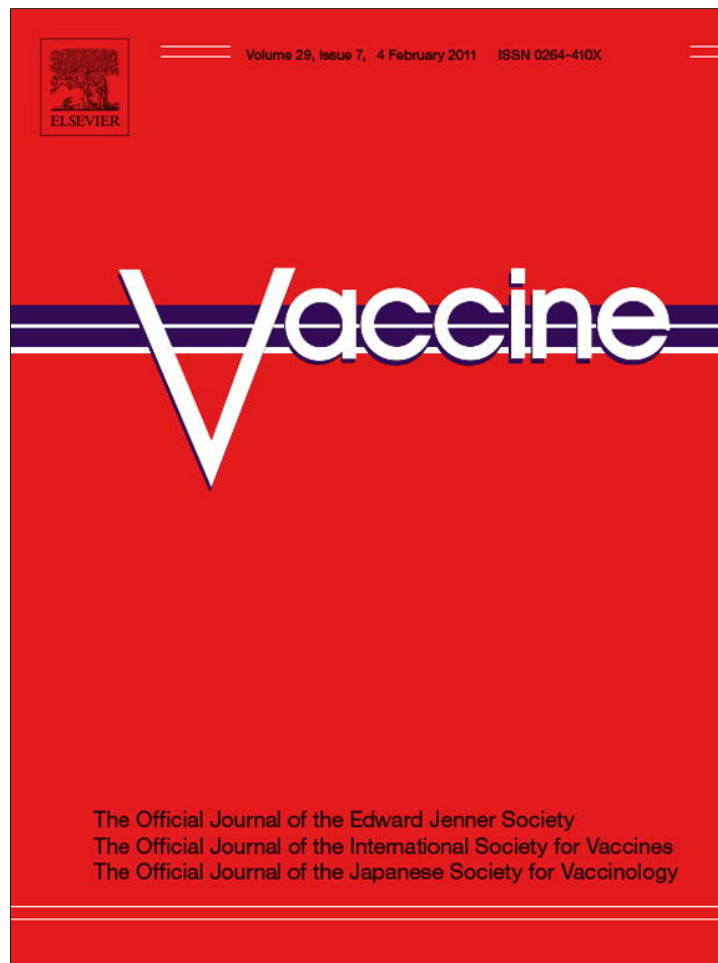


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## Letter to the Editor

**2009 H1N1 influenza vaccines in pregnant women: The French Pharmacovigilance survey**

Pregnant women are at high risk of A(H1N1) 2009 influenza complications: respiratory distress, death [1,2]. From April to August 2009, 788 cases of A(H1N1) influenza in pregnant women were reported in United States to the Centres for Disease Control and Prevention (CDC). Among them, 65% were hospitalized and 3.8% died. It has been postulated that the risk of influenza complications might be higher in the second and third trimester of pregnancy. These data support the decision of public health authorities to consider pregnant women as a priority group for vaccination. In France, it has been recommended to vaccinate all pregnant women from the second trimester of pregnancy with a nonadjuvanted vaccine. Several studies suggest that inactivated seasonal influenza vaccines are safe during pregnancy [3–8] but there is no available data about effects of new A(H1N1) vaccines (new antigen) on pregnant women. Thus, using the French Pharmacovigilance network, it was the aim of the present study to describe Adverse Drug Reactions (ADRs) occurring in vaccinated pregnant women during winter 2009.

The French Pharmacovigilance system consists of a network of 31 Regional Centres. According to the law, physicians must report “serious” or “unexpected” ADRs as defined by WHO. During winter 2009, an intensive pharmacovigilance survey of H1N1 influenza was performed by the French network of Regional Pharmacovigilance Centres. We investigated spontaneous reports of ADRs following A(H1N1) vaccination in pregnant women recorded during the whole vaccination campaign. During this period, 6 million persons were vaccinated and pregnant women were the second group who had priority to access to the vaccine after health professionals.

Between October 20, 2009 (beginning of the vaccination campaign) and March 28, 2010, 30 “serious” ADRs occurring in pregnant women were notified to the French network of Pharmacovigilance: among them, 13 intra-uterine deaths and 12 spontaneous abortions. Mean age of the 30 women was 31.8 (SD=5.9; range 19–45) years. Intra-uterine deaths were diagnosed 7.9 (SD=7.5; range 1–23) days after vaccination. Mean gestational age of intra uterine death occurrence was 28 (SD=4) weeks of pregnancy. In 6 cases of intra-uterine death, risk factors were identified (umbilical cord striction, eclampsia, molar pregnancy, infections). Spontaneous abortions were reported at 11 (SD=4) weeks of pregnancy. They occurred 17.2 (SD=16; range 1–56) days after vaccination. In 3 cases of spontaneous abortion, other potential causes were identified: 1 umbilical cord striction, 1 infection HHV8 in a VIH infected woman and 1 anaphylactic shock 1 h after vaccination. The 5 other ADRs were neonatal death, fetal tachycardia, uterine contractions/fetal arrhythmia, respiratory distress and anamnios/intra-uterine growth retardation.

Intra-uterine death rates range from 2 to 9 per 1000 of pregnancies in European countries [9]. The number of vaccinated pregnant women in France during winter 2009 was around 100,000 [10]. Thus, the estimated number of vaccinated pregnant women who could have experienced a fetal death would be between 200 and 900. According to Black et al. [11], 397 per 1 million vaccinated pregnant women would be predicted to have a spontaneous abortion within 1 day of vaccination (basal risks without vaccine). Thus, the numbers of notified intra-uterine deaths and spontaneous abortion are considerably lower than the expected number of cases.

This report summarizes initial French data about spontaneous notifications of ADRs following A(H1N1) 2009 vaccination in pregnant women. Despite limits of this kind of survey (especially underreporting), this study does not allow detecting any safety signal of concern at least with a short term follow-up (5 months). Other epidemiological studies are necessary to evaluate long term potential risk of A(H1N1) 2009 vaccines in pregnant women.

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I. Lacroix\*

C. Damase-Michel

*Laboratoire de Pharmacologie Médicale et Clinique,  
Centre Midi-Pyrénées de Pharmacovigilance,  
de Pharmacopépidémiologie et d'Informations sur le  
Médicament, Equipe de Pharmacopépidémiologie,  
INSERM U1027, Université de Toulouse,  
Faculté de Médecine, Centre Hospitalier Universitaire,  
Toulouse, France*

C. Kreft-Jais

A. Castot

*Agence Française de Sécurité Sanitaire des Produits  
de Santé (AFSSAPS), France*

J.L. Montastruc,

*Laboratoire de Pharmacologie Médicale et Clinique,  
Centre Midi-Pyrénées de Pharmacovigilance,  
de Pharmacopépidémiologie et d'Informations sur le  
Médicament, Equipe de Pharmacopépidémiologie,  
INSERM U1027, Université de Toulouse,  
Faculté de Médecine, Centre Hospitalier Universitaire,  
Toulouse, France*

The French Association of Regional  
Pharmacovigilance Centres<sup>1</sup>

\* Corresponding author at: Laboratoire de  
Pharmacologie Médicale et Clinique,  
Faculté de Médecine, 37 allées Jules Guesde,  
31 000 Toulouse, France.  
Tel.: +33 5 61 14 59 77;  
fax: +33 5 61 25 51 12.  
E-mail address: [lacroix@cict.fr](mailto:lacroix@cict.fr)  
(I. Lacroix)

<sup>1</sup> F. Bavoux, A. Bénard-Larivière,  
N. Bernard, F. Colin, S. Crepin, S. Dos Santos,  
P. Eftekhari, S. Gautier, M.J. Jean-Pastor,  
A.P. Jonville-Bera, J. Lacotte, C. Le Beller,  
C. Riché, J. Scala-Bertola, E. Schir, M.A. Thompson,  
M.B. Valnet-Rabier, M. Zenut.

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