Autism and thimerosal containing vaccines

Anders Hviid - Statens Serum Institut - March 29 2011
**EPIDEMIOLOGY:**
**When an Entire Country Is a Cohort**

Lone Frank

Denmark has gathered more data on its citizens than any make this vast array of statistics even more useful.

For years, any woman who got an abortion had to accept more she also faced an elevated risk for breast cancer. At least that suggested before Mads Melbye, an epidemiologist at the State largest effort ever to explore the link. He and his colleagues obtain national Abortion Register, then checked how many of the sam Their foray into the two databases led to a surprising result: As
Materials

- CPR registry (’68)
- Vaccination registry (´90-)
- Hospital registries (’77)

1,3 mil. + children

Methods

- Survival analysis
- Poisson regression

Incidence rate ratios
Why autism and vaccines / thimerosal?

• Little is known about the etiology
• Increasing secular trends
• Symptoms coinciding with vac. schedule

• Thimerosal, a vaccine preservative, contains mercury.

• Mercury is neurotoxic.

• 1990s, US: More and more TCVs.

• TCVs increases risk of Autism.
Thimerosal in the Danish schedule

- Jan 1, 1970 – May 31, 1992: Whole-cell pertussis (1 dose ~ 100 µg thiomersal ~ 50 µg ethylmercury), ½ dose at 5 weeks, 1 dose at 9 weeks, and 1 dose at 10 months.

Total amount of ethylmercury received through vaccination in the Danish schedule and in the US schedule.
Study Design – Determining Thiomersal exposure

Cohort
All children born in Denmark
Jan 1, 1990 – Dec 31, 1996

N = 467,450

Unvaccinated (no wcP)
N = 20,755 (4.4%)

Thiomersal-containing wcP
(At least 1 dose)
N = 138,953 (29.7%)

Thiomersal-free wcP
(At least 1 dose and no thimerosal-containing doses)
N = 307,742 (65.9%)

Study period
## Results I

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>OSD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thimerosal +</strong></td>
<td>0.85 (0.60 – 1.20)</td>
<td>1.12 (0.88 – 1.43)</td>
</tr>
<tr>
<td><strong>Trend per 25 µg</strong></td>
<td>0.98 (0.90 – 1.06)</td>
<td>1.03 (0.97 – 1.09)</td>
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</tbody>
</table>
# Results II – Association in subgroups

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Autism</th>
<th>RR 95% CI</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td></td>
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<tr>
<td>&lt; 2500 g</td>
<td>1.71 (1.06-2.76)</td>
<td>1.10 (0.47-2.57)</td>
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<tr>
<td>2500-2999 g</td>
<td>1.14 (0.82-1.59)</td>
<td>0.63 (0.28-1.42)</td>
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<tr>
<td>3000-3499 g</td>
<td>1 Referent</td>
<td>1.00 (0.61-1.65)</td>
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<tr>
<td>3500-3999 g</td>
<td>1.02 (0.79-1.32)</td>
<td>0.97 (0.59-1.60)</td>
<td></td>
</tr>
<tr>
<td>&gt;= 4000 g</td>
<td>1.28 (0.96-1.72)</td>
<td>0.77 (0.41-1.45)</td>
<td></td>
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<tr>
<td>Gestational age</td>
<td></td>
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<tr>
<td>&lt; 37 weeks</td>
<td>0.93 (0.59-1.47)</td>
<td>0.85 (0.28-2.63)</td>
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<tr>
<td>37 - 41 weeks</td>
<td>1 Referent</td>
<td>0.95 (0.66-1.38)</td>
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<tr>
<td>&gt;=42 weeks</td>
<td>0.82 (0.56-1.21)</td>
<td>0.68 (0.26-1.74)</td>
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<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Girl</td>
<td>1 Referent</td>
<td>0.93 (0.53-1.64)</td>
<td></td>
</tr>
<tr>
<td>Boy</td>
<td>4.05 (3.19-5.15)</td>
<td>0.83 (0.58-1.20)</td>
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</tbody>
</table>

(Not published)
Study strengths and weaknesses

Strengths

- Large (Autism, 440 cases, Other Autistic-Spectrum Disorder, 787 cases)
- Nationwide, population-based
- All data used were collected independently and prospectively
- A comparison of children vaccinated with thiomersal-containing vaccine with children vaccinated with a thiomersal-free formulation of the same vaccine

Weaknesses

- Date of diagnosis instead of date of "onset of symptoms"
Pros

+ Nationwide complete
+ Large
+ Danish pop. homogenous.
+ Denmark “egalitarian” society
+ Easy access to outcomes and potential confounders
+ Changes in schedule in the 90s
Cons

- Outcomes not available through the nationwide outcome registries
- Outcomes not specific enough in the –”–
- Vaccines not included in the Danish schedule
- Not large enough to study some rare outcomes
- Not large enough to study vaccination effects in more detail, i.e. genetics etc.
- Reaction time is dependent on updates (sporadic)
- Funding issues, no core funding for vaccine safety research
Thimerosal Exposure in Infants and Developmental Disorders: A Retrospective Cohort Study in the United Kingdom Does Not Support a Causal Association

Nick Andrews, MSc*; Elizabeth Miller, MBBS, FRCPath, FFPHM‡; Andrew Grant, PhD*; Julia Stowe, BA§; Velda Osborne, BSc||; and Brent Taylor, PhD, MBCHB§

Design:

Amount of Hg by 3 mo. / 4 mo. / All
“To help assess the feasibility of a multi-country collaboration England and Denmark, who have established vaccine safety systems, undertook to work to a common protocol and share results and data to estimate the risk of idiopathic thrombocytic purpura (ITP) following measles-mumps-rubella (MMR) vaccination.”

“very similar estimates of the relative incidence in the 6 weeks after vaccination and a pooled relative incidence estimate of 2.13 (95% confidence interval 1.55-2.94)”.

“performed using the self controlled case series method which is particularly suited to collaborative studies because of its implicit control for individual level confounding.”

“The study therefore shows the potential for vaccine safety collaborations across Europe to detect true associations through use of common protocols and sharing of results or data.”