Vaccine Safety Monitoring

Part 1: How does it work now?

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8 September 2017
Outline

- Components
- Current Process
- Future activities
Components of a vaccine vigilance system

- The Medicines Act 1981
- Immunisation programme
- We can always use more
- Yes – keep listening
- Official Information Act
- WHO

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Vaccine Safety

Intrinsic safety
- Compare yellow fever vaccine with influenza

User-dependent safety
- Avoid live vaccines in immunosuppressed

Population vs Individual
- Regulator concerned with population as a whole, health professionals need to care for individual
Vigilance Process

- Signal Detection
- Signal Investigation and Assessment
- Signal Response Measures
What is a Signal?

WHO Definition:
‘reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously….’
Sources of Signals

- Spontaneous reporting schemes
  - Centre for Adverse Reactions Monitoring (CARM)
  - WHO, sponsors

- Data from formal studies
  - Pre-clinical, clinical trials, observational studies

- Published Literature

- Unpublished data
  - Sponsors, other regulators, healthcare professionals
Who Reports?

- Nurses: 44%
- Hospital doctors: 18%
- GPs: 6%
- Other healthcare professionals: 5%
- Public: 3%
- Community pharmacists: 6%
- Hospital pharmacists: 17%
- Other: 1%

2016
Spontaneous Reporting - Strengths

- Proven to identify new reactions
- Sensitivity is potentially high
- Inclusive (all medicines for life)
- Can be rapid
- Can be applied widely
- Fairly cheap
- Harnesses the reporter’s intelligence

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Spontaneous Reports - Weaknesses

- Under reporting
- Poor for certain reactions
- Frequency of reaction can’t be determined
- Uncertainty regarding causality
- Data can be misinterpreted/abused

*Beware* of stimulated reporting
Tools for Detecting Signals from Spontaneous Reports

- Individual case analysis – WHO causality criteria
- Seriousness
- Trend analysis
  - Reporting rates
  - Reaction profile
  - Data mining- Proportional reporting ratio (PRR)
Causality assessment

- Temporal relationship (including dechallenge/rechallenge)
- Alternative causes
- Nature of event (skin reactions)
- Plausibility (class effect, pharmacology)
Beware of the Nocebo Effect

Skin reaction to vaccination before injection

Every time an injection was given the girl had an immediate significant rash on her arm.

Her mother (a doctor) took her to hospital to give the next HPV-injection.

When approaching the site with an injection needle, the mother witnessed the appearance of an all too familiar rash. The skin reacted in anticipation before the needle even touched it.

doi.org/10.1016/j.vaccine.2009.12.044
Seriousness

- Highlight and prioritise
- Proportion of serious events does not reflect safety
- Determined based on what happens to patient – no impact on causality

Criteria (ICH E2D)-

- Death
- Life-threatening (real not hypothetical)
- Hospitalisation (or prolongation)
- Persistent or significant disability
- Birth defect
- Medically important (intervention- agreed lists)
# Reporting Rates

## Influenza vaccine hypersensitivity (HS)

![Image](www.medsafe.govt.nz/safety/EWS/2015/influenza-vaccine-hypersensitivity.asp)

<table>
<thead>
<tr>
<th>Year</th>
<th>HS Reactions</th>
<th>HS Reports</th>
<th>Total Influenza Reports</th>
<th>HS/ Total Reports %</th>
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<td>2013</td>
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<td>2014</td>
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<td>76</td>
<td>53</td>
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Reaction Profile

Crude AEFI rate per 10,000 doses of Gardasil from CARM reports 2008 to 2017

N.I.R. denominator = 749,383
### Data mining

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<tr>
<th>Medicine</th>
<th>Reaction (MedDRA PT)</th>
<th>listed in data sheet?</th>
<th>No. of cases</th>
<th>No. medicine-reaction reports</th>
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