

# Investigation of Reports to VAERS of Death after Vaccination

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# What is the Vaccine Adverse Event Reporting System (VAERS)?

- National system for surveillance of adverse events after vaccination initiated by National Childhood Vaccine Injury Act 1986 and established 1990
- Jointly managed by FDA and CDC
- Reports received from health professionals, vaccine manufacturers, and the public
- All death and serious (hospitalization, prolongation of hospitalization, life-threatening illness, or permanent disability ) reports receive follow-up

# Uses of VAERS

- Detecting unrecognized adverse events
- Monitoring known reactions
- Identifying possible risk factors
- Vaccine lot surveillance

# Limitations of VAERS

- Reported diagnoses are not verified
- Lack of consistent diagnostic criteria
- Wide range in data quality
- Underreporting
- Inadequate denominator data
- No unvaccinated control group
- **Usually not possible to assess whether a vaccine caused the reported adverse event**

# Analysis of VAERS Data

- Describe characteristics and look for patterns to detect “signals” of adverse events plausibly linked to a vaccine
- Signals detected through analysis of VAERS data almost always require confirmation through a controlled study



# Background

- When apparently healthy people die shortly after immunization, it is reasonable to ask if the vaccine caused or contributed to the death
- Controlled studies of vaccines do not show increased risk of death among vaccinees
- The widespread administration of vaccines may result in some temporal, but not causal, associations with deaths
- It is possible that vaccination rarely causes death at rates too low to allow detection in controlled studies
- Reports of death after vaccination to VAERS provide an opportunity to possibly detect such cases

# Background (cont.)

- The FDA and the Institute of Medicine (IOM) reviewed 206 deaths reported to VAERS during 1990-1991.
  - One death was believed to have resulted from a vaccine
- The IOM concluded that the vast majority of deaths reported to VAERS are temporally but not causally related to vaccination.

Institute of Medicine. Editors: Stratton KR, Howe CJ, Johnston RB, Jr. Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality. National Academy Press: Washington, DC. 1994; P.274-304.



# The Epidemiology of Fatalities Reported to VAERS 1990-1997

- 1, 266 fatalities reported to VAERS
- Median age 0.4 years (range 1 day to 104 years)
- Higher percentage of deaths reported to VAERS (16.8%) in “low-birth weight” infants than US general population
- Nearly half of reported deaths attributed to SIDS
- Number of reported deaths peaked in 1992-1993
  - Pattern follows the decline in deaths in the US attributed to SIDS since “Back to Sleep” program
- Conclusion: Data support prior controlled studies showing that association between infant vaccination and SIDS is not causal

Silvers LE, Ellenberg SS, Wise RP, Varriccho FE, Mootrey GT, Salive ME. The epidemiology of fatalities reported to the Vaccine Adverse Event Reporting System 1990-1997. *Pharmacoepidemiology and Drug Safety*. 2001; 10:279-285.



# Reported Deaths after Vaccination by Age and Gender (VAERS, US 1990-1997)

Age in Years	<i>n</i>	Percentage	Percentage female
Overall	1199	100.0	42
< 1	808	67.4	39
1 – 4	117	9.8	43
5 – 9	18	1.5	50
10 – 17	17	1.4	29
18 – 45	43	3.6	56
46 – 64	55	4.6	44
≥ 65	141	11.7	55



Excludes 67/1266 cases with unreported age. The stratification by gender excludes 28/1199 cases due to unreported gender

# Causes of Death (VAERS, US 1990-1997)

Cause of Death	<i>n</i>	Percentage	Percentage female
Overall	1244	100.0	42
SIDS	592	47.6	36
Congenital	38	3.1	46
Infectious	164	13.2	42
Neoplastic	15	1.2	67
Other	261	21.0	48
Unknown	147	14.0	48

Gender was unknown for 53 cases. Cases with unknown gender were excluded for this calculation.



# Pediatric Deaths Reported after Vaccination: The Utility of Information Obtained from Parents

- Structured interviews of parents and healthcare providers (HCP) of 100 consecutive pediatric deaths reported to VAERS to determine value of parental information compared with HCP information
- In general the information was equivalent in quality
- Parents were more likely to know child's position when found in distress
- Conclusion: None of the additional information obtained from parents provided a signal or confirmation of a causal link between vaccine and death

Silvers LE, Varriccho FE, Ellenberg SS, Krueger CL, Wise RP, Salive ME. Pediatric deaths reported after vaccination: The utility of information obtained from parents. *American Journal of Preventive Medicine* 2002; 22:170-176.



# Neonatal Deaths after Hepatitis B Vaccine: VAERS, 1991-1998

- 18 deaths in 1,771 neonatal reports
  - 8 boys, 9 girls, 1 unclassified
- 17 Autopsy Reports
  - 12 SIDS, 3 infection, 1 intracerebral hemorrhage, 1 accidental suffocation, 1 congenital heart disease
- **Conclusion: No evidence to suggest Hepatitis B vaccination implicated in neonatal deaths**

Niu MT, Salive ME, Ellenberg, SS. Neonatal deaths after hepatitis B vaccine: the Vaccine Adverse Event Reporting System, 1991-1998. Archives of Pediatrics and Adolescent Medicine. 1999; 153:1279-82.



# Published Surveillance Summaries Including Review of Reports of Death Following Vaccination

- Ball R, Braun MM, Mootrey GT (2001). Safety data on meningococcal polysaccharide vaccine from the Vaccine Adverse Event Reporting System. *Clin.Infect.Dis.*, 32(9), 1273-1280.
- Braun MM, Mootrey GT, Salive ME, Chen RT, Ellenberg SS (2000). Infant immunization with acellular pertussis vaccines in the United States: assessment of the first two years' data from the Vaccine Adverse Event Reporting System (VAERS). *Pediatrics*, 106(4), E51
- Lathrop SL, Ball R, Haber P, Mootrey GT, Braun MM, Shadomy SV, Ellenberg SS, Chen RT, Hayes EB. (2002). Adverse event reports following vaccination for Lyme disease: December 1998-July 2000. *Vaccine*, 20(11-12), 1603-1608.
- Wise RP, Salive ME, Braun MM, Mootrey GT, Seward JF, Rider LG, Krause PR. (2000). Postlicensure safety surveillance for varicella vaccine. *JAMA*, 284(10), 1271-1279.
- Zanardi LR, Haber P, Mootrey GT, Niu MT, Wharton M (2001). Intussusception among recipients of rotavirus vaccine: reports to the vaccine adverse event reporting system. *Pediatrics*, 107(6), E97



# Follow-up Procedures for Reports to VAERS of Death after Vaccination

- Contract nurse-initiated follow-up of all serious cases including death
- Documents requested (where appropriate)
  - Medical records
  - Discharge summary
  - Death Certificates
  - Autopsies/Medical Examiner reports
  - Misc (ER records, physician notes/summaries, consultant reports)
- Standardized data collection instruments completed
  - Adult death supplemental follow-up questionnaire
  - Pediatric death supplemental follow-up questionnaire



# Follow-up Results

## 10/1/00-9/30/02

- 562 initial reports of death
  - 163 Autopsy Reports Received (29.0%)
    - Avg Time 67.2 Days
- Of the 562
  - 17 or younger - 413 (73.5%)
  - 18 or older - 113 (20.1%)
  - No Response – 36 (6.4%)

# Review of Reports to VAERS of Death after Vaccination

- FDA pathologist reviews all reports and associated documentation as information arrives
- FDA medical officers review deaths reported for vaccines they monitor on a weekly basis
- Review of reported deaths by lot at weekly meeting
  - If 3 or more deaths are reported in a given lot, the reports are examined for unexpected patterns in causes of death and reporting rate by lot, if warranted



# Death Reports of Interest

- Yellow fever vaccine-associated viscerotropic disease

- Vaccine strain virus detected in tissue

Martin M, Tsai TF, Cropp B, et al. Fever and Multisystem Organ Failure associated with 17D-204 yellow fever: A report of four cases. *Lancet* 2001; 358:98-104.

Chan RC, Penney DJ, Little D, Carter IW, Roberts JA and Rowlinson WD. Hepatitis and death following vaccination with 17D-204 yellow fever vaccine. *Lancet* 2001; 358: 121-2.

- Intussusception after Rotavirus vaccine

- 1 death from intussusception but not possible to conclusively determine if caused by vaccine

- VAERS has limited ability to detect rare events



# Summary

- Limitations of VAERS prevent definitive assessment of vaccine causality
- However, intensive review of death reports and vaccine surveillance summaries have found no clear evidence of an association between vaccination and death except in rare instances (e.g. yellow fever vaccine and viscerotropic disease)
- Routine follow-up and review of reports and lot-specific screening continues to be conducted by FDA medical officers

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