New medicines and vaccines
– Monitor safety in emergency situations
The Swedish experience of the 2009-2010 pandemic flu vaccination

Uppsala Health Summit October 10, 2017

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Outline

What happened?

Setting and regulatory aspects

What actions did we take?

What have we learnt?

How can we prepare for the future?
The flu broke out.....

Mexico swine flu outbreak triggers global pandemic fears

Up to 70 dead as swine flu outbreak sweeps Mexico, crosses US border and prompts worldwide pandemic panic

A killer virus that has caused at least 20 deaths and sparked widespread panic in Mexico has the potential to become a global pandemic, warn health experts.

The World Health Organisation stopped short of issuing a worldwide alert over the swine flu strain - a unique mix of human, pig and bird viruses - but its director general, Dr Margaret Chan, said the option remained "on the table".

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Swine Flu and Narcolepsy: What Was the Link?

By Erica Zane - November 11, 2015

Back in 2009, a nasty strain of the flu, namely swine flu, raced around the globe knocking people down like bowling pins.

ScienceNordic

Flu vaccine may cause narcolepsy

September 19, 2013 - 08:32

The influenza vaccine Pandemrix has been associated with an abrupt increase in the incidence of childhood narcolepsy in Finland and Sweden.

Pandemrix - AstraZeneca/Covis and earlier costs, Medscape, Frommers

Great increases in Sweden and Finland in 2009-2010. In the same period in narcolepsy cases was correlated with the swine flu pandemic. In 2008-2010, in Finland, 312 cases of narcolepsy were recorded, and in Sweden, 152 cases were reported, of which were below the age of 18.

The swine flu vaccine Pandemrix...
The setting – and the actors

- **Sweden**
  - 10milj inhabitants, public and tax funded health care,
  - decisions on vaccination programs, pandemic vaccination, reimbursement of drugs/vaccines taken at the national level (Public Health Agency)

- **EU- EC, EMA-NCAs, ECDC, WHO**
  - approval of vaccines and drugs/biologics, safety assessment and risk management planning
  - declaration of pandemic state and severity
Why regulation of medicines?

- Safeguard adequate testing prior to marketing
- Balance scientific (un)certainty vs medical need

Pandemic particulars:
- Mock-up vaccine
- Disease risk “moving target”
- Treating healthy children
- Public fear – flu vs vaccination
SE case-inventory study. Population Incidence Rates for narcolepsy: Jan 1 2009- Dec 31 2010, by quarters of years

- Pre-Pandemic: 0.31/100’ p-yrs
- Pandemic-vaccination: 5.78/100’ p-yrs
- Post Pandemic-vaccination: 0.79/100’ p-yrs
What actions did we take?
Capture of the signal in the spontaneous reporting system

![Graph showing adverse event reports from healthcare professionals regarding suspected narcolepsy after vaccination with Pandemrix (2010–2014). *Start of Medical Products Agency narcolepsy investigations.*](image-url)
From safety signal to benefit/risk assessment

Signal generation → Signal detection → Signal verification → Risk assessment → Causality assessment → Risk minimization → B/R

Feed-back driven actions and communication

2017-10-19  N Feltelius UHS 2017
What actions did we take?

- April 2009
  - H1N1 flu starts

- 9 okt 2009
  - Vaccination starts

- August 2009
  - Increasing no of ADRs

- 4 maj 2010
  - ADRs summary report

- 18 Augusti
  - NUI on narcolepsy (EU)

- 27 Augusti
  - Article 20 proc starts

- Sept
  - MPA case inventory starts

- 1 Sept
  - Expert meeting at MPA

- 29 January 2011
  - Parents info meeting

- Spring 2011
  - VAESCO case control study

- 16 Oct – 4 May
  - Compilation of ADRs

- 27 Augusti
  - Article 20 proc starts

- Sept
  - MPA case inventory starts

- SE regional registry study

- 1 fEB 2011
  - Report from FI (THL)

- 29 March
  - National registry study (MPA)

- 2009 2009 2010

- 2009
  - 4 maj 2010

- 2009 2010

- 2010

- 2011

- August 2010 – July 2011
  - CHMP meetings
  - narcolepsy

- 30 June
  - Result CI study (MPA)

- 12 July
  - Expert meeting (EU)

- 21 July (Art 20)
  - Restricted use of Pandemrix

- 25 August
  - Beijing study
What actions did we take?(II)

- Iterative parents/patients consultations
- Repeated media activities
- Research projects
- Health care supporting activities

2012 - 2016
Overview of Pandemrix related activities in Sweden

- EU vaccine safety measures
- Registry studies
- Case inventory and long-term follow-up
- Spontaneous AE reports

- 4-region study (narcolepsy)
- 7-region (neurol./autoimm.)
- Infectious epidemiol
- Clinical report
- Genetics
- Immunology
- Biobanking
- VAESCO

- Disease mechanism?
- New treatment?

NUI

Spontaneous AE reports

Quality registry

Cont analyses

Art 20 report

Case control

Case inventory and long-term follow-up

4-region study (narcolepsy)

4-region (long-term)

Infectious epidemiol

Clinical report

Genetics
Some scientific reports generated through the MPA narcolepsy research package


What have we learnt? Identified problems

• Data/analytical
  – Insufficient exposure (vaccination) and outcome data
  – Poor information on flu/infection geographical spread and severity
  – Poor knowledge of disease background incidences
  – Confounding by media-driven reporting bias
• Organization/procedural
  – Lack of sufficiently powered and skilled analytic capacity
  – Difficult to transform WHO, ECDC pandemic scenario information to national vaccination recommendations
• Communication
  – Media and public reactions difficult to predict
  – We informed too little on benefits with vaccination
  – Rare adverse reactions not avoidable – Overall trust in vaccinations will be harmed
What have we learnt? How can we prepare for the future?

• Data/analytical
  – Set up data collection structures before pandemic out-break (exposure, outcomes, back-ground incidences)
  – Social media to follow disease spread(?)

• Organizational/procedural
  – Identify scientific networks prepared to give support in emergency situations
  – Train rapid analytic procedures (external collaborations or in-house capacities)
  – Take on a distinct organizational and scientific leadership as soon as an emergency situation is identified

• Communication
  – Accept that rare adverse effects will occur – and must be communicated
  – Establish a functioning relationship with media
  – Prepare for direct discussions with patients/relatives
  – Provide convincing data on vaccination benefits
  – Counteract fake news with focus on social media
Thank you for your attention!

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