

HPV Vaccine Safety and Adverse event reporting

Dr. Almath Spooner BSc.Pharm, PGDip.Stat, PhD, MPSI
PhVWP Delegate for Ireland,
Human Products Safety Monitoring
Irish Medicines Board



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Presentation Topics

- Regulatory information on Gardasil - licensed indications, posology, safety profile, recommendations for safe and effective use.
- Irish Medicines Board Pharmacovigilance Strategy for vaccines
- Post marketing monitoring of vaccine safety - learning from experience.



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Gardasil – Safety Profile

- Gardasil has been authorised for use across the European Union since 2006.
- The vast majority of suspected adverse reactions have related either to the signs and symptoms of **recognised side effects listed in the product information** or were **due to the injection process** and not the vaccine itself (i.e. 'psychogenic' in nature).
- The most common side effects with Gardasil (seen in more than 1 patient in 10 in studies) were **pyrexia, pain, erythema and swelling at the injection site.**



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Gardasil - Contraindications

- Gardasil should not be used in people who may be hypersensitive to the active substance or any of the other ingredients. If a patient shows signs of an allergy after a dose of Gardasil, she should not receive further doses of the vaccine.
- Administration of Gardasil should be postponed in individuals suffering from an acute severe febrile illness. (However, the presence of a minor infection, such as a mild upper respiratory tract infection or low-grade fever, is not a contraindication for immunisation.)



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Safety profile - syncope

- Fainting (or vasovagal syncope) and panic attacks, including mass episodes, can occur during, following, or even before, vaccination especially in adolescents and young adults.
- Syncope, sometimes associated with falling, has occurred after vaccination with Gardasil. Therefore, vaccinees should be carefully observed for an appropriate period of time after administration of Gardasil
- Faints or panic attacks occurring during or very shortly after vaccination are usually a psychogenic response to the needle injection and not a true side-effect of the vaccine.



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Safety profile - anaphylaxis

- Anaphylaxis is a very rare side-effect of all injectable vaccines.
- As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a serious allergic reaction and possibly a rare anaphylactic event following the administration of the vaccine. An appropriate post-vaccination monitoring period should be observed in line with local guidance.



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Safety profile – allergic reactions

Gardasil should not be used in people who may be hypersensitive to the active substance or any of the other ingredients. If a patient shows signs of an allergy after a dose of Gardasil, she should not receive further doses of the vaccine.

Yeast allergy?

Yeast is used in the manufacturing process for Gardasil. Therefore, Gardasil may contain low levels of yeast host cell protein. In September 2008, the US prescribing information for Gardasil was updated and a statement was added to the contraindications section regarding use of Gardasil in patients with a severe allergy to yeast.



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Vaccine Pharmacovigilance

- The most effective tools available for prevention and control of infectious diseases.
- Controversial because of concerns about safety
 - Administered to healthy people,
 - Universally used in infants and children
 - Short duration of exposure with a long-term response
 - Mass vaccination campaigns

⇒ Active post-authorisation monitoring



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Safety Monitoring of Vaccines

- Many challenges to assessment of vaccine safety
 - ⇒ Huge media and public attention
 - ⇒ Public needs frequent reassurance of vaccine safety
 - ⇒ Careful interpretation of vaccine safety signals is crucial to detect real reactions to vaccine



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Vaccine

Vigilance

Temporal and geographical clustering of rare events can occur by pure coincidence

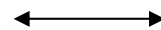
Media

A single case in temporal association

=

causal association

coincidence is not accepted!



Agencies – PhV

Temporal association only one criterion (which can be misleading)

Importance of background rates of disease in assessment of vaccine safety during mass immunisation



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Initial alarm in the media but no link to vaccination – coincidental and unrelated events regrettably associated with vaccination.

TIMES ONLINE

September 29, 2009

Friends pay tribute to schoolgirl cancer jab victim Natalie Morton



Natalie Morton: The schoolgirl died hours after having the cervical cancer jab



MHRA press release Sept 2009:
The risk/benefit profile for Cervarix remains positive and that the safety and efficacy of the vaccine had been extensively researched in clinical trials before licensing.

More than 1.4 million doses of HPV vaccine have now been administered in the United Kingdom and there have only been a little more than two thousand reports of adverse reactions.

Many women's lives will be saved in the future as a direct result of this vaccine.



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Alternative aetiology established – death unrelated to vaccination



Tragic Natalie 'not killed by cancer jab'

By ANDREW PARKER

Published: 30 Sep 2009

 [Add a comment \(48\)](#)

TRAGIC schoolgirl Natalie Morton did NOT die as a result of a cancer jab, it was thought last night.

Early tests on the 14-year-old showed she had "a serious underlying medical condition".


Natalie died hours after being given a Cervarix injection as part of a school inoculation programme.

There was chaos last night as some health and schools chiefs suspended vaccinations while the batch used at her school in Coventry was tested.



There ARE
side-effects that
we're NOT being told
about

Published: 06 Oct 2009

 [Add a comment \(6\)](#)

MUMS are fighting back over the controversial cervical cancer jab being dished out to young Scots schoolgirls.

Challenges in Vaccine Vigilance – unconfirmed concerns

- Attention on unconfirmed risks which were linked with the use of some vaccines:
 - demyelinating diseases and hepatitis B vaccines
 - Type one diabetes mellitus and vaccines (Hib vaccines)
 - Measles, mumps, and rubella (MMR) vaccines and autism



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Why does this happen?

Factors that contributed to the quick acceptance of several of these false assumptions of causal association were:

- a lack of understanding of how passive reports of adverse events can be interpreted
- a poor understanding of the scientific methods used to assess causality.

Black et al. Lancet 2009



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Post Marketing Risk Evaluation

- Data collection
- Signal detection
- Signal evaluation
- Decision making
- Communication
- Collaborations



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Monitoring of Vaccine safety

CIOMS/WHO VACCINE PHARMACOVIGILANCE WORKING GROUP

- Adverse Event Following Immunization (AEFI):

“any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the administration of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease”.



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Data Collection

- Adverse Event Following Immunization (AEFI) may be causally related or happen coincidentally. Prioritise reporting of those considered to be causally associated.
- **Spontaneous reporting:** Cornerstone of safety monitoring: in particular with regard to rare, serious adverse reactions with a low background event rate.
- **Ideally provided:** complete and accurate records:
 - date of vaccination, product administered, manufacturer, batch number, site and route of administration, detailed description, concomitant drugs, and course of the adverse event/reaction as well as therapeutic intervention should be provided where feasible.
 - Details about the event in question help to determine whether it meets a case definition such as those developed by the Brighton Collaboration

Data collection

- Background incidence rates
- A critical aspect of the analysis of spontaneous reporting data and data from studies is the collection of background information on incidence of AEs.
- Assessment of causality for events associated with vaccines will be aided by knowledge of their background incidence rates. (Observed vs. Expected

Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines

Steven Black, Juhani Eskola, Claire-Anne Siegrist, Neal Halsey, Noni MacDonald, Barbara Law, Elizabeth Miller, Nick Andrews, Julia Stowe, Daniel Salmon, Kirsten Vannice, Hector S Izurieta, Aysha Akhtar, Mike Gold, Gabriel Oselka, Patrick Zuber, Dina Pfeifer, Claudia Vellozzi

www.thelancet.com Published online October 31, 2009

RD

Risk evaluation

Causality assessment

is complex...

“In most cases, there are no specific tests to prove a causal association between a vaccine and an AEFI. In contrast there may be several tests that can confirm an event is due to a specific cause other than immunization, i.e. a coincidental event.”

Reporting ADRs/AEFIs

- Anaphylaxis is a very rare side-effect of most vaccines.
- It is essential that we distinguish between reports of anaphylaxis and less serious allergic reactions or psychogenic events.
- If you suspect a true case of anaphylaxis has occurred, **please report it as such**, providing as much **detail** as possible.
- When reporting less severe allergic reactions, please report as 'allergic reaction' or provide another relevant description as the **primary diagnosis**.
- Any **signs or symptoms** of anaphylaxis or other allergic reactions should be reported as '**additional information**' on the report form rather than as the primary adverse reaction.



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Reporting Suspected Adverse Reactions

What & When?

- Any suspected adverse reaction, but in particular
 - Serious, suspected reactions to established medicines
 - Any suspected increase in the frequency of non-serious reactions

We strongly encourage you to report online at www.imb.ie or alternatively use the Yellow Card system:

Post-paid Report Cards (Yellow-Cards)

- On request from IMB (Tel: 01 6764971)
- Available from website



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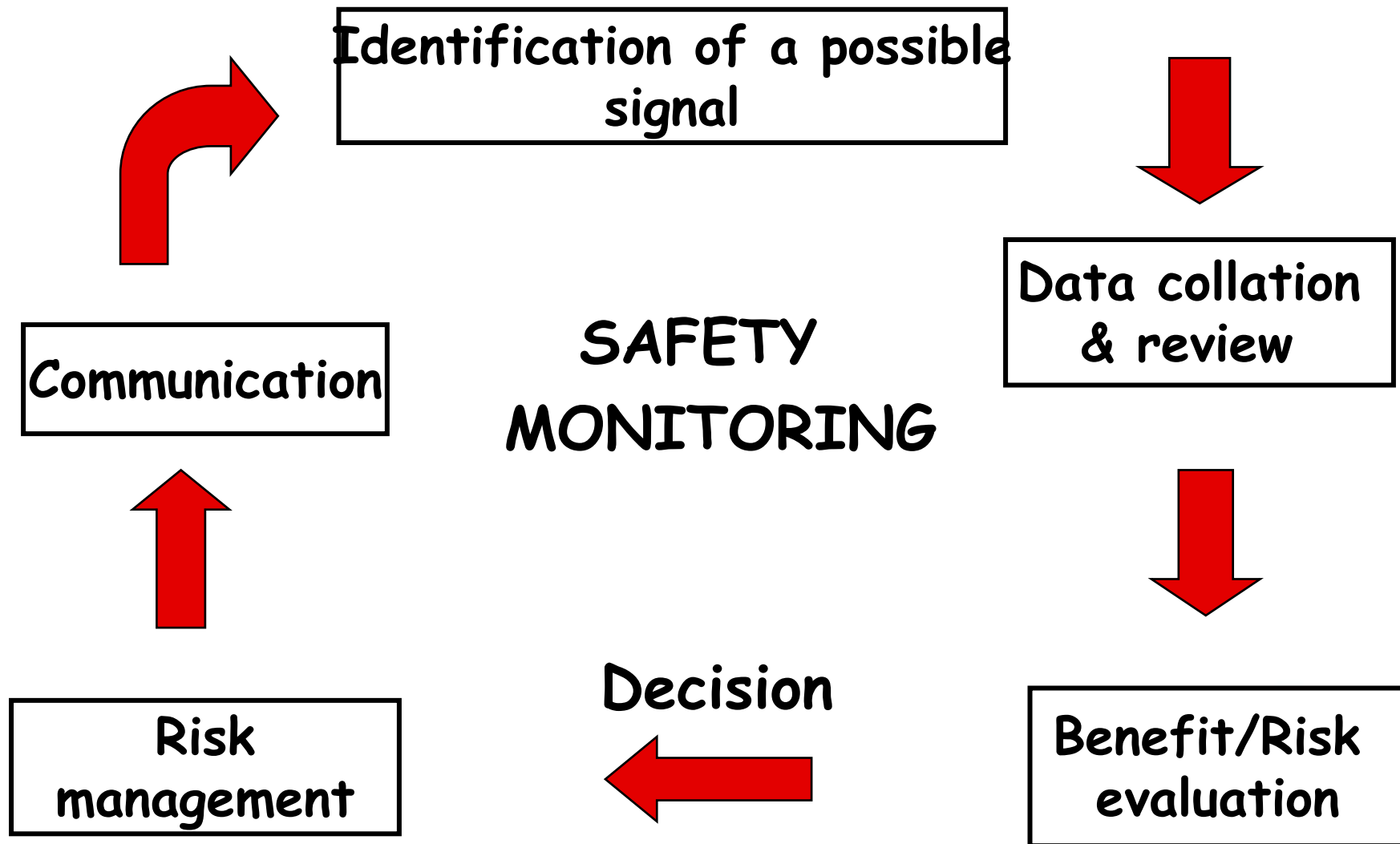
High Quality/Added value Reports...

- Please report adverse reactions that you suspect may have been caused by Gardasil.
- Please prioritise reporting of adverse reactions that you suspect may be related to the vaccine and not those associated with the injection process or procedure .
- Please remember to provide details of the batch number and the brand name of the vaccine to facilitate traceability.



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Evaluation of Pharmacovigilance Data



Conclusions

- Vaccines are ‘specific drugs’.
- Many challenges to assessment of vaccine safety.
- Active post-authorisation monitoring is required.
- Spontaneous reporting: Cornerstone of safety monitoring.
- Importance of background incidence of potential AEFIs in assessment of vaccine safety.
- Public confidence based on the assessment of the safety signals in a timely and adequate manner.
- Appropriate action and adequate communication needed.



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Regulatory Information Sources

- www.imb.ie
- <http://www.ema.europa.eu/>
- Product Information –
Summary of Product Characteristics
(SmPC) and Package Leaflet (PL)
IMB Drug Safety Newsletter
Web updates



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