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Karen Trévennec, P Lekcharoensuk, Francois Roger

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K. Trévennec[1]*, P. Lekcharoensuk[2], F. Roger[1]
[1]CIRAD, AGIRs Unit, Campus International de Baillarguet, 34398 Montpellier Cedex 5, France.
[2] Kasetsart University - Phahonyothin Road, Chatuchak, Bangkok, 10900, Thailand.
*Corresponding author
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Introduction

Although the first three Flu pandemics were of avian origins, the most recent human pandemic H1N1 2009 has urged scientists to play more attention on the pivotal role of pigs in the process of emerging pandemic strain [1]. Considering the lack of data related to swine influenza virus (SIV), surveillance activities need to be improved very urgently all over the world [1], especially in East and South-East Asia, which produced around 516 millions of pigs (and 8.2 billions of poultry) in 2008, and represents more than the half of the world pig production (FAO).
Pigs are the main reservoir of H1N1, H3N2 and H1N2 subtypes [2, 3]. The H1N1 and H3N2 emergence in swine occurred consecutively to cross-species transmission from birds or humans. The early detection of emerging/new swine influenza viruses should be based on a surveillance program of rare events. However, the surveillance modalities to detect the cross-species transmissions or to early detect new strains are still unclear. New methods or epidemiological tools must be developed and adapted. We propose alternative surveillance strategies to assess the risk of emergence and spreading of new strains.

Swine influenza in East and South East Asia

The literature review shows that only a few countries are publishing some data on SIV, and there is a lack of knowledge in central countries South East Asia, which are probably as infected as theirs neighbours. The typing and the phylogenetic analysis show a real diversity of circulating strains. But, there is a strong evidence of a usual low isolation rate, on average less than 2% (non published data), wherever the samples were collected: in the abattoirs, in healthy farms or in farms with clinical signs. The seroprevalence of influenza virus type A in pigs in South East Asia varies around 20%, with a between-herd seroprevalence high than 50% (non published data). There are virological and serological evidences of co-circulating strains within swine population: H1N1, H3N2, H1N2 [4, 5], and unusual subtypes H5N1[6], H9N2 [7] or H3N8 [8]…

Surveillance systems to capture the suspected cases

Scanned (passive) surveillance: this strategy is based on the detection of influenza-like illness within pigs by farmers, veterinarians or traders [4]. Swine influenza illness caused by H1N1, H3N2 and H1N2 is well documented. The disease acts as a respiratory syndrome, characterized by a cough, nasal discharge, dyspnoea, added to fever, anorexia, apathy, a great loss of weight or abortions [10]. Although the clinical signs of swine infection with H4N6, H3N1, H3N3 and avian or human H1N1 seem to be similar [11-13], we must be aware that the specific infections with other unusual subtypes can be variable [14]. On the other hand, swine influenza virus is involved in 10% to 20% of the porcine respiratory disease complex (PRDC) cases [15, 16], as a single infection in more than 60% of cases, or associated with the Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) or *Pasteurella multocida* in 20% of cases [15]. For this reason, the swine influenza clinical surveillance cannot be separated from the global surveillance of respiratory syndromes, which is one of the most prevalent syndromes in industrial systems.
In conclusion, the scanned surveillance involving the spontaneous reports by the swine workers is exposed to several difficulties. A sensitive clinical case definition will generate many suspicions which might represent a heavy cost in term of logistic, manpower and diagnostic tests for the country. The laboratories might be overwhelmed during the critical season. Moreover, the farmer interest for swine influenza might be low, as it causes economic loss but no mortality. Other diseases, with similar clinical manifestation as swine influenza, might break the farmer reports because of their heavy consequences. For example, the emergent highly pathogenic PRRSV is a sensitive topics because the authorities have culled millions of pigs in East and Southeast Asia [17]. The early detection of emergences cannot rely only on swine workers. For these reasons, the clinical surveillance program must be completed by a more targeted surveillance program.

Risk-based syndromic surveillance on sentinel farms: The Risk-based surveillance strategy is a specific strategy defined as “A surveillance programme in the design of which exposure and risk assessment methods have been applied together with traditional design approaches in order to assure appropriate and cost-effective data collection" [18]. Contrarily to repeated cross-sectional surveys, which are based on random sampling, risk-based surveillance studies display stratification in the probability of harbouring the hazard and/or the consequences of the occurrences of the hazard [18]. A risk assessment approach needs to be performed in order to identify various strata of the population according to their risk of swine influenza emergence and cross-species transmissions. The at-risk units (farms, markets…) must be identified and must be monitored as sentinels through a traditional study design. This might lead to a syndromic surveillance strategy, which is defined by CDC as "an investigational approach where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor disease indicators in real-time or near real-time to detect outbreaks of disease earlier than would otherwise be possible with traditional public health methods". In the context of pig supply chain, an abnormal increase of PRDC prevalence or unusual variation of trade and production rates in sentinel farms and/or sentinel markets could be a sign of a possible emergence. This needs to predetermine precise indicators and thresholds beyond which the rate fluctuations are considered as abnormal.

*Slaughterhouses as sentinels***:** more than the simple monitoring, the disease can be surveyed in a network of sentinel abattoirs in at-risk areas or during the at-risk seasons. Surveys in slaughterhouse require a low logistic investment in terms of manpower, time and cost. First, sample collection in slaughterhouse will increase the chance to isolate the virus, as the influenza RNA is detected mainly in the bronchial and bronchiolar epithelial cells [19]. In non vaccinating countries, the serological follow up with a screening sensitive test affords the detection of abnormal increasing prevalence, which can be a sign of emergence. The threshold beyond which the prevalence of influenza type A is considered abnormal and a random variation beyond which the variation is considered unusual are still unclear. The cut-off value will depend on the location, the period, the population and need to be adapted to the country context.

When the capacities allow an individual identification of animals, the matching of virological and serological status is largely preferable. However, in non automated small slaughterhouses, a long time passes between the bleeding and the evisceration. If the manpower or financial resources are limited, a global survey, without taking into account the individual level, could be the best way to maximize the probability to detect the virus or to improve the precision of the prevalence and seroprevalence measures.

Confirmation of emergence by highly specific tools

The positives results of the serological screening test will be confirmed with a more specific test. The sensitivity and specificity of the HI test in the field depends on the antigenic match between antigens used in the test and the circulating strains. The detection of unusual subtype or unusual antigen reaction could be a sign of emergence. This leads to the issue of the serological diagnosis taking into account cross-reactions and the choice of the right antigens.

Molecular surveillance represents the final way to confirm an emergence and to follow the genetic evolution of the virus. Genetic analyses highlight the origin of the strains and whether it comes from a single or repeated cross-species transmission. Moreover, it helps to identify possible candidates for cross-species transmissions.

The shedding period starts 1 day post-infection and lasts less than 7 days. In the field, the simple clinical surveillance of PRDC and the monitoring in slaughterhouses might miss to detect the swine influenza virus. The low isolation rate remains the main limiting factor. For this reason, although the virological surveillance brings the final proof of an emergence, it remains unsuitable for early detection of emergences because it requires huge sample collection and high level of laboratory capacities.

Conclusion

In a context of weak infrastructures and lab capacities, the surveillance system should be effective and must improve its sensitivity in order to capture the maximum of suspected/probable cases. However, the laboratories might be rapidly overwhelmed by the reports of the influenza-like illness surveillance. The optimal surveillance system should be adapted according to the risk of emergence. A risk-based surveillance design could start to set up a simple clinical monitoring in low-risk strata, completed by active surveillance protocols, based on a sentinel monitoring in higher risk strata. The abattoir in at-risk areas could have a central role to monitor the disease as it centralises many individuals from large areas. A syndromic surveillance can be based on screening sensitive serological tests in order to study prevalence variations and to detect unusual increases. According to this method, a cut-off level should be defined, which is the critical value to measure the disease risk for each strata. The choice of the surveillance strategy must optimize the equation between the resource investment and the risk level. Each proposal must be adapted to the socio-economic context and must be tested and then validated in the different countries.

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