Investigation of Reports to VAERS of Death after Vaccination

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for
IOM Immunization Safety Review Committee
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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.

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

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

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>$n$</th>
<th>Percentage</th>
<th>Percentage female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1199</td>
<td>100.0</td>
<td>42</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>808</td>
<td>67.4</td>
<td>39</td>
</tr>
<tr>
<td>1 – 4</td>
<td>117</td>
<td>9.8</td>
<td>43</td>
</tr>
<tr>
<td>5 – 9</td>
<td>18</td>
<td>1.5</td>
<td>50</td>
</tr>
<tr>
<td>10 – 17</td>
<td>17</td>
<td>1.4</td>
<td>29</td>
</tr>
<tr>
<td>18 – 45</td>
<td>43</td>
<td>3.6</td>
<td>56</td>
</tr>
<tr>
<td>46 – 64</td>
<td>55</td>
<td>4.6</td>
<td>44</td>
</tr>
<tr>
<td>≥ 65</td>
<td>141</td>
<td>11.7</td>
<td>55</td>
</tr>
</tbody>
</table>

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)

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

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


• 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

Published Surveillance Summaries Including Review of Reports of Death Following Vaccination


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

• **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 viscerotrophic disease)
• Routine follow-up and review of reports and lot-specific screening continues to be conducted by FDA medical officers
Acknowledgements

• Analytical Sciences, Inc (VAERS contractor)
  – Steve Gordon

• FDA
  – Sean Shadomy, Bob Wise, M. Miles Braun, Susan Ellenberg