



# Specifics of vaccine Pharmacovigilance

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DCVMN training on PV,  
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# Definition vaccine PV

- “Vaccine pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and communication of adverse events following immunization and other vaccine- or immunization-related issues, and to the prevention of untoward effects of the vaccine or immunization.”

CIOMS working group on vaccine pharmacovigilance 2012



# What is different in PV for vaccines?

- Vaccines are primarily a public health asset
- Universal mass vaccination leads to huge exposure numbers (almost everyone exposed)
- Some specific questions
- Very low tolerance for most AEs
- Events of concern/interest mostly rare to very rare



# Public health asset (but too successful?)

Disease	Pre-Vaccine Era	2000	% change
Diphtheria	31,054	4	99.99
Measles	390,852	81	99.98
Mumps	161,500	323	99.80
Pertussis	117,998	6,755	95.40
Polio (wild)	4,953	0	100.00
Rubella	9,941	152	99.70
Cong. Rubella Synd.	19,177	7	99.10
Tetanus	246	26	98.00
Invasive Hib Disease	18,556	167	99.10
Total	754,277	7,515	98.67
<b>Vaccine Adverse Events</b>	<b>0</b>	<b>13,497<sup>^</sup></b>	<b>+++</b>

Ref: (1)

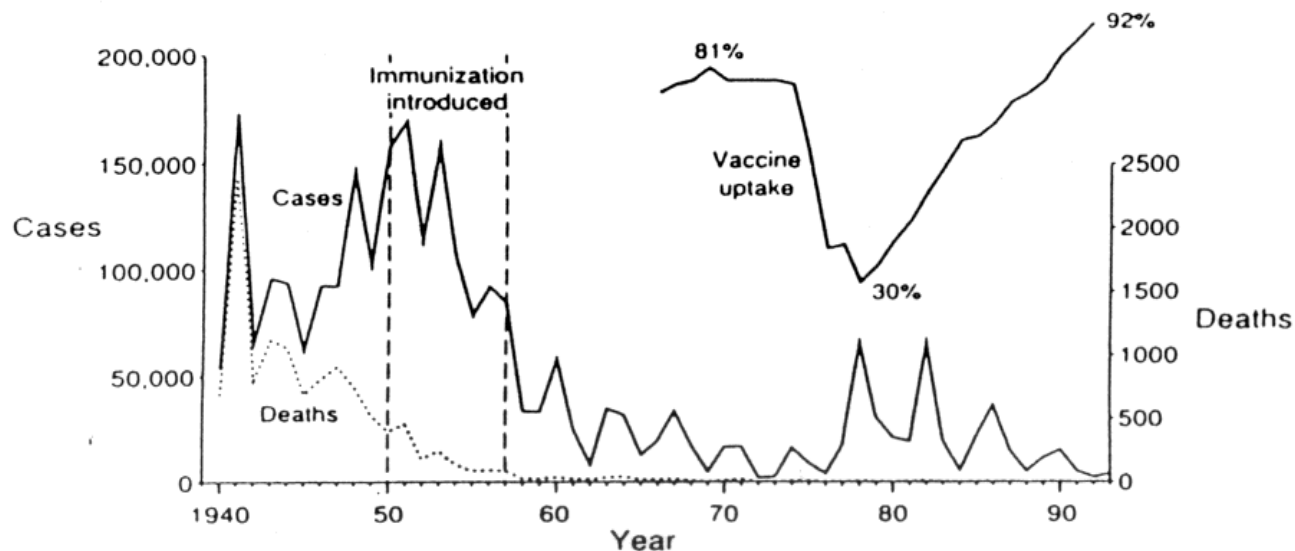
Maximum cases reported in pre-vaccine era and year

<sup>^</sup> Adverse events after vaccines against diseases shown on Table = 5,296



# Large (near universal) exposure

Whooping cough notifications : cases and deaths, England and Wales, 1940-1993  
(source : OPCS. Prepared by CDSC)



Reference : Begg N., Cutts F.T., *The Role of Epidemiology, In Vaccination, Successes and Challenges*, ed. Cutts F.T. & Smith P.G.; John Wiley & Sons, 1994.



# Specific concerns to be monitored for vaccines

- transmission of infectious agent, especially for live viral vaccines (eg rotavirus, varicella, polio)
- genetic stability
- epidemiological shifts of prevented disease: eg pneumococcal serotypes
- safety in special groups such as premature children, immunocompromised

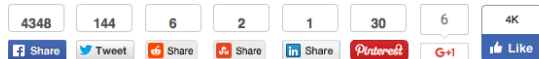


# Very low tolerance

## Family's pain as girl, 13, dies just five days after cancer jab having been sent home from hospital hours earlier

Investigation launched into claims tragic Shazel was 'bride of a 'leaky child'

Gardasil Vaccine Hoax: Vaccine Side Effect Risks Higher than Cervical Cancer Risks



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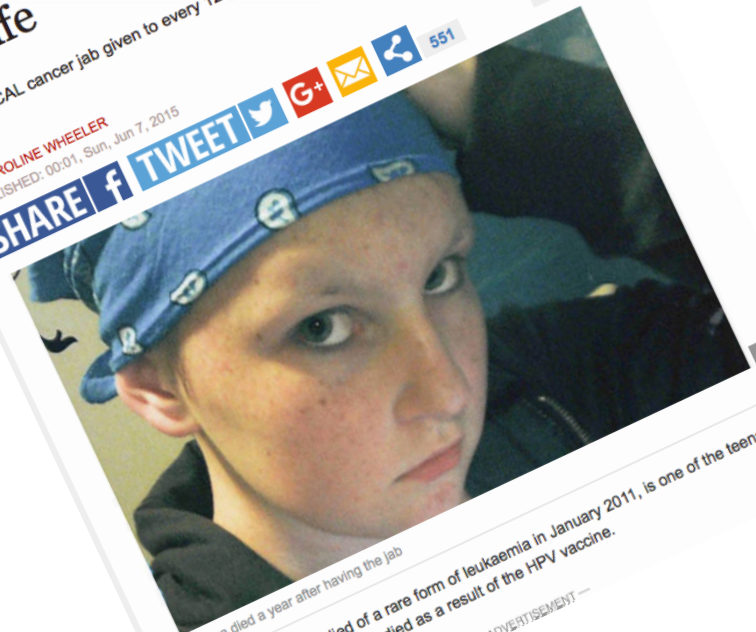
Duty to Warn: Gardasil and Cervical Cancer: Are We Witnessing a Hoax in the Making?

(Exploring Big Pharma's Assertion that Gardasil Will Prevent/Cervical Cancer)

## Cervical cancer jab cost our girl her life

A CERVICAL cancer jab given to every 12-year-old girl in Britain has been linked to four deaths.

By CAROLINE WHEELER  
PUBLISHED: 00:01, Sun, Jun 7, 2015



Rebecca Kerr, who died of a rare form of leukaemia in January 2011, is one of the teenagers whose parents believe she died as a result of the HPV vaccine.

— ADVERTISEMENT —



# Events of concern/interest mostly rare to very rare

The NEW ENGLAND JOURNAL of MEDICINE

## ORIGINAL ARTICLE

### Safety of Influenza A (H1N1) Vaccine in Postmarketing Surveillance in China

Xiao-Feng Liang, M.D., Li Li, M.D., Ph.D., Da-Wei Liu, M.D., Ke-Li Li, M.D., Wen-Di Wu, M.D., Bao-Ping Zhu, M.D., Hua-Qing Wang, M.D., Ph.D., Hui-Ming Luo, M.D., Ling-Sheng Cao, M.D., Jing-Shan Zheng, M.D., Da-Peng Yin, M.D., Lei Cao, M.P.H., Bing-Bing Wu, M.D., Hong-Hong Bao, M.D., Di-Sha Xu, M.D., Wei-Zhong Yang, M.D., and Yu Wang, M.D., Ph.D.

## ABSTRACT

### BACKGROUND

On September 21, 2009, China began administering vaccines, obtained from 10 different manufacturers, against 2009 pandemic influenza A (H1N1) virus infection in priority populations. We aimed to assess the safety of this vaccination program.

### METHODS

We designed a plan for passive surveillance for adverse events after immunization with the influenza A (H1N1) vaccine. Physicians or vaccination providers were required to report the numbers of vaccinees and all adverse events to their local Center for Disease Control and Prevention (CDC), which then reported the data to the Chinese CDC through the online National Immunization Information System's National Adverse Event Following Immunization Surveillance System. Data were collected through March 21, 2010, and were verified and analyzed by the Chinese CDC.

### RESULTS

A total of 89.6 million doses of vaccine were administered from September 21, 2009, through March 21, 2010, and 8067 vaccinees reported having an adverse event, for a rate of 90.0 per 1 million doses. The age-specific rates of adverse events ranged from 31.4 per 1 million doses among persons 60 years of age or older to 130.6 per 1 million doses among persons 9 years of age or younger, and the manufacturer-specific rates ranged from 4.6 to 185.4 per 1 million doses. A total of 6552 of the 8067 adverse events (81.2%; rate, 73.1 per 1 million doses) were verified as vaccine reactions; 1083 of the 8067 (15.4%; rate, 12.1 per 1 million doses) were rare and more serious (vs. common, minor events), most of which (1050) were allergic reactions. Eleven cases of the Guillain-Barré syndrome were reported, for a rate of 0.1 per 1 million doses, which is lower than the background rate in China.

### CONCLUSIONS

No pattern of adverse events that would be of concern was observed after the administration of influenza A (H1N1) vaccine, nor was there evidence of an increased risk of the Guillain-Barré syndrome.

“Eleven cases of the Guillain-Barré syndrome were reported, for a rate of 0.1 per 1 million doses, which is lower than the background rate in China.”<sup>(2)</sup>

From the Chinese Center for Disease Control and Prevention, National Immunization Program (X.-F.L., L.L., D.-W.L., K.-L.L., W.-D.W., H.-Q.W., H.-M.L., L.-S.C., J.-S.Z., D.-P.Y., L.C., B.-B.W., H.-H.B., D.-S.X., W.-Z.Y., Y.W.); and the Chinese Field Epidemiology Training Program (B.-P.Z.) — both in Beijing. Address reprint requests to Dr. Yu Wang at the Chinese Center for Disease Control and Prevention, Beijing 100050, China, or at wangyu@chinacdc.cn.

This article (10.1056/NEJMoa1008553) was published on February 2, 2011, and updated on April 13, 2011, at NEJM.org.

N Engl J Med 2011;364:638-47.

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# Other specifics of vaccines (PV)

- Overlap between age of vaccination and high frequency some diseases (eg Intussusception, sudden infant deaths)
- Errors in vaccine handling (transport, storage, administration)
- Combination vaccines: which antigen is to blame for the AE (or the adjuvant, the excipient, the solvent etc)?
- Co-administration: which vaccine is to blame for the AE?
- Lot specific analyses
- Generic analyses (eg all live viral, all adjuvanted, all influenza etc)



# References

- (1): Chen et Orenstein in Infectious Disease Epidemiology
- (2): Liang XF1, Li L, Liu DW et al. Safety of influenza A (H1N1) vaccine in postmarketing surveillance in China. N Engl J Med. 2011 Feb 17;364(7):638-47.
- + CIOMS : Definition and Application of Terms for Vaccine Pharmacovigilance (Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance)