

VAXXED



UNVAXXED

The Science (Part 9)

Children's
Health Defense



Pandemrix Flu Shot Increases Odds of Narcolepsy by 14.4X in Children and Adolescents

BMJ. 2013 Feb 26;346:f794. doi: 10.1136/bmj.f794.

Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis.

Miller E¹, Andrews N, Stellitano L, Stowe J, Winstone AM, Shneerson J, Verity C.

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Abstract

OBJECTIVE: To evaluate the risk of narcolepsy in children and adolescents in England targeted for vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine (Pandemrix) from October 2009.

DESIGN: Retrospective analysis. Clinical information and results of sleep tests were extracted from hospital notes between August 2011 and February 2012 and reviewed by an expert panel to confirm the diagnosis. Vaccination and clinical histories were obtained from general practitioners.

SETTING: Sleep centres and paediatric neurology centres in England.

PARTICIPANTS: Children and young people aged 4-18 with onset of narcolepsy from January 2008.

MAIN OUTCOME MEASURES: The odds of vaccination in those with narcolepsy compared with the age matched English population after adjustment for clinical conditions that were indications for vaccination. The incidence of narcolepsy within six months of vaccination compared with the incidence outside this period measured with the self controlled cases series method.

RESULTS: Case notes for 245 children and young people were reviewed; 75 had narcolepsy (56 with cataplexy) and onset after 1 January 2008. Eleven had been vaccinated before onset; seven within six months. In those with a diagnosis by July 2011 the odds ratio was 14.4 (95% confidence interval 4.3 to 48.5) for vaccination at any time before onset and 16.2 (3.1 to 84.5) for vaccination within six months before onset. The relative incidence from the self controlled cases series analysis in those with a diagnosis by July 2011 with onset from October 2008 to December 2010 was 9.9 (2.1 to 47.9). The attributable risk was estimated as between 1 in 57,500 and 1 in 52,000 doses.

CONCLUSION: The increased risk of narcolepsy after vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine indicates a causal association, consistent with findings from Finland. Because of variable delay in diagnosis, however, the risk might be overestimated by more rapid referral of vaccinated children.

Comment in

Is the adjuvant solely to blame? [BMJ. 2013]

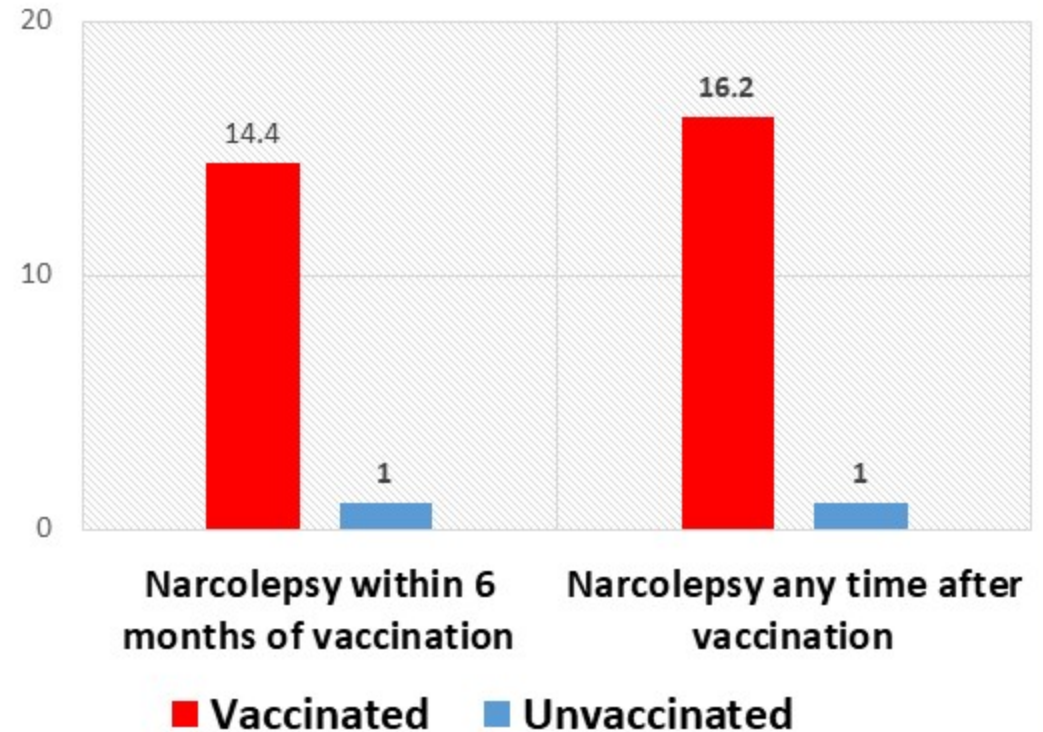
Is the risk of narcolepsy also increased with non-adjuvanted flu vaccines? [BMJ. 2013]

PMID: 23444425 DOI: 10.1136/bmj.f794

Miller et al. 2013 British Medical Journal
doi: 10.1136/bmj.f794

Odds between vaccinated and unvaccinated children

Odds of Narcolepsy Diagnosis After Pandemrix Flu Shot



“The increased risk of narcolepsy after vaccination with AS03 adjuvanted pandemic A/H1N1 2009 vaccine indicates a causal association, consistent with findings from Finland.”

Influenza Vaccination Increases Inflammatory Response by 39% in Pregnant Women

Vaccine. 2011 Nov 8;29(46):8982-7. doi: 10.1016/j.vaccine.2011.09.039. Epub 2011 Sep 22.

Inflammatory responses to trivalent influenza virus vaccine among pregnant women.

Christian LM¹, Iams JD, Porter K, Glaser R.

© Author information

Abstract

OBJECTIVE: In the U.S., seasonal trivalent influenza virus vaccine (TIV) is currently universally recommended for all pregnant women. However, data on the maternal inflammatory response to vaccination is lacking and would better delineate the safety and clinical utility of immunization. In addition, for research purposes, vaccination has been used as a mild immune trigger to examine in vivo inflammatory responses in nonpregnant adults. The utility of such a model in pregnancy is unknown. Given the clinical and empirical justifications, the current study examined the magnitude, time course, and variance in inflammatory responses following seasonal influenza virus vaccination among pregnant women.

METHODS: Women were assessed prior to and at one day (n=15), two days (n=10), or approximately one week (n=21) following TIV. Serum interleukin (IL)-6, tumor necrosis factor (TNF)- α , C-reactive protein (CRP), and macrophage migration inhibitory factor (MIF) were determined by high sensitivity immunoassay.

RESULTS: Significant increases in CRP were seen at one and two days post-vaccination (ps<05). A similar effect was seen for TNF- α , for which an increase at two days post-vaccination approached statistical significance (p=.06). There was considerable variability in magnitude of response; coefficients of variation for change at two days post-vaccination ranged from 122% to 728%, with the greatest variability in IL-6 responses at this timepoint.

CONCLUSIONS: Trivalent influenza virus vaccination elicits a measurable inflammatory response among pregnant women. There is sufficient variability in response for testing associations with clinical outcomes. As adverse perinatal health outcomes including preeclampsia and preterm birth have an inflammatory component, a tendency toward greater inflammatory responding to immune triggers may predict risk of adverse outcomes, providing insight into biological mechanisms underlying risk. The inflammatory response elicited by vaccination is substantially milder and more transient than seen in infectious illness, arguing for the clinical value of vaccination. However, further research is needed to confirm that the mild inflammatory response elicited by vaccination is benign in pregnancy.

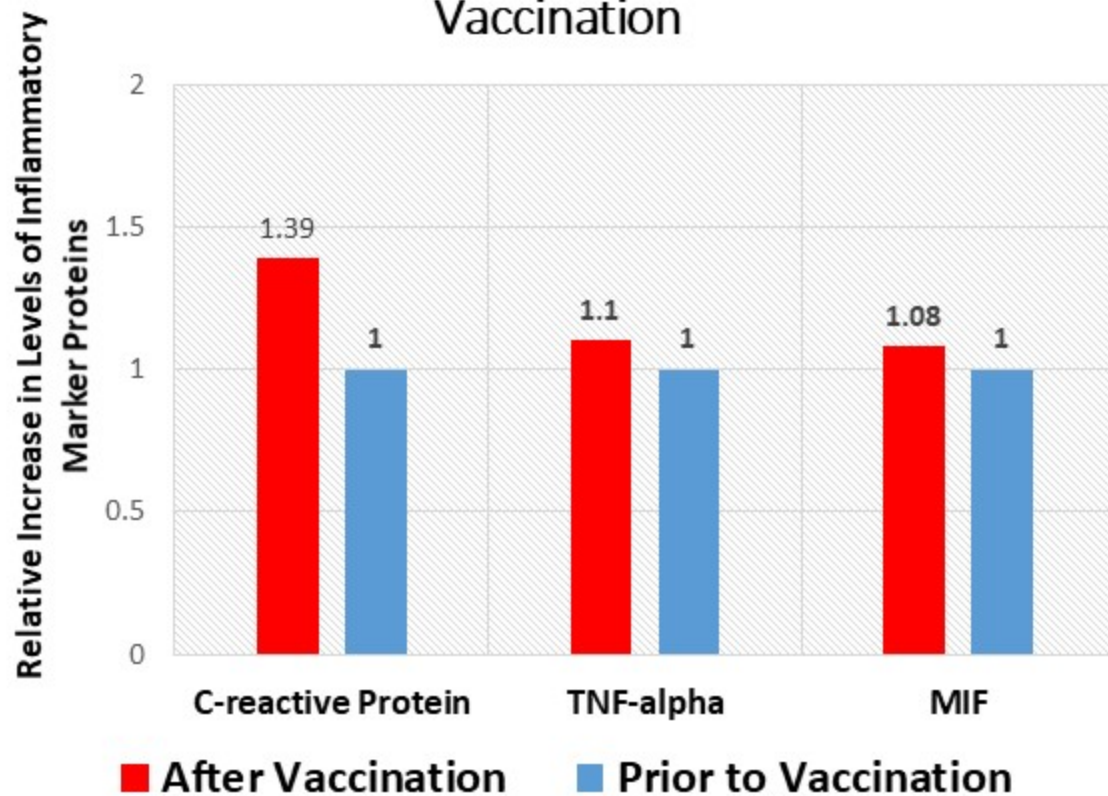
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PMID: 21945263 PMCID: PMC3204610 DOI: 10.1016/j.vaccine.2011.09.039

Christian et al. Vaccine 2011

doi:10.1016/j.vaccine.2011.09.039

Increases in Inflammatory Markers After Vaccination



“In sum, this study demonstrates that trivalent influenza virus vaccine (TIV) elicits a measurable inflammatory response during pregnancy, and that considerable variability is seen between women in the magnitude of this response.”

Influenza Vaccination Increases Inflammatory Response by 173% and Induces Platelet Activation and Cardiac Imbalance

J Intern Med. 2011 Jan;269(1):118-25. doi: 10.1111/j.1365-2796.2010.02285.x. Epub 2010 Oct 22.

Inflammation-related effects of adjuvant influenza A vaccination on platelet activation and cardiac autonomic function.

Lanza GA¹, Barone L, Scalone G, Pittocco D, Sposola GA, Mollo R, Nerla R, Zaccardi F, Ghirlanda G, Crea F.

© Author information

Abstract

BACKGROUND: Inflammation, platelet reactivity and cardiac autonomic dysfunction increase the risk of cardiovascular events, but the relationships between these prognostic markers are poorly defined. In this study, we investigated the effect of an inflammatory stimulus (influenza A vaccine) on platelet activation and cardiac autonomic function.

METHODS: We measured serum C-reactive protein (CRP) and interleukin-6 levels, monocyte-platelet aggregates (MPAs) and monocyte/platelet receptor expression before and after adjuvant influenza A vaccination in 28 patients with type II diabetes (mean age 62.1 ± 8 years, 18 men). Twenty-four-hour Holter electrocardiogram was recorded 24 h before and after vaccination; heart rate variability (HRV) was assessed as a measure of cardiac autonomic function.

RESULTS: Inflammatory cytokines, MPA formation and monocyte/platelet receptor expression increased after vaccination. CRP was 2.6 ± 2.8 and 7.1 ± 5.7 mg L⁻¹ 48 h before and after vaccination, respectively (P < 0.0001). HRV parameters decreased after vaccination compared to baseline, with very low-frequency amplitude showing the most significant change (34.6 ± 11.8 and 31.0 ± 10.2 ms 48 h before and after vaccination, respectively; P = 0.002). A significant correlation was found between percentage changes in CRP levels and in most HRV variables, with the most significant correlations between changes in CRP levels and changes in standard deviation of all normal RR intervals (r = 0.43; P = 0.02).

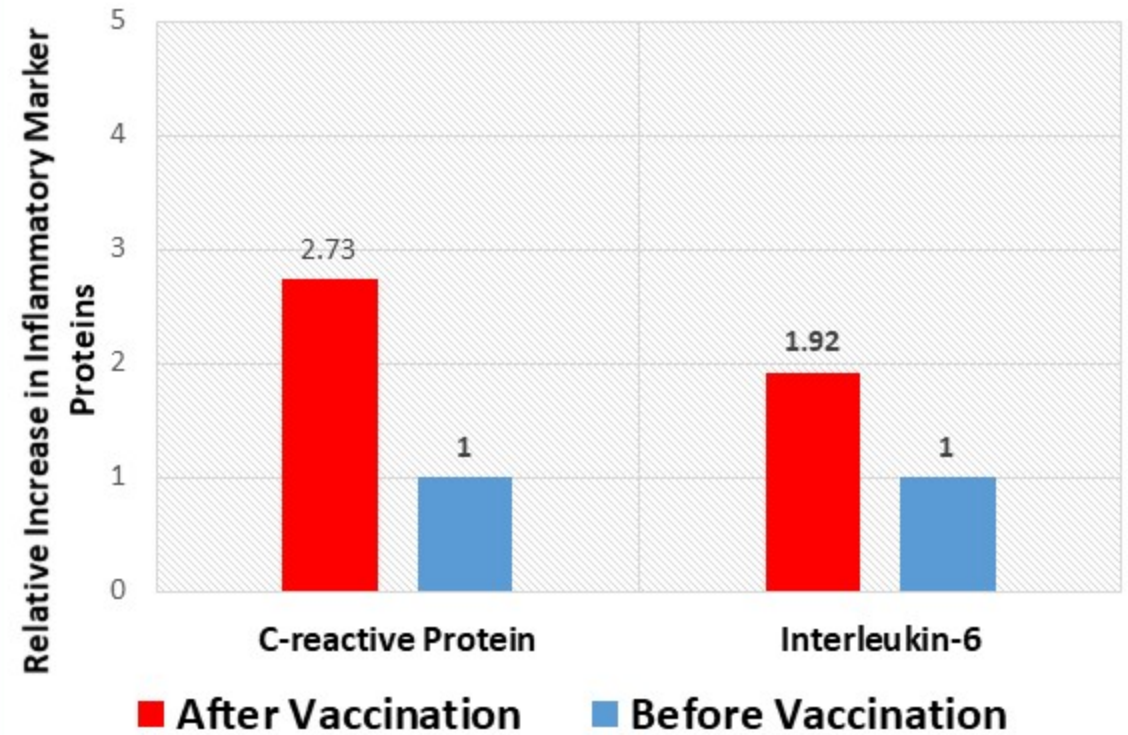
CONCLUSIONS: Together with an inflammatory reaction, influenza A vaccine induced platelet activation and sympathovagal imbalance towards adrenergic predominance. Significant correlations were found between CRP levels and HRV parameters, suggesting a pathophysiological link between inflammation and cardiac autonomic regulation. The vaccine-related platelet activation and cardiac autonomic dysfunction may transiently increase the risk of cardiovascular events.

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PMID: 20964738 DOI: 10.1111/j.1365-2796.2010.02285.x

Lanza et al. 2011 J Intern Med
doi: 10.1111/j.1365-2796.2010.02285.x

Inflammatory Markers Prior to and After Vaccination



“Together with an inflammatory reaction, influenza A vaccine induced platelet activation and sympathovagal imbalance towards adrenergic predominance... The vaccine-related platelet activation and cardiac autonomic dysfunction may transiently increase the risk of cardiovascular events.”

Influenza Vaccination Increases Susceptibility to and Damage Caused by Non-Target Flu Strains

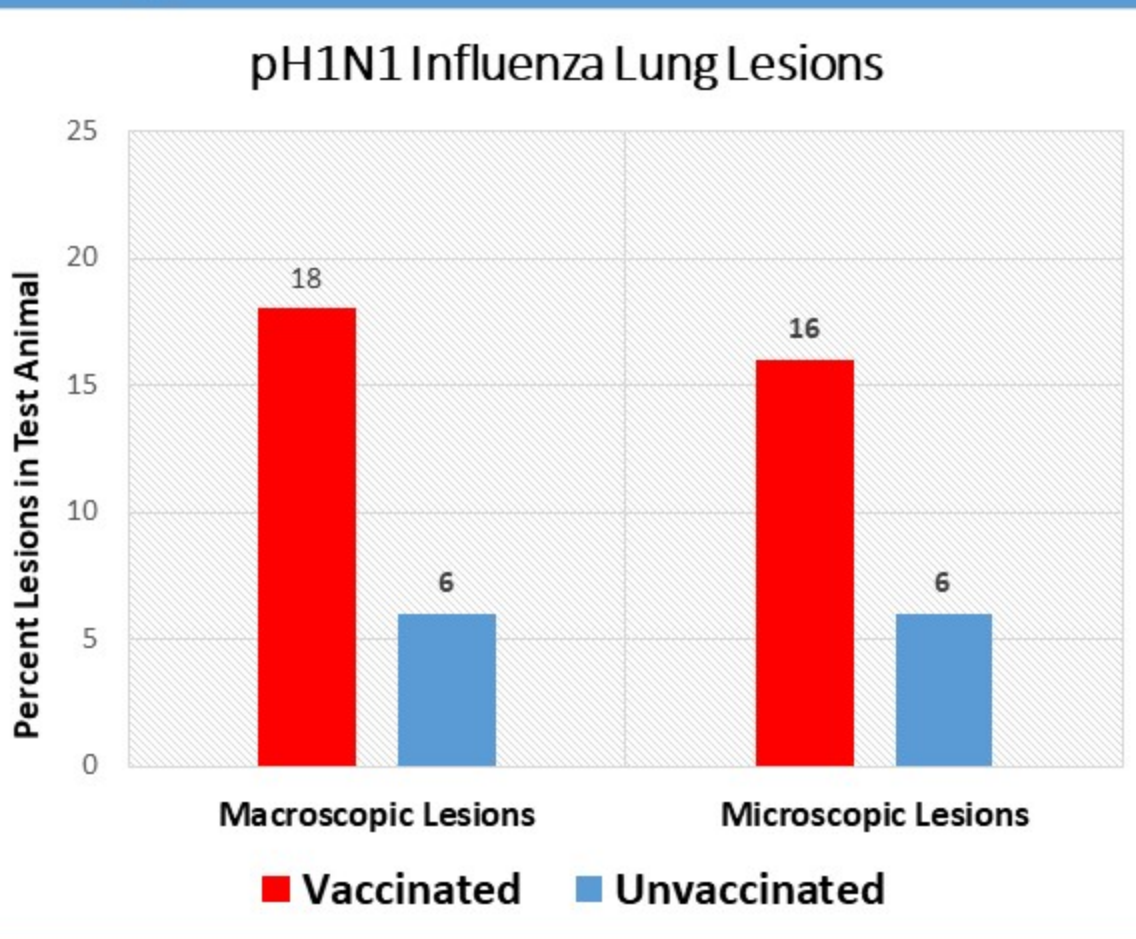
INFLUENZA

Vaccine-Induced Anti-HA2 Antibodies Promote Virus Fusion and Enhance Influenza Virus Respiratory Disease

Surender Khurana,¹ Crystal L. Loving,² Jody Manischewitz,¹ Lisa R. King,¹ Phillip C. Gauger,³ Jamie Henningson,⁴ Amy L. Vincent,^{2*} Hana Golding^{1*}

Vaccine-induced disease enhancement has been described in connection with several viral vaccines in animal models and in humans. We investigated a swine model to evaluate mismatched influenza vaccine-associated enhanced respiratory disease (VAERD) after pH1N1 infection. Vaccinating pigs with whole inactivated H1N2 (human-like) virus vaccine (WIV-H1N2) resulted in enhanced pneumonia and disease after pH1N1 infection. WIV-H1N2 immune sera contained high titers of cross-reactive anti-pH1N1 hemagglutinin (HA) antibodies that bound exclusively to the HA2 domain but not to the HA1 globular head. No hemagglutination inhibition titers against pH1N1 (challenge virus) were measured. Epitope mapping using phage display library identified the immunodominant epitope recognized by WIV-H1N2 immune sera as amino acids 32 to 77 of pH1N1-HA2 domain, close to the fusion peptide. These cross-reactive anti-HA2 antibodies enhanced pH1N1 infection of Madin-Darby canine kidney cells by promoting virus membrane fusion activity. The enhanced fusion activity correlated with lung pathology in pigs. This study suggests a role for fusion-enhancing anti-HA2 antibodies in VAERD, in the absence of receptor-blocking virus-neutralizing antibodies. These findings should be considered during the evaluation of universal influenza vaccines designed to elicit HA2 stem-targeting antibodies.

Khurana et al. 2013 Sci Translational Med
DOI: [10.1126/scitranslmed.3006366](https://doi.org/10.1126/scitranslmed.3006366)



“Vaccinating pigs with whole inactivated H1N2 (human-like) virus vaccine (WIV-H1N2) resulted in enhanced pneumonia and disease after pH1N1 infection.”

Influenza Vaccination Increases Hospitalizations in Asthmatic Patients by 2.97X

CM4 VIRAL INFECTIONS IN CHILDHOOD RESPIRATORY DISEASE / Mini Symposium / Tuesday, May 19/1:30 PM-4:00 PM / Room 3 (Upper Level) San Diego Convention Center

Flu Vaccination in Asthmatics: Does It Work?

A. Y. Joshi, MD¹, V. N. Iyer, MD,MPH¹, M. F. Hartz, MD¹, G. W. Volcheck, MD,Ph.D¹, A. M. Patel, MD¹ and J. T. Li, MD,Ph.D¹.
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INTRODUCTION: Influenza is known to be associated with asthma exacerbation but the effectiveness of the trivalent inactivated flu vaccine (TIV) in asthmatics is unknown.

METHODS: We conducted a *cohort study* of all pediatric subjects (6 months to 18 years age) who were evaluated at Mayo Clinic, Rochester, MN, USA who had laboratory confirmed influenza during each flu season from 1999–2006 to evaluate the efficacy of TIV. A case control analysis was performed with the cases and the controls being the subjects with asthma who did and did not require hospitalization with the influenza illness respectively.

RESULTS:

There were 236 subjects with laboratory confirmed influenza from 1996–2006.

In assessing the effectiveness of the TIV for preventing hospitalization with influenza in all subjects, there was an overall trend towards higher rates of hospitalization in subjects who got the TIV as compared to the ones who did not get the TIV (OR:2.97, CI: 1.3,6.7). Using Cochran–Mantel–Haenszel (CMH) test for Asthma status stratification, there was a significant association between hospitalization in asthmatic subjects and TIV ($P=0.006$).

In the asthmatic subset:

There was no association between ER visit and receiving the TIV, severity of asthma and the risk of hospitalization or the hospital length of stay and receiving the TIV.

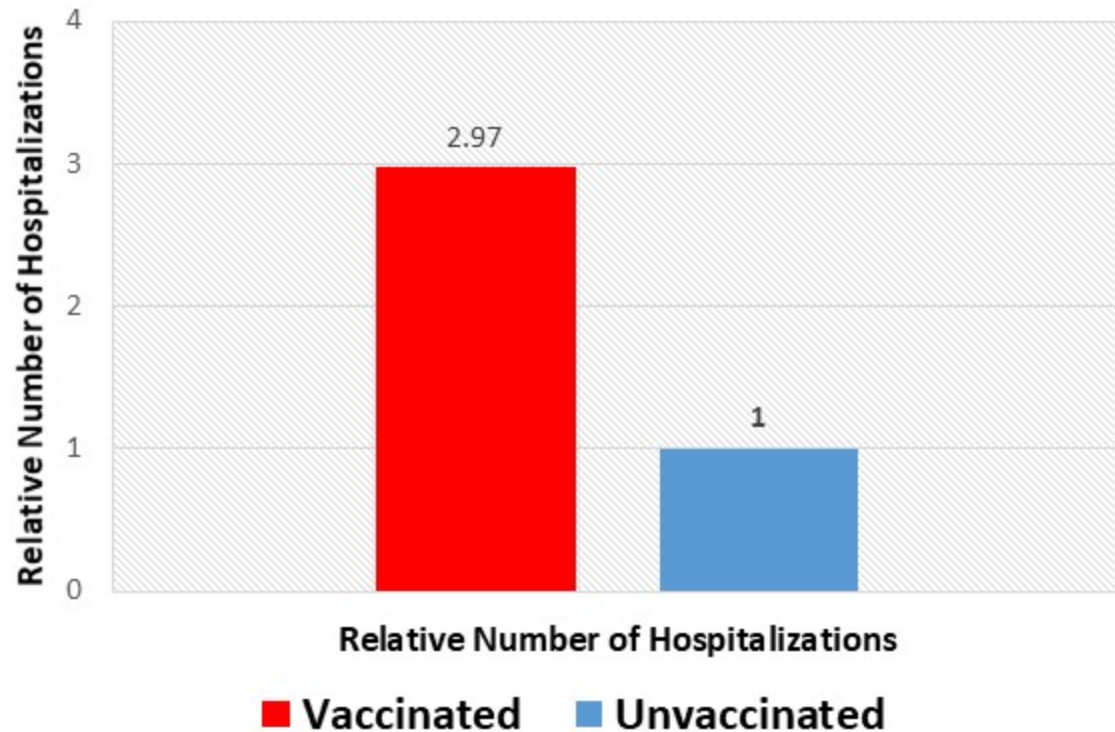
In assessing access to medical care, there was no association between hospitalizations and health care insurance plans (Odds ratio:0.3, $P=0.13$)

CONCLUSION:

1) TIV did not provide any protection against hospitalization in pediatric subjects' esp. children with asthma. On the contrary, we found a 3– fold increased risk of hospitalization in subjects who did get the TIV vaccine. This may be a reflection not only of the vaccine effectiveness but also the population of children who are more likely to get the vaccine.

2) More studies are needed to assess not only the immunogenicity but also efficacy of different influenza vaccines in asthmatic subjects.

Hospitalizations in Asthmatics Receiving Influenza Vaccine



Joshi et al. 2009 American Thoracic Society Conference Abstract

“In assessing the effectiveness of the TIV for preventing hospitalization with influenza in all subjects, there was an overall trend towards higher rates of hospitalization in subjects who got the TIV as compared to the ones who did not get the TIV (OR:2.97, CI: 1.3,6.7).”

Multiple Vaccinations Given Simultaneously Increases Odds of Cardiac Events in Premature Infants by 3.62X

Primary Immunization of Premature Infants with Gestational Age <35 Weeks: Cardiorespiratory Complications and C-Reactive Protein Responses Associated with Administration of Single and Multiple Separate Vaccines Simultaneously

MASSROOR POURCYROUS, MD, SHELDON B. KORONES, MD, KRISTOPHER L. ARHEART, PhD, AND HENRIETTA S. BADA, MD

Objective To determine the incidence of cardiorespiratory events and abnormal C-reactive protein (CRP) level associated with administration of a single vaccine or multiple separate vaccines simultaneously.

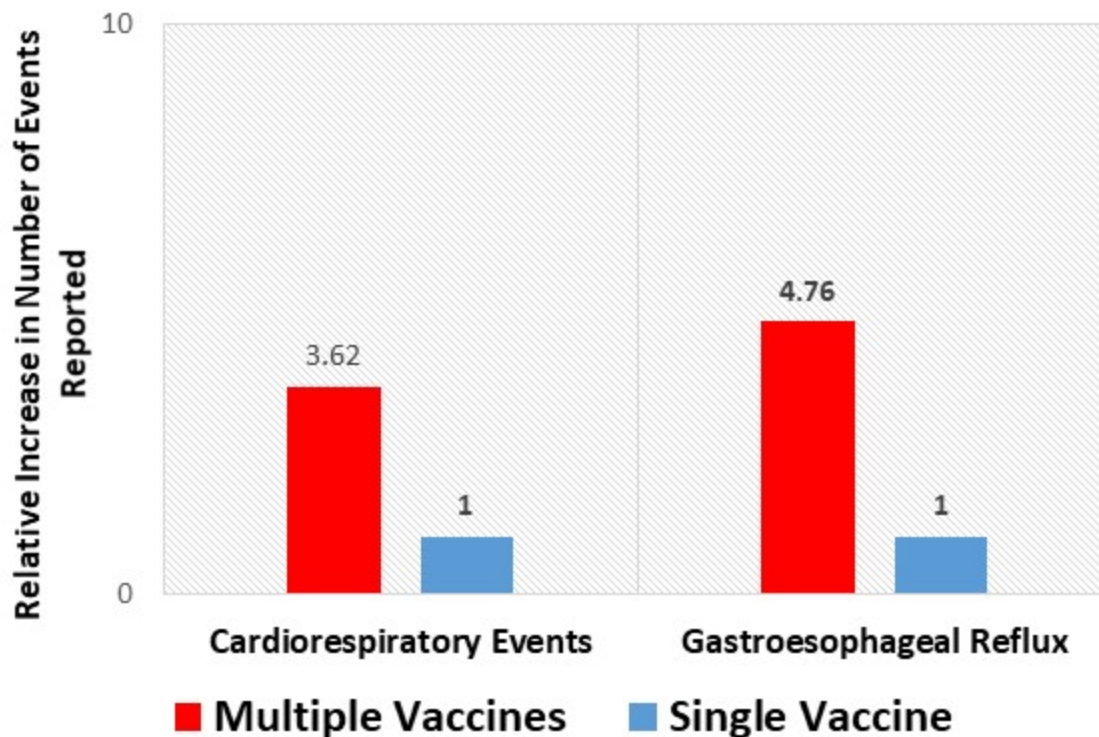
Study design Prospective observational study on 239 preterm infants at ≥ 2 months of age in the neonatal intensive care unit (NICU). Each infant received either a single vaccine or multiple vaccines on one day. CRP levels and cardiorespiratory manifestations were monitored for 3 days following immunization.

Results Abnormal elevation of CRP level occurred in 85% of infants administered multiple vaccines and up to 70% of those given a single vaccine. Overall, 16% of infants had vaccine-associated cardiorespiratory events within 48 hours postimmunization. In logistic regression analysis, abnormal CRP values were associated with multiple vaccines (OR, 15.77; 95% CI 5.10-48.77) and severe intraventricular hemorrhage (IVH) (OR, 2.28; 95% CI 1.02-5.13). Cardiorespiratory events were associated marginally with receipt of multiple injections (OR, 3.62; 95% CI 0.99-13.25) and significantly with gastroesophageal reflux (GER) (OR, 4.76; 95% CI 1.22-18.52).

Conclusion CRP level is expected to be elevated in the 48 hours following immunization. In a minority of infants immunized, cardiorespiratory events were associated with presumed need for intervention. Underlying medical conditions and possibly multiple injections are associated with cardiorespiratory events. Precautionary monitoring following immunizations is warranted. (*J Pediatr* 2007;151:167-72)

Pourcyrous et al. 2007 J Pediatr
DOI 10.1016/j.jpeds.2007.02.059

Increase in Events Due to Multiple Vaccines Given Simultaneously



“Cardiorespiratory events were associated marginally with receipt of multiple injections (OR, 3.62; 95% CI 0.99-13.25) and significantly with gastroesophageal reflux (GER) (OR, 4.76; 95% CI 1.22-18.52).”