness, an increased need for hospitalization or admission to an intensive care unit, as well as death. The World Health Organisation estimates that worldwide, inter-pandemic influenza (seasonal flu outbreaks that occur between worldwide epidemics) are estimated to result in about 3 to 5 million cases of severe illness, and about 290 000 to 650 000 respiratory deaths in total.[4] A local study done in 2006 estimated the annual influenza-associated all-cause deaths, underlying pneumonia and influenza deaths, and underlying circulatory and respiratory deaths in Singapore to be 14.8, 2.9, and 11.9 per 100,000 person-years, respectively. This translated to an estimated 588 deaths (3.8% of total deaths) due to influenza annually.[5]

Risks of influenza infection

Maternal

Influenza infection in pregnancy is associated with a higher likelihood of developing severe illness, hospitalization and admission to an intensive care unit compared to that of the general population. Mortality rates are also higher in the pregnant patient.

Fetal

There have been reports of influenza infection in pregnancy being associated with an increased risk of obstetric complications such as spontaneous abortion, preterm delivery, low birth weight and fetal death, as well as a potential increased risk of congenital abnormalities for influenza or influenza-related illness in the first trimester. The effect of maternal hyperthermia as a result of influenza illness may also increase the risk of certain birth defects.

Neonatal

Infants less than 6 months old who experience influenza virus infection have the highest rates of hospitalization and death of all children.

Rationale for antenatal influenza vaccination

The efficacy of inactivated influenza vaccine among adults has been demonstrated in various randomized placebo-controlled trials with the outcome of laboratory-confirmed influenza. A recent meta-analysis reported a pooled vaccine efficacy of 59% (95% confidence interval, 51–67%) for the trivalent inactivated influenza vaccine among adults aged 18–64 years.[6] The immunogenicity and safety of the quadrivalent vaccine is similar to that of the trivalent vaccines.[7] Antenatal influenza vaccination thus helps to protect the pregnant mother and reduce the risk of serious maternal medical complications whilst providing passive protection to the neonate via trans-placental transmission of antibodies, especially in the early few months of life.

Inactivated influenza vaccine

The inactivated influenza vaccine is safe in all trimesters of pregnancy, with studies conducted by the Centre for Disease Control and Prevention (CDC) showing no evidence of a link between vaccination and pregnancy complications or adverse fetal outcomes. The vaccine is administered as a single dose repeated yearly with the updated vaccine.

Common side effects experienced after influenza vaccination include soreness, redness or swelling from the shot, fainting, headache, fever, muscle aches, nausea and fatigue. If these side effects occur, they usually begin soon after the shot is administered and can last for about 1 to 2 days. Rarely, influenza vaccines can cause serious problems such as severe allergic reactions. People who have had a severe allergic reaction (e.g. anaphylaxis) after a previous dose or a severe allergy to any of the vaccine components should abstain from getting the vaccine.

Table 1. Current international guideline recommendations

UK (Public Health England)	Inactivated influenza vaccine should be offered to pregnant women at any stage of pregnancy (1 st , 2 nd or 3 rd trimesters), ideally before influenza viruses start to circulate.
CDC Advisory Committee on Immunization Practices and American College of O&G (ACOG)	All women who are pregnant or will be pregnant during influenza season should receive inactivated influenza vaccine, regardless of trimester.
Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)	Influenza vaccination is recommended for all pregnant women regardless of gestation and for women planning pregnancy. Vaccination early in the season and regardless of gestational age is optimal, but unvaccinated pregnant women should be immunized at any time during influenza season as long as the vaccine supply lasts.
Society of Obstetricians and Gynaecologists of Canada (SOGC)	Pregnant women should be offered the influenza vaccine when pregnant during the influenza season.

Table 2. Current local guideline recommendations

Clinical Practice Guidelines on Adult Vaccination (April 2016)	Routine influenza (inactivated) vaccine for pregnant women is strongly recommended.
Ministry of Health (Singapore) National Adult Immunisation Schedule (NAIS)	Women at all stages of pregnancy should receive 1 dose of influenza vaccine annually.

PERTUSSIS VACCINATION IN PREGNANCY

Pertussis infection

Pertussis, also known as whooping cough, is a highly contagious respiratory disease caused tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) by the bacterium Bordetella pertussis. It is transmitted from person to person usually via coughing or sneezing or via close contact in an enclosed environment. Symptoms usually develop within 5 to 10 days after exposure, but sometimes not for as long as 3 weeks. Pertussis has an insidious onset with catarrhal symptoms that are indistinguishable from those of minor respiratory tract infections. The cough, which is initially intermittent, becomes paroxysmal. In typical cases paroxysms terminate with an inspiratory whoop and post-tussive vomiting can follow. The cough typically persists for 1 to 6 weeks or more.

There has been an increase in the number of reported cases of pertussis since the 1980s worldwide. Several factors may have contributed to this observation, and these include: 1) increased awareness and recognition of pertussis among healthcare practitioners; 2) greater access to and use of laboratory diagnostics; 3) increased surveillance and reporting of pertussis infections to public health departments; 4) waning immunity from vaccines.

Burden of disease

In 2015, the World Health Organization (WHO) reported 142,512 pertussis cases globally, and estimated that there were 89,000 deaths. However, a recent publication modeling pertussis cases and

deaths estimates that there were 24.1 million pertussis cases and 160,700 deaths in children younger than 5 years in 2014 worldwide – numbers significantly higher than what had been reported by the WHO.[8]

Locally, according to the statistics published by the Ministry of Health (MOH), the number of whooping cough cases has more than doubled since 2012 – the number of laboratory confirmed cases of pertussis increased from 24 in 2012[9] to 57 in 2015[10] and to 86 in 2016.[11] More than half of the cases reported in 2015 and in 2016 occurred in infants aged less than six months.

Risks of pertussis infection

Maternal

There is no evidence of pertussis infection in pregnancy being more severe compared to the general population, nor is there any evidence that pertussis infection is associated with increased obstetric complications in pregnancy.

Fetal

There is no evidence of pertussis infection in pregnancy being associated with an increased risk of fetal complications.

Neonatal

Neonates and infants are particularly at risk of serious pertussis infection as they remain vulnerable until they can be vaccinated at 2 months of age. Unvaccinated or incompletely vaccinated infants less than 12 months of age have the highest risk of severe illness including hospitalization and death. In this particular group, about half need treatment in a hospital, most commonly in infants less than 6 months of age.

Of infants with pertussis who need treatment in a hospital, approximately 61% will have apnoea, 23% suffer from pneumonia, 1.1% will have seizures, 1% will die and 0.3% will have encephalopathy as a result of hypoxia from coughing or from toxins.

Rationale for antenatal pertussis vaccination

The main aim of antenatal Tdap vaccination is to provide passive protection to the neonate/infant via trans-placental transmission of antibodies so as to reduce the risks of pertussis infection in infancy and its potential complications discussed above. A CDC evaluation found that Tdap vaccination during the 3rd trimester of pregnancy prevents more than 3 in 4 cases of whooping cough in babies younger than 2 months old, thus protecting babies until they are old enough to receive the pertussis vaccine at 2 months of age.[12] Also, for babies who do acquire pertussis, the infection is typically also less serious if their mother had received Tdap antenatally during pregnancy, with Tdap during the 3rd trimester of pregnancy protecting 9 in 10 babies from infections serious enough to need hospital treatment.[12]

Vaccination is recommended with each pregnancy to provide maximal protection to every infant as vaccine-induced pertussis antibodies wane over time and the protective antibody level required in newborn infants is unknown. The above CDC evaluation found that Tdap given at any point before pregnancy was only 50.8% (95% CI, 2.1%–75.2%) effective at preventing infant pertussis, whereas the overall effectiveness of vaccination between 27–36 weeks' gestation was 78.4% (95% CI,49.8%–90.7%).[12]

Tetanus toxoid, reduced diphtheria toxoid and a cellular pertussis (Tdap) vaccine

The Tdap vaccine is safe for use in pregnancy with studies showing no link between Tdap vaccine administration and increased risk of pregnancy complications such as low birth weight or preterm delivery. The vaccine is administered as a single dose intramuscularly, preferably at the deltoid area. Maternal immune response to the vaccine peaks about 2 weeks after administration.

Common side effects experienced after Tdap vaccination include erythema, swelling, pain and tenderness at the injection site, body ache, fatigue and fever. Rarely, Tdap vaccines can cause serious

problems such as severe allergic reactions. People who have had a severe allergic reaction (e.g. anaphylaxis) after a previous dose or a severe allergy to any of the vaccine components should not receive the vaccine.

CONCLUSION

Antenatal vaccination against influenza and pertussis infection has been shown to be safe, effective and beneficial. There has been heightened awareness of the importance of antenatal vaccination in improving maternal outcomes in pregnancy as well as neonatal outcomes in the first few months of life in recent years, especially what with the marked increase in the incidence of pertussis in the world as well as increasing recognition of the detrimental impact of influenza on pregnant mothers. As obstetricians, we are primarily responsible for the care and health of our pregnant women and their unborn children. It is thus essentialfor us toeducate our patients, promote influenza and Tdap vaccination as an integral component of routine antenatal care, and support them through their decision-making processes to do what is best for them and their babies.

Table 3. Current international guideline recommendations

UK (Public Health England)	All women should be offered pertussis vaccination during each pregnancy, ideally between weeks 16 and 32 of pregnancy to maximize the likelihood that the baby will be protected from birth.
CDC Advisory Committee on Immunization Practices and American College of O&G (ACOG)	Pregnant women should receive a single dose of Tdap vaccine during every pregnancy, preferably at 27 through 36 weeks of gestation. Tdap is recommended only in the immediate postpartum period before discharge from the hospital or birthing centre for new mothers who have never received Tdap before or whose vaccination status is unknown.
Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)	Tdap vaccine is recommended as a single dose during the 3rd trimester of each pregnancy. The optimal time for vaccination is early in the 3rd trimester between 28 and 32 weeks.

Table 4. Current local guideline recommendations

Clinical Practice Guidelines on Adult Vaccination (April 2016)	Pertussis vaccination during the third trimester of every pregnancy is recommended regardless of interval from the last Tdap vaccination.
Ministry of Health (Singapore) National Adult Immunisation Schedule (NAIS)	Pregnant women should receive the Tdap vaccine between the 16 th to 32th weeks of each pregnancy, so as to provide maximal protection to each infant, including pregnancies which are closely spaced (less than 2 years). Tdap can also be considered after 32 nd week of gestation during each pregnancy. Maternal vaccination in this period may afford less protection for infants, but would potentially protect the mother from pertussis infection and thereby reduce the risk of exposure to her infant.

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