



# *Influenza A/H1N1*

## *Lesson learned*

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# Outline of the presentation

- Background on the human epidemic
- Background on Influenza A viruses
- What is new about Influenza type A H1N1
- Why it has been associated with swine
- Role of pigs
- New challenges and perspectives



# The epidemic

- An unprecedented influenza A strain of the subtype H1N1 has been causing infections among humans since April 2009. The virus has been described as a new subtype of Influenza A/H1N1 not previously detected in swine or humans.
- The novel virus in humans was first identified in Mexico.



# The epidemic

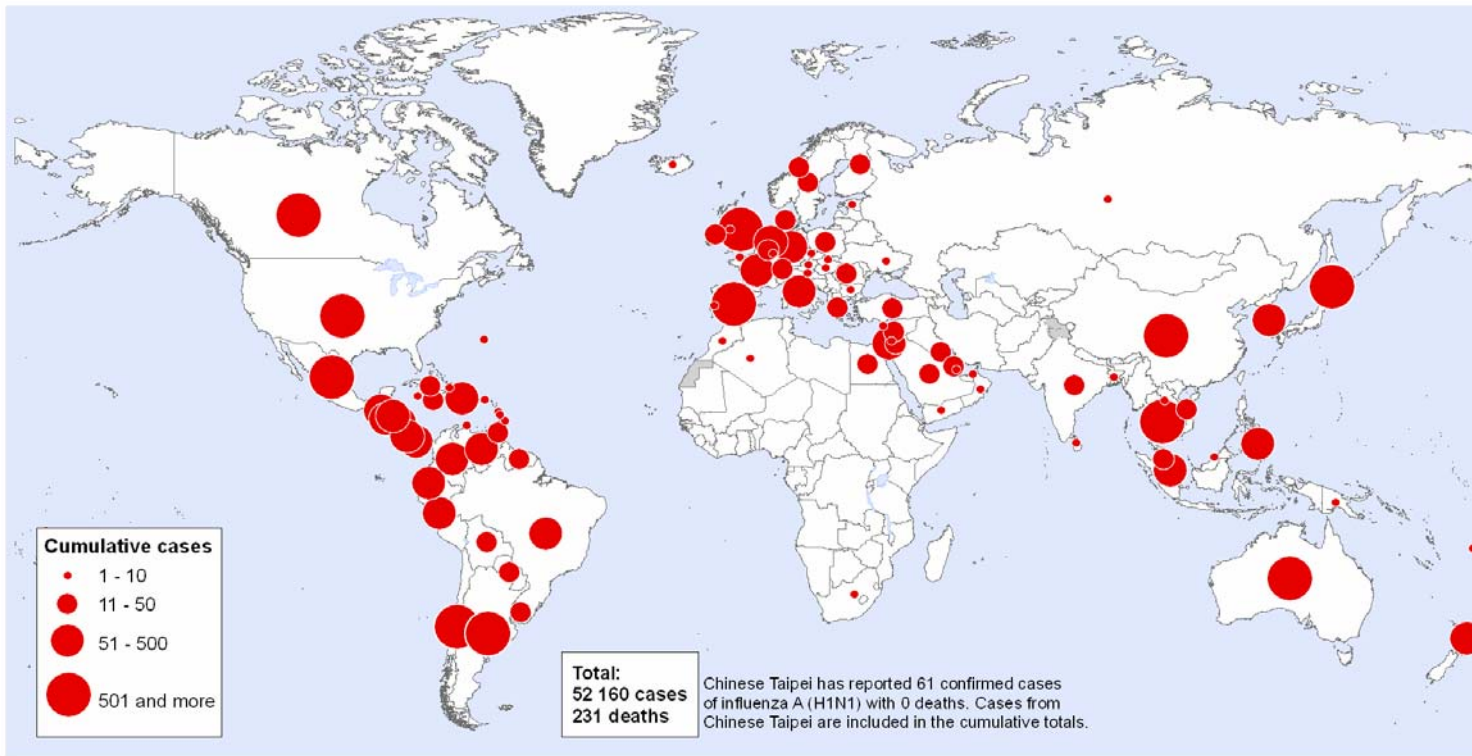
- The Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), the World Health Organization (WHO), the Animal and Plant Inspection Service of the United States Department of Agriculture (USDA), the Centers for Disease Control and Prevention (CDC) and other partners are monitoring the situation on a daily basis.



# The epidemic

New Influenza A (H1N1),  
Number of laboratory confirmed cases as reported to WHO

Status as of 22 June 2009  
06:00 GMT



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 22 June 2009 06:55 GMT

Data Source: World Health Organization  
Map Production: Public Health Information  
and Geographic Information Systems (GIS)  
World Health Organization



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# The epidemic

- Due to the rapid spread, the WHO increased the phases of its pandemic alert scale at various points, reaching phase 6 (i.e. pandemic) on 11 June 2009;
- WHO considers the overall severity of the influenza pandemic to be moderate. This assessment is based on scientific evidence available to WHO, as well as input from its Member States on the pandemic's impact on their health systems, and their social and economic functioning.



# The epidemic

- The observation on the genetic structure and components of the implicated virus has led, in an early stage of the epidemics in humans, to speculate that this particular combination of gene segments had originated in swine;



# Influenza A viruses

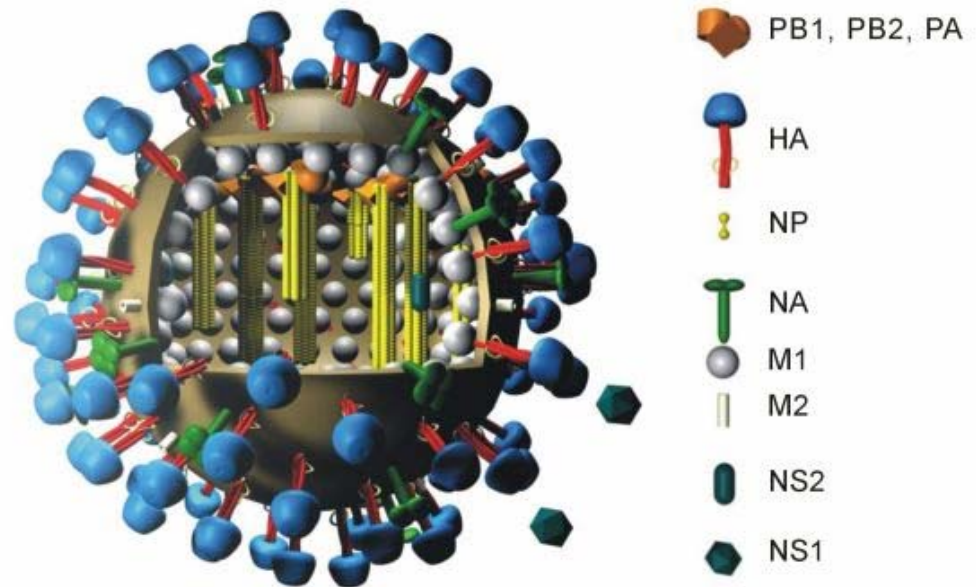
- What has led to indicate swine as a possible origin of the implicated virus ?





# Influenza A viruses

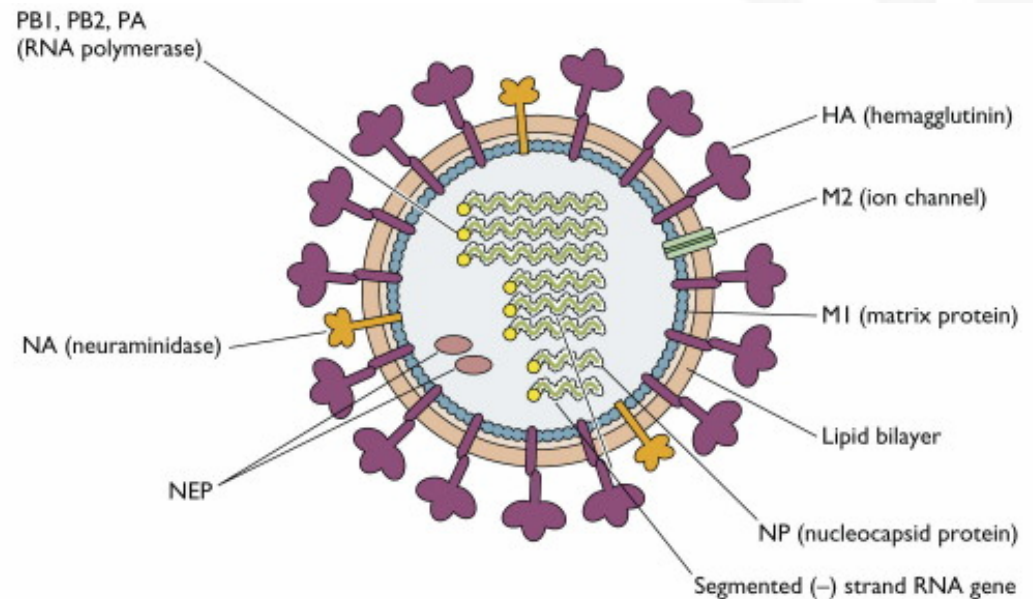
- Family of Orthomyxoviridae
- Single stranded RNA (negative sense)
- Classification based on Haemoagglutinin (HA – from H1 to H16) and Neuroaminidasis (NA – from N1 to N9)





# Influenza A viruses

- The nucleic acid is composed by 8 distinct segments
- Those 8 segments recognize gene tracts that encode for 10 different proteins





# Influenza A viruses

- The **HA** gene encodes the haemagglutinin (HA)
- The **NA** gene encodes the neuraminidase (NA)
- The **NP** gene encodes the nucleoprotein (Influenza A, B, and C viruses have different nucleoproteins)
- The **M** gene encodes two proteins: a matrix protein (M1) and an ion channel (M2) spanning the lipid bilayer
- The **NS** gene encodes two different non-structural proteins (namely NS1 and NS2, also known as NEP). These are found in the cytoplasm of the infected cell but not within the virion itself
- The remaining three segments (**PA**, **PB1** and **PB2**) encode for each of the 3 corresponding subunits of the RNA polymerase (PA, PB1 and PB2)



# Influenza A viruses

- New strains of the influenza virus may emerge due to a gradual process known as **antigenic drift**, in which mutations within the virus antibody-binding sites accumulate over time. Through this mechanism, the virus is able to circumvent the body's immune system, which may not be able to recognize and confer immunity to a new influenza strain even if an individual has already built up immunity to a different strain of the virus. Both A and B influenza viruses continually undergo antigenic drift.



# Influenza A viruses

- Influenza A also experiences another type of mutation called **antigenic shift** that results in a new subtype of the virus. Antigenic shift is a change in antigenicity caused by the recombination of the influenza genome, which can occur when a cell becomes simultaneously infected by two different strains of type A influenza. The broad range of hosts susceptible to influenza A appears to increase the likelihood that this event will occur.
- The mixing of strains that can infect birds, pigs, and humans is thought to be responsible for most antigenic shifts.



# Influenza A viruses

- What is new with the novel type A H1N1 ?
- The novel virus possess:
  - **PB2** and **PA** genes of North America avian origin;
  - **PB1** gene of a human H3N2 virus;
  - **HA**, **NP** and **NS** genes of classical swine virus origin;
  - **NA** and **M** genes of Eurasian avian-like swine origin
- This combination of gene segments had never been observed before.



# Influenza A viruses

- Apparently a triple re-assortment (H3N2 human/avian/swine) was started to be observed early in 1997-1998 (Neumann G. et al, 2009; Smith G.J.D. et al, 2009; Nature, vol 459; 2009) which spread widely within North American pig population;
- Co-circulation and mixing of this triple H3N2 re-assorted virus with well established swine lineages has generated further re-assorted H1N1 and H1N2 virus in pigs that sporadically have infected humans;



# Influenza A viruses

- The insertion of gene segments encoding for **N1** and **M** proteins of Eurasian avian-like swine origin is the new event detected in the genetic structure of the virus (quadruple re-assortment);
- When and in which species this event has taken place has not been established;



swine influenza.exe





# Influenza A viruses

- This particular combination with a prevalent gene segments of swine origin has led to speculate that this re-assortment had taken place in swine;
- As a consequence at the initial stage of the epidemic pigs had been identified as the source for this novel virus;
- Both of those statements have not been demonstrated yet.



# Influenza A viruses

- This putative association has created shock markets for the pig industry because of significant reduction of consumption of pork meat products;
- This has led FAO-OIE-WHO to issue a joint statement stressing the inaccuracy of the early “swine influenza” denomination and recommending the change to novel influenza virus A/H1N1;



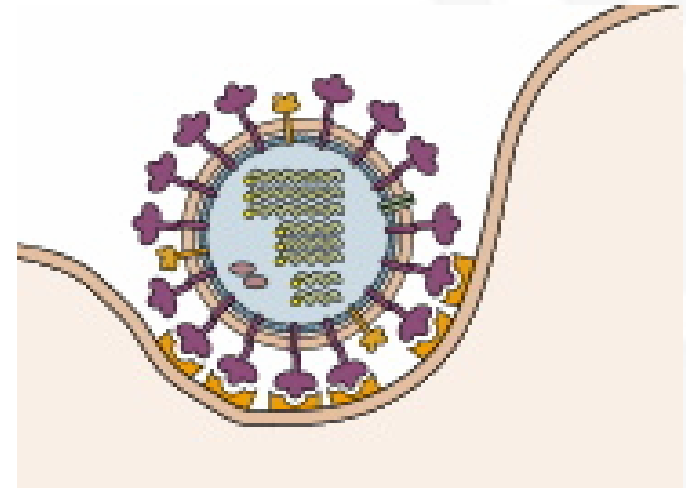
# Influenza A viruses

- What is the role of pigs in the ecology of Influenza viruses and why this animal species is considered so important ?



# Role of pigs

- Pigs may play an important role in the ecology of influenza virus as **mixing vessels**;
- Determinants of host susceptibility (in humans and avian species) is the presence and distribution of specific acid sialic receptors for the HA protein of the influenza virus;
- The two most common receptors are the **SA $\alpha$ 2,6Gal** (prevalent on epithelial cells of human trachea) and **SA $\alpha$ 2,3Gal** (prevalent on epithelial cells in the intestinal tract of waterfowl, main replication site of avian influenza viruses);





# Role of pigs

- The reason why pigs are suggested to be a major mixing vessels of human and avian influenza virus is because they express high levels of both **SA $\alpha$ 2,6Gal** and **SA $\alpha$ 2,3Gal** in their upper respiratory epithelium;
- If simultaneously infected with human influenza and avian influenza virus a re-assortment could occur between the two viruses resulting in a third new virus;



## Role of pigs

- It is noteworthy to mention that the susceptibility of humans to Highly Pathogenic Avian Influenza H5N1 correlates to the expression of **SA $\alpha$ 2,3Gal** in bronchiole and alveolar type II cells in the lung (in fact in humans pneumonia is commonly seen and not an upper respiratory tract infection where those receptors are not present).



## Role of pigs

- While the origin of the implicated virus is still a question mark there is ample evidence of human-to-human transmission;
- Influenza viruses circulating in humans have the potential to be transmitted to pigs and occurrence of infection by this novel virus in a pig farm has been reported from Canada;



## Role of pigs

- The initial findings suggested that the pig herd may have contracted the virus from a worker who had recently returned from an infected country;
- The completion of the analysis of the virus isolates in Canada confirmed that the novel 2009 strain of A (H1N1) influenza virus was responsible for the infection in pigs.





## Role of pigs

- Very recently the novel H1N1 has been identified in a pig farm in Argentina;
- It is under investigation possible links with human cases;
- Information available suggest that, as in the case of Canada, the disease in pigs is mild



## Role of pigs

- Field observation in the Canada pig herd and preliminary results of recent inoculation studies in pigs with the novel A/H1N1 strain done in the Veterinary Laboratories Agency (VLA) have shown that pigs are susceptible to the A/H1N1 virus and show typical signs of influenza;
- No mortality was observed;
- Peak shedding was noted mainly via nasopharyngeal route 3-5 days post infection;
- Transmission to other pigs occurred.



# New challenges

- The One-World-One-Health approach recognizes the intimate linkages among the human, animal and ecosystem health domains (which appears to be the most appropriate for addressing issues such as Influenza A/H1N1 and more in general the issue of Influenza viruses);
- It proposes an international, interdisciplinary, cross-sectoral approach to disease surveillance, monitoring, prevention, control and mitigation of emerging diseases, as well as to environmental conservation.



# New challenges

- The major lesson learned (from the Highly Pathogenic Avian Influenza H5N1 but can be extended to other diseases) is the central importance of efficient surveillance, effective intersectoral collaboration, a well-designed national strategy and sustained political will.



# New challenges

- Where any of these elements has been absent or insufficient, countries have been less able to detect and control the spread of infection such as HPAI H5N1, with the result that in some countries the disease has become entrenched in poultry and thereby increasing the possibility of human infection.



# New challenges

- Should swine influenza be included among the list of notifiable diseases?
- What should be done if detected in pigs?
- Should the surveillance system for influenza viruses be seen as a multi-component system incorporating different animal species (including humans) under a single framework?



Thanks for your attention

