

# **Safety aspects of influenza vaccine**

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**World Health  
Organization**

# General safety profile of seasonal influenza vaccines

## WHO position paper 2005

- Efficacious and safe inactivated vaccines remain the cornerstone of influenza prophylaxis in most countries.
  - Influenza vaccines can offer 70–90% protection when optimal match against clinical disease in healthy adults
  - In elderly people vaccines may reduce hospitalizations by 25–39% and overall mortality by 39–75% during influenza seasons.
  - Influenza vaccination in pregnancy is considered safe and is recommended for all pregnant women during influenza season.
- There is conclusive evidence for a risk of anaphylaxis (0.7 cases per million doses).

# General safety profile of pandemic influenza vaccines

## GACVS

- Safety information for the pandemic influenza vaccines continues to be reassuring.
- No new proven safety signals other than association of narcolepsy/cataplexy with 1 ASO3 adjuvanted pandemic influenza vaccine in Finland and Sweden, Norway and Ireland (age: 4 – 19 years)
- No major safety concerns on possible association between influenza A(H1N1)pdm09 vaccines and certain autoimmune and other clinical syndromes. (need for further analysis).

# Example: Lack of evidence for increased risk of Guillain-Barré-Syndrome

- Preliminary analyses of active surveillance studies for Guillain–Barré syndrome following Pandemic Vaccine (adjuvanted and unadjuvanted vaccines) in the US:
  - this finding has not been replicated elsewhere to date.
  - there may be a small risk associated with vaccination (1–2 cases per million doses of vaccine administered).
  - Apart from some smaller studies suggesting the possibility of a smaller effect, data do not provide conclusive evidence for an increased risk.
- If confirmed: risk would be
  - much lower than that observed following the 1976 swine influenza vaccination campaign in US
  - similar to the risk that has been associated in some, but not all, studies with the use of seasonal influenza vaccine (an excess risk of the order of 1–2 cases/million doses).

# Safety of vaccines containing Thiomersal (1)

- **1999:** concerns were raised in the US about exposure to mercury in vaccines as cumulative amount of mercury in infant immunization schedule potentially exceeded recommended threshold for methyl mercury set by government.
- Thiomersal contains ethyl mercury:
  - Half-life of ethyl mercury is less than 1 week compared with that of methyl mercury 1.5 months.
  - Ethyl mercury is actively excreted via the gut, whereas methyl mercury accumulates in the body.
- GACVS reviewed several studies, which however did not confirm any association.

# Safety of vaccines containing Thiomersal

## GACVS analysis

- Periodical review of available information on thiomersal in humans (including low birthweight infants)
- Assessment of validity of animal models in studying hypothetical associations between thiomersal and neuro-developmental disorders in humans.
- Identification of two ways to further investigate safety of thiomersal:
  - epidemiological studies on the effects of ethyl mercury and
  - pharmacokinetic studies in infants.

# Safety of influenza vaccines in pregnancy (1)

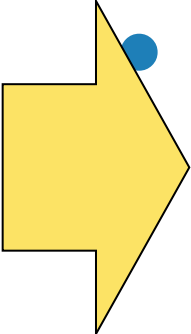
- Influenza vaccination (TIV) is an essential element of prenatal care because pregnant women are at increased risk of serious illness due to influenza
- Vaccination is recommended at any time in pregnancy, before and during the influenza season
- No study to date has shown an adverse consequence of inactivated influenza vaccine in pregnant women or their offspring
- Data from an observational cohort study in Canada and from a birth and infant health registry in the United States did not point to any safety concerns related to pandemic vaccines among women during gestation or their offspring. Several studies on the safety of pandemic vaccines among pregnant women are still being completed in other regions.
- GACVS has established a subgroup on safety during pregnancy issues that is reviewing safety issues related to the use of influenza vaccines during pregnancy and lactation.

**ACOG Committee Opinion, Obstet Gynecol Vol116;No.4:1006,Oct.2010**

# Safety of influenza vaccines in pregnancy (2)

- Data available includes

- Prospective clinical trials \*
- Retrospective and database studies\*
- Post-marketing passive reporting systems \*\*
  - VAERS or VSD in the US
  - Yellow Card System in the UK
- Other vaccine safety systems using databases that link vaccination history and medical outcomes
- Post-marketing Pregnancy Registries\*\*



● Data available supports safety of vaccination of pregnant women with inactivated influenza vaccine, with potential to benefit both mother and infant.  
(Maternal Influenza Immunization Convening London, June 2011)

\* Limitations: Design and statistical power (N)

\*\* Limitations: 1. Under reporting; 2. In addition to number of events, calculation of a rate or attributable risk (using # persons vaccinated as denominator) is necessary to evaluate relationship/causality; 3. Confounders; 4. Insufficient power



# **GACVS advice:**

## **Safety of Influenza vaccines in pregnancy (3)**

- Safety information for influenza vaccines continues to be reassuring.
- Significant morbidity due to vaccine-preventable diseases among women and infants could be prevented by immunization of pregnant women.
- Despite lack of apparent safety issues precautions and contraindications limiting vaccines' benefits to women are often included in product labelling on pregnancy and lactation.
- Further action by GACVS (Dec 2011):
  - continue to monitor and report adverse events in pregnant women following the use of influenza vaccines
  - review relevant evidence
  - include methodological points for planning and analysis of clinical trials and post marketing studies.

# Safety of influenza vaccines in < 2 year olds

- Febrile seizures after seasonal influenza vaccine registered by Australia's regulatory authority in 2010
- Increased reports of fever and febrile convulsions in children aged <5 years following administration of seasonal inactivated influenza vaccine (Fluvax) made by CSL.
  - Data suggested increase in febrile seizures, primarily in children <5 in 24 hour period after vaccination (2010 Southern Hemisphere seasonal influenza vaccine made by CSL).
  - Approximately 75% children who had febrile seizures received only CSL TIV.
  - No increased febrile seizure risk with non-CSL influenza vaccine products.
  - Estimated rate of “up to 9 per 1,000” compared to estimated <1 per 1,000 for Panvax
  - “No biological, clinical, or epidemiological factors identified to explain these higher than expected rates of febrile convulsions”
  - Extensive testing of retention and field samples of vaccine have revealed no abnormalities
  - No increased risk for febrile seizures observed for 2009 H1N1 monovalent influenza vaccine
- GACVS has not detected reports of increased fever or febrile convulsions from other 2010 seasonal vaccines.

\*(Parkville, Victoria, Australia)

# Live, attenuated influenza vaccines

- For several years, live, attenuated influenza vaccines for nasal application have been used successfully in the Russian Federation and in the USA.
- USA: Cold-adapted influenza vaccine licensed only for healthy people (5–49 years),
  - after reported increase in reactive airway disease in vaccinees <5 years of age
  - insufficiently documented protective efficacy in older people.

**Thank you for your  
attention.**