Priority Public Health Interventions before and during influenza pandemics

Klaus Stöhr

Department for Communicable Diseases Surveillance and Response

Before and during influenza pandemics

- Before pandemics: interpandemic period
  - New human influenza strain emerges: one case
  - Two or more human cases: but virus essentially non-human
Events with pandemic potential since 1968

- 1976: H1N1 Swine influenza USA (1 †)
- 1986: H1N1 Swine virus derived from avian source: one severe pneumonia
- 1988: H1N1 Swine virus USA: pregnant woman died after contact to sick pigs
- 1993: H3N2 Swine virus H3N2 recombinant with Avian H1N1 Netherlands: 2 children with mild disease
- 1995: H7N7 duck virus UK: adult mild conjunctivitis
- 1997: H5N1 avian influenza Hong Kong: 18 cases/6 †
- 1999: H9N2 quail virus: 2 mild cases
- 2003: H5N1 avian virus Hong Kong: 1 †; 1 disease +1 related † from pneumonia
- 2003: H7N7 avian virus Netherlands: 1 †; 80+ conjunctivitis; few respiratory symptoms
- 2003: H5N1 avian virus Guangdong: 1 †
- 2003: H9N2 avian virus Hong Kong: 1 disease
- 2004: H5N1 disease and death in Vietnam and Thailand (34 cases/23 †)
- 2004: H7N3 avian virus Canada: 2 cases (conjunctivitis)
- More recently...

Before and during influenza pandemics

- **Before pandemics: interpandemic period**
  - New human influenza strain emerges: one case
  - Two or more human cases: but virus essentially non-human
  - Human-to-human spread; localized outbreaks
    - Through Ag shift; mutation of non-human virus

- **During pandemics**
  - Pandemic virus circulates; efficient human-to-human transmission
Phases of an influenza pandemic

**WHO Pandemic Preparedness Plan**

- Duration of interpandemic phase and levels may vary
- New: 1997 → direct transmission
- New: 2004: long + widespread presence of type of known human pathogenicity; multiple transmission to humans; co-circulation of human virus but no reassortment

**Interpandemic phase**

- Level 1: new human strain emerged
- Level 2: two or more human cases
- Level 3: human-human spread; localized outbreaks

**Pandemic**

- Slowing down spread

**Interpandemic phase**

Duration of interpandemic phase and levels may vary

New: 1997 → direct transmission

New: 2004: long + widespread presence of type of known human pathogenicity; multiple transmission to humans; co-circulation of human virus but no reassortment

---

**H5N1 influenza in humans and poultry**

→ 21 March 2004

[Map showing H5N1 influenza in humans and poultry]
Phases of an influenza pandemic

WHO Pandemic Preparedness Plan

- Duration of interpandemic phase and levels may vary
- New: 1997 → direct transmission
- New: 2004: long + widespread presence of type of known human pathogenicity; multiple transmission to humans; co-circulation of human virus but no reassortment

Priority Public Health Interventions

International

- Generic
  - Surveillance
  - Research
  - Risk assessment and communication
- Medical interventions
  - Vaccines
  - Antivirals
  - Treatment of viral and secondary bacterial pneumonia (antimicrobials)
- Non-medical interventions → objectives
  - Aversion of pandemic → package of activities aiming at elimination of new subtype with increasing fitness
  - Slowing down spread of pandemic virus → packaged of activities to reduce transmission/infection rate
→ An national levels: combination might vary
  - Reducing morbidity or mortality or economical implications
**Priority Public Health Interventions**

**Surveillance**

- **Objective**
  - Early warning: rapid detection of emerging strain, unusual clusters of cases and occurrence of human-to-human transmission
    - at the earliest possible stage, when PH interventions have the greatest chance to prevent or delay further national and international spread
  - Global reporting to support national planning
  - Foundation of
    - Research, risk assessment and policy development (allocation of resources)
    - Pandemic vaccine prototype selection and development

- **Challenges**
  - WHO Global Influenza Surveillance System exists but
    - Surveillance capacities insufficient in several priority countries
    - Access to strains and shipment costs are limiting factors

**Priority Public Health Interventions**

**Research**

- **Objective**
  - Obtain evidence for policy making
  - Understand and assess evolution of key clinical, epidemiological and virological parameters
    - Epidemiological parameter: risk groups, IKP, Ab, duration of infectivity; impact
    - Virological: diagnostic test kits; pandemic vaccine content; antiviral resistance
    - Clinical: treatment and diagnostic guidelines

- **Challenges**
  - National and international coordination planning
  - Availability of epi study and clinical trial protocols and research cooperation before next outbreak
  - Academic competition versus rapid access to data for PH policy making
Priority Public Health Interventions
Risk assessment and communication

An influenza pandemic is a public health emergency that rapidly takes on significant political, social, and economic dimensions. As with other emerging infectious diseases, the course of its evolution is governed by factors – including the properties of a new causative agent – that cannot be known in advance and require some time to understand.

In the phases moving from the pre-pandemic period to a full-fledged pandemic, health authorities will need to make a series of emergency decisions in an atmosphere of considerable scientific uncertainty and fragile public confidence. (WHO/CDS/CSR/2004.09)

Priority Public Health Interventions
Risk assessment and communication

● Objective
  – Evidence based policy making during an evolving epidemiological situation;
  – Providing free and rapid access to existing information (epi, clinical, virological; human and animals; economics and medical; ...)

● Challenges
  – Rapid information sharing ➔ internet fundamental tool
  – Mechanisms required to obtain international consensus
  – Coherent approaches to risk assessment and communication
    • countries not taking decisions in isolation
      – Decisions in one country will have implications elsewhere
  – Evidence of effectiveness lacking for most of the non-medical interventions; PH decisions to be taken on incomplete scientific data


Priority Public Health Interventions
Vaccines

- Vaccines major pillar for reduction of morbidity and mortality if timely available...

- Challenges
  - Rapid strain identification/characterization; evolutionary surveillance
    - WHO Global Influenza Surveillance Network; WHO CC
  - Significant problems with rapid and significant vaccine manufacturing
    - Lack of surge capacity (up- and down-stream; CC-vaccines no option yet…)
    - Expedited licensing: clinical testing; GMO
    - Paucity of clinical data on immunogenicity of pandemic vaccines
    - Technical problems: IP right for use of reverse genetics; GMO

Spread of H2N2 influenza in 1957
“Asian influenza”
Availability of Influenza Pandemic Vaccine
European Country

Priority Public Health Interventions
Vaccines

- Vaccines major pillar for reduction of morbidity and mortality → if timely available...

- Challenges
  - Rapid strain identification/characterization; evolutionary surveillance
    - WHO Global Influenza Surveillance Network; WHO CC
  - Significant problems with rapid and significant vaccine manufacturing
    - Lack of surge capacity (up- and down-stream; CC-vaccines no option yet...)
    - Expedited licensing: clinical testing; GMO
    - Paucity of clinical data on immunogenicity of pandemic vaccines
    - Technical problems: IP right for use of reverse genetics; GMO
  - Location of production capacity: haves and not-haves
Vaccine production capacities

- 70% of global vaccine production located in Europe (5 companies)
  - 50% of that production is exported outside of Europe

Source: EVM Press Release 30 April 2004

Priority Public Health Interventions

Antivirals

- Stockpiling possible; could be major pillar for reduction of morbidity and mortality? if timely available...

- Challenges
  - Significant problems with rapid and significant production and access
    - Lack of production and surge capacity
  - Neuraminidase inhibitors
    - Costs; shelf-life; application; treatment versus prophylaxis
  - Amantadines
    - Anti-viral resistance; side affects and toxicity
    - Effectiveness on reduction of mortality anticipated but not measured
    - Stockpiling: only developed countries...

- Location of production capacity: haves and not-haves
Priority Public Health Interventions
Summary: vaccines and antivirals

- Will not be available during initial phase of pandemic
  - Irrespective of the pathway of emergence of pandemic strain
- There will be only limited supply during later phase of pandemic: haves (some developed) and non-haves (all developing countries)
  → Non-medical interventions will be the principal control measures pending the availability of adequate supplies of an effective vaccine and antivirals.
    - In some resource-poor settings, might be the only control measures available throughout the course of a pandemic

Priority Public Health Interventions
Non-medical interventions

- Objective
  - Reduce transmission and spread (during levels 1-3 and first phase pandemic; entire pandemic for resource poor countries)
- Challenges
  - Use during different phases of pandemic has not been systematically evaluated
- WHO Consultation
  - More than 30 interventions
    - Assessed in terms of feasibility and likely effectiveness
    - Wide range: personal hygiene, wearing masks to quarantine and passenger screening
    - Considered separately for use at national and international levels and during various interpandemic and pandemic phases
    - Considered resource implications and social and economical disruption
Priority Public Health Interventions
Non-medical interventions: international

- Measures at borders
  - for persons entering or exiting a country
  - for international travellers coming from or going to affected countries
- Entry and exit screening
- Measures for countries with porous borders adjoining affected areas
- Measures for travelers on board of international conveyances from affected areas

Priority Public Health Interventions
Aversion of a pandemic (level 1-3)

- Objective
  - Extinguish pre-pandemic strain (like H5N1 Asia 2004)
  - Package of medical and non-medical measures on risk reduction
    - to prevent reassortment and drift
    - to avoid international spread
  → Direct country support
- Challenge
  - Elimination of animal reservoir
    - Bringing together public health and agriculture objectives
      - Surveillance and reporting approaches; control measures
    - Outbreaks in resource poor countries
  - Reduce exposure of and transmission to humans
    - PPE; Irrespective of the pathway of emergence of pandemic strain
  - Avoid co-circulation of human viruses
    - Vaccination with human epidemic vaccines and prophylactic use of antivirals
    → Access to vaccines; use of international antiviral stockpile?
WHO specific contribution to pandemic preparedness and response 1

- **Surveillance**
  - Detection of emerging strain; continuous strain assessment; WHO diagnostic test kits for all countries
  - Global surveillance and reporting mechanism/guidelines

- **Immediate response**
  - Outbreak detection/reporting;
  - Direct support to countries: treatment/management of cases; diagnosis; use of PPE
  - Use of non-medical interventions at international levels
    - antiviral stockpile
  - Research coordination
  - Risk communication

WHO specific contribution to pandemic preparedness and response 2

- **Vaccines**
  - Development of prototype strain vaccine; standardizing reagents

- **Advocacy, international leadership, guidance**
  - Support to countries
    - Model national plans, vaccine+antiviral use, self-assessment tools
  - Critical assessment of armamentarium of non-medical interventions to slow down spread
  - Access to vaccines and antivirals
    - Very wide range of activities....
  - Advocate for developing countries

⇒ WHO is one player in a team....
Global Agenda on Influenza

4 areas/themes of high priority
- Improve surveillance nationally and globally
- Increase knowledge on health and economical burden
- Increase vaccine usage
- Accelerate national and international action on pandemic preparedness

17 priority activities with 47 action items