Be aware the next pandemic pathogen can be very different: Experience of H5N1?

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Medicines Patent Pool
In 2006, all eyes were focused on Influenza A/H5N1

• There is scientific ground to fear an avian flu pandemic:
  – The Spanish flu in 1918-19 was caused by a mutation of an avian flu virus into a subtype that easily transmitted between humans. It killed 40 million people in 10 months time
  – Recently there have been outbreaks of avian flu viruses in men, which resulted in 273* infections of which 166 died
  – Scientists agree that it isn’t a question of if there will be a pandemic outbreak but rather a question of when it will happen and by which strain it will be caused

• A flu pandemic would cause high morbidity, as vaccine supply isn’t sufficient
  – Scenarios predict between millions of deaths as experts believe that an outbreak would contaminate up to 30% of the global population within 80-90 days.
  – Vaccinations remain the cornerstone of prevention but current global capacity for flu vaccines is still several billion doses short of the expected demand at the time of the pandemic outbreak
  – Moreover, vaccine coverage would be extremely low in Asia, from which a pandemic is likely to start

* In Feb 2007
WHO initiated the Global Action Plan to increase supply of pandemic influenza vaccines in 2006

- In order to strengthen pandemic-influenza preparedness and response, WHA 58.5 requested to WHO secretariat to seek solutions with international and national partners, including the private sector, to reduce the potential global shortage of influenza vaccines for both epidemics and pandemics, including vaccination strategies that economize on the use of antigens, and development and licensing of antigen-sparing vaccine formulations.

I. Increase use of seasonal influenza vaccine

II. Increase production capacity for pandemic vaccines, independent of seasonal vaccine use

III. Research and develop new technologies
High-income countries started stockpiling H5N1 Vaccine

Moreover:

- H5N1 influenza vaccines were shown to induce cross-clade immunogenicity in humans

- When this was tested, H5N1 vaccines were demonstrated to induce both homologous and heterologous protection in ferrets

- All preparations tested were shown to be safe
But H5N1 threat changed the status quo

- **Seasonal vaccine**
  - Use mainly in industrialized countries
  - Vaccine production met market needs
  - Free sharing of influenza viruses and sequences for over 50 years

- **H5N1/pandemic vaccine**
  - Human zoonotic infections mainly in developing countries
  - Threat of pandemic greater than anytime since 1968
  - Need in both high and low-income countries
  - Production capacity would not meet global need
In early June 2007, Minister Supari said the government would no longer report human H5N1 cases and deaths promptly to the WHO. Media outlets reported that she planned to report cases after they were reported in the news media or only at 6-month intervals.
Jakarta Meeting, March 2007: Sharing the benefits of virus sharing

- Maintain best practices/review operational procedures and develop new terms of reference for WHO Collaborating Centres:
  - Increased transparency in specimen handling
  - Intensified laboratory exchange/training possibilities
  - More involvement of developing country scientists

- Identify short term mechanisms to make H5N1 and pandemic vaccines available as a compliment to GAP
Results from WHO Survey

Results from 45 countries which had completed the WHO Global online survey

- **4/45 Countries (9%)** had stockpiles of H5N1 vaccine (Australia, New Zealand, Singapore and Solomon Islands)

In addition, many high-income countries were known to have secured access to H5N1 vaccine, among which Austria, Canada, Germany, France, UK, USA

- **37/45 Countries (82%)** indicated that they would require H5N1 Vaccine from WHO Stockpiles. However, only 20 countries were able to identify the required number of doses.

- **24/45 Countries (53%)** had plans which prioritized essential workers
### Three primary options considered for vaccine strategies

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<th>Produce vaccines at time of pandemic</th>
<th>Pre-pandemic vaccine stockpiling</th>
<th>Priming population</th>
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- **Produce vaccines at time of pandemic**
  - Timeline typically requires **3-6 months** for sufficient ramp-up

- **Pre-pandemic vaccine stockpiling**
  - [Image of syringes]

- **Priming population**
  - [Image of a caregiver administering a vaccine to a child]

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**World Health Organization**

**R&D Blueprint**

*Powering research to prevent epidemics*
Each vaccine strategy offers pros and cons

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<th>Pros</th>
<th>Cons</th>
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| Produce vaccine only at the time of pandemic | • Exact strain should provide maximum protection  
• Avoids waste in stockpiling ineffective vaccine  
• Saves cost of stockpiling vaccines |
|                        | • Can only vaccinate the survivor of the initial pandemic wave  
• May potentially fail in ramping up needed supply of vaccines  
• Vaccine distribution could be challenging |                        |
| Pre-pandemic vaccine stockpiling | • Ensures vaccine is available from day 1 of outbreak  
– Produced during low production period  
• Offers potential cross-protection to mitigate impact of pandemic | • Could be less effective than exact strain  
• Significant costs of stockpiling and/or cold storage |}

| Priming population | • Priming populations may improve broader immunity against H5 infection  
• Stimulates vaccine demand to guarantee capacity  
• Avoids storage costs | • Effect of vaccine is controversial before pandemic really happens  
• Risk of side effects |
SAGE Recommendations, 2007
Review of current knowledge

- Sufficient evidence for WHO to create a stockpile H5N1 influenza vaccine for countries without influenza vaccine production capacity or ability to purchase stockpiles of H5N1 vaccines.

- Establish mechanisms for ensuring access to pandemic vaccine, should a pandemic be declared by the Director General, for distribution to developing countries without influenza vaccine production capacity or resources to purchase such vaccines.
Lessons learnt

1. Never presume of which virus will cause the next pandemic!
2. Generic preparedness – including using a «family approach» and focusing on Pathogen X - will likely be more effective
3. Equity should be built from the start in pandemic preparedness plans

So, at the end of the day…

1. High-income countries stockpiled at high cost H5N1 «pre-pandemic vaccine» which was never used;
2. After several extensions of expiry date, all H5N1 vaccine was destroyed.
The current challenges of Research and Innovation are a problem that can be solved.

Let’s solve it together!