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Controlling Avian Flu and Protecting People's Livelihoods in the Mekong Region

HPAI Research Brief | No.19 - Year: 2009

H5N1 Incidence, Viral Evolution, and Policy Implications

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Key Findings

- H5N1 is now a widely dispersed threat to poultry and livelihoods associated with this sector, but this virus is now differentiated both genetically and in terms of local persistence.
- Policy needs to adapt to this reality, and we define and discuss a classification scheme for heterogeneous risk conditions to support this.

incidence based on both H5N1 genetic variation and epidemiological conditions such as recurrence, within country mutagenic transition, etc.

Viral Evolution of H5N1

During the long history of its association with human pandemic risk, avian influenza has established a reputation for rapid genetic mutability and, as Figure 1 indicates, the H5N1 member of this viral family has already developed dozens of variants (clades).¹ This evolution is both natural and inevitable, but it makes the challenge of risk management

¹ We are indebted to K. Inui of FAO Viet Nam for collecting the data used in this analysis.

more complex because the disease becomes a moving target for containment/eradication. All attributes of a virus, including contagion, mortality, vaccine efficacy, etc., are subject to change with genotype, but in ways that are notoriously difficult to predict. What is certain, however, is that effective responses must adapt when conditions change.

Figure 1: Viral Evolution - Clades of H5N1

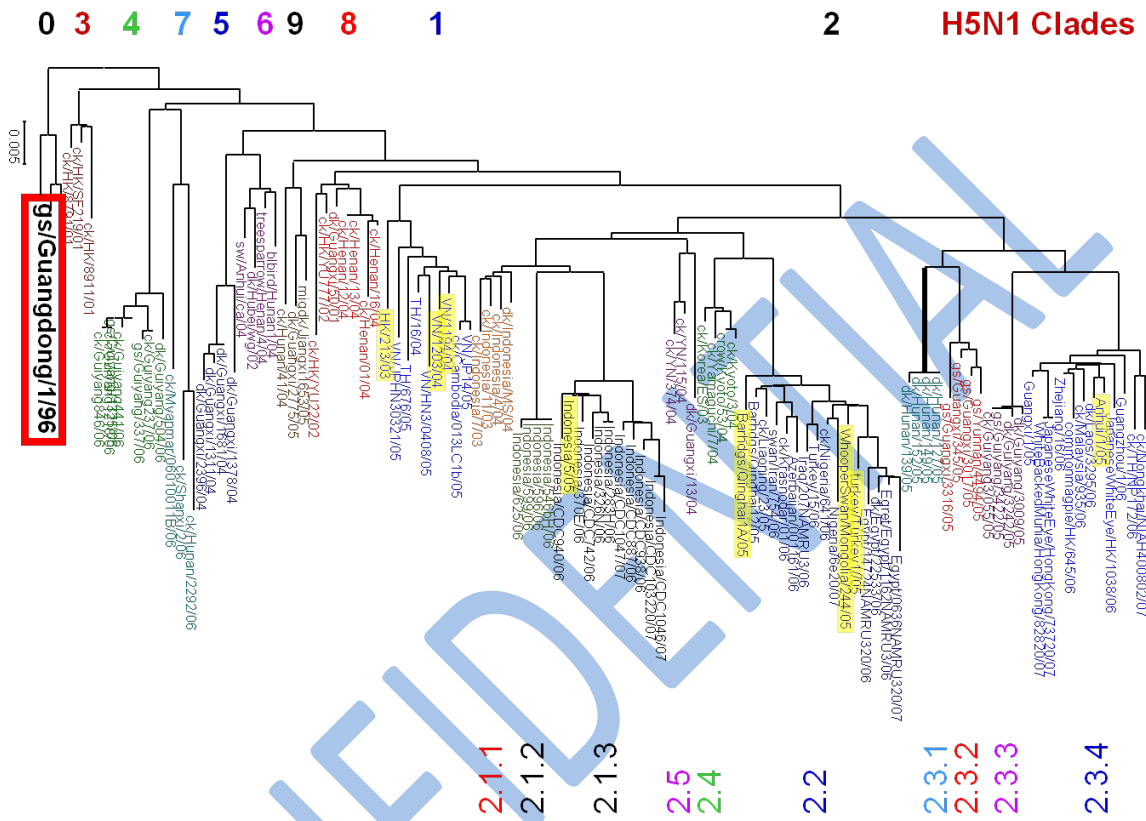


Figure 2: Emergent Clades of in China

Year	HA Clades																	Total	
	0	1	2.1	2.2	2.3				2.4	2.5	3	4	5	6	7	8	9		Out
					1	2	3	4											
96-99	9																		9
2000	8												1						9
2001	17									8			1				1	1	28
2002	12	6	1					2				4	2	1		3	2	8	41
2003	4	9	1		1	1		14	4	1		1	3		1	1	6	4	51
2004	4				3	11	1		9	1			16	3	3		13	3	67
2005				19	12	41	5	34	2	0		1			7		9	1	131
2006				4		3		63		2		5			1		1		79
2007																			0
Total	37	15	2	23	16	56	6	97	27	7	9	11	22	4	12	4	32	17	397

Geographic Dispersion of H5N1

Ideally, policy adaption should be evidence based, but at the present time genetic variation in H5N1 is relatively confined geographically and the observed basis of evidence may be narrower than the actual scope of the underlying process. In particular, most of the currently observed clades have been identified only in China and Viet Nam, with the majority confined to the former. Figure 2 tabulates clade identification in China between 1996 and 2006. Cells in red indicate so-called dominant clades, i.e. those variants that were most often reported in each year. Aggregating these detailed clades indicates a clear progression (Figure 3, arrow) across major clade types. Both the number of clades and their systematic transition suggest a well established mutagenic process that is producing viable successor variants continuously. This poses a serious ongoing challenge for disease risk management and, from a pandemic perspective, should be a focal point for intensive policy intervention. Moreover, in light of the public good nature of contagious disease prevention, it suggests an essential opportunity for multilateral cooperation.

Figure 3: Transition of Dominant Clades in China

Year	HA Clades											Total	
	0	1	2	3	4	5	6	7	8	9	Out		
96-99	29												29
2000	7			3		1							21
2001	1			43		1					1	2	65
2002	17	17	3		7	3	1		7	2		8	65
2003	4	25	33	1	1	5		1	1	7		8	86
2004	4		49			16	3	3		14		5	265
2005	3	11	170		1			7	1	9	1		304
2006	5	5	122		5			1		1			139
2007		12	94										22
Total	97	342	471	47	14	26	4	12	9	34	24	1080	

Major clade of the year
Existing clade

Important examples of these issues can be found by comparing detailed clade incidence in other countries. The spatial dispersion of clades in Viet Nam, for example, is illustrated in Figure 4. Here we see important diversity between two very disjoint and differentiated ecosystems. In the Red River Delta, more recent H5N1 variants dominate. By contrast, in the southern Mekong Delta, the original clade of N5H1 is ubiquitous. This comparison has many implications, the most prominent of which are that proximity to China may confer adaptive challenges on Viet Nam, and the appearance that H5N1 is endemic in the Mekong Delta.

The transboundary issue is even more apparent in Figure 5, where it is clear that dominant clade transition in northern Viet Nam mirrors that of its northern neighbour, while that of South Viet Nam mirrors that of its southern neighbour Thailand. These findings reinforce a perception that disease risk management in the Mekong Region could be more effective

with a multilateral approach that limits re-infection risk and, where possible, coordinates to an extent that facilitates containment and progressive eradication.

Figure 4: Dispersion of Clades in Viet Nam 2007-8

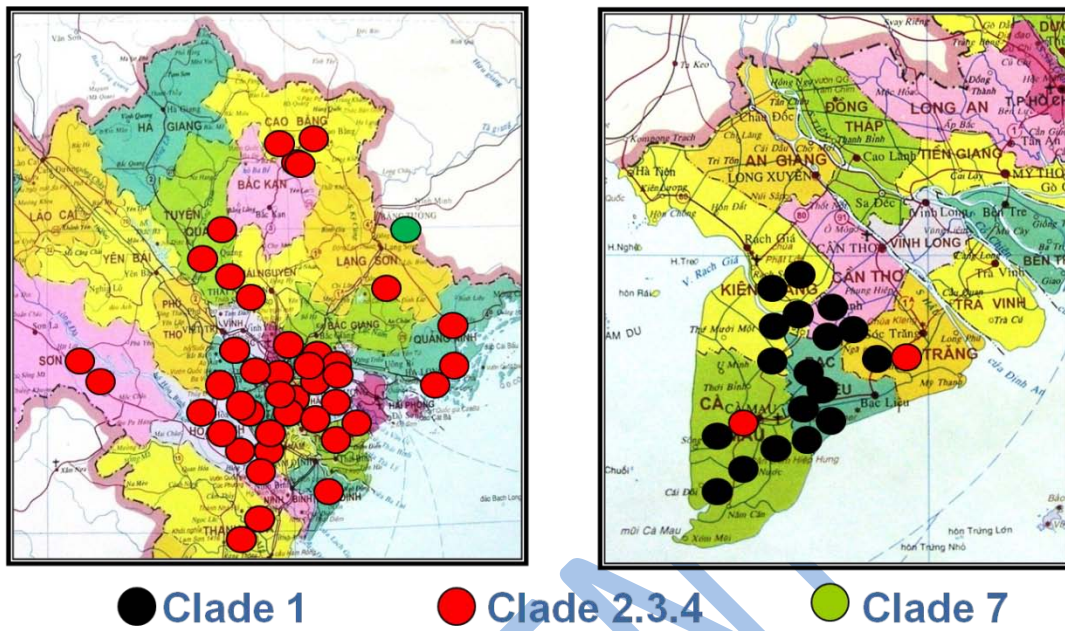
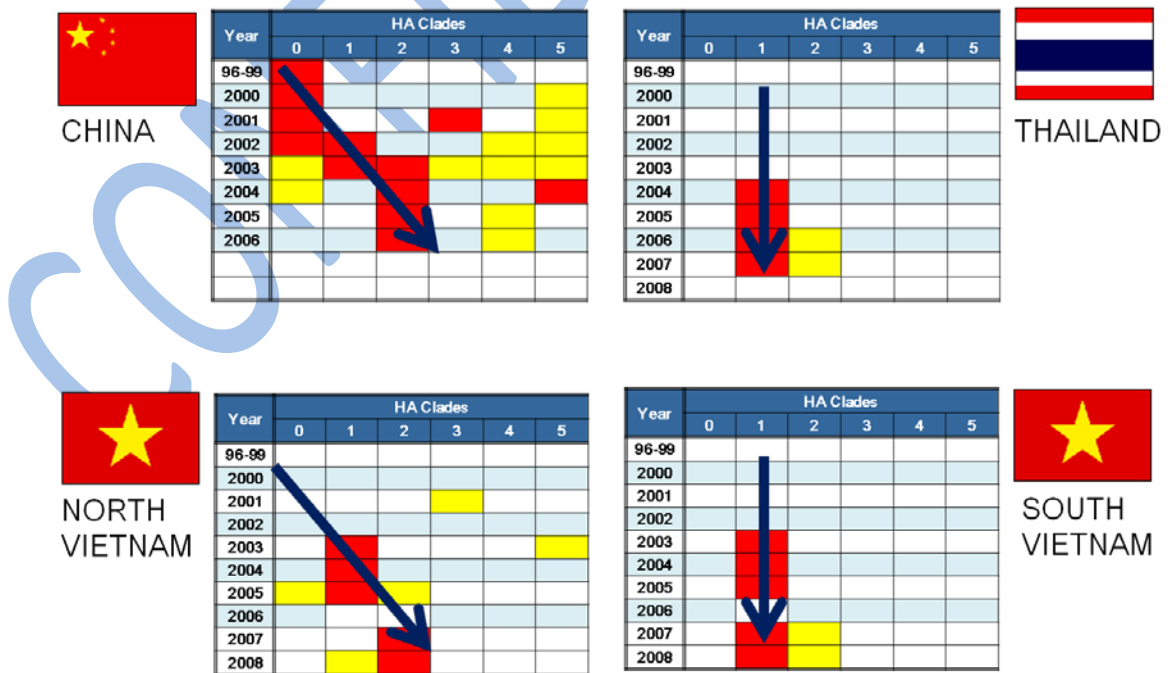
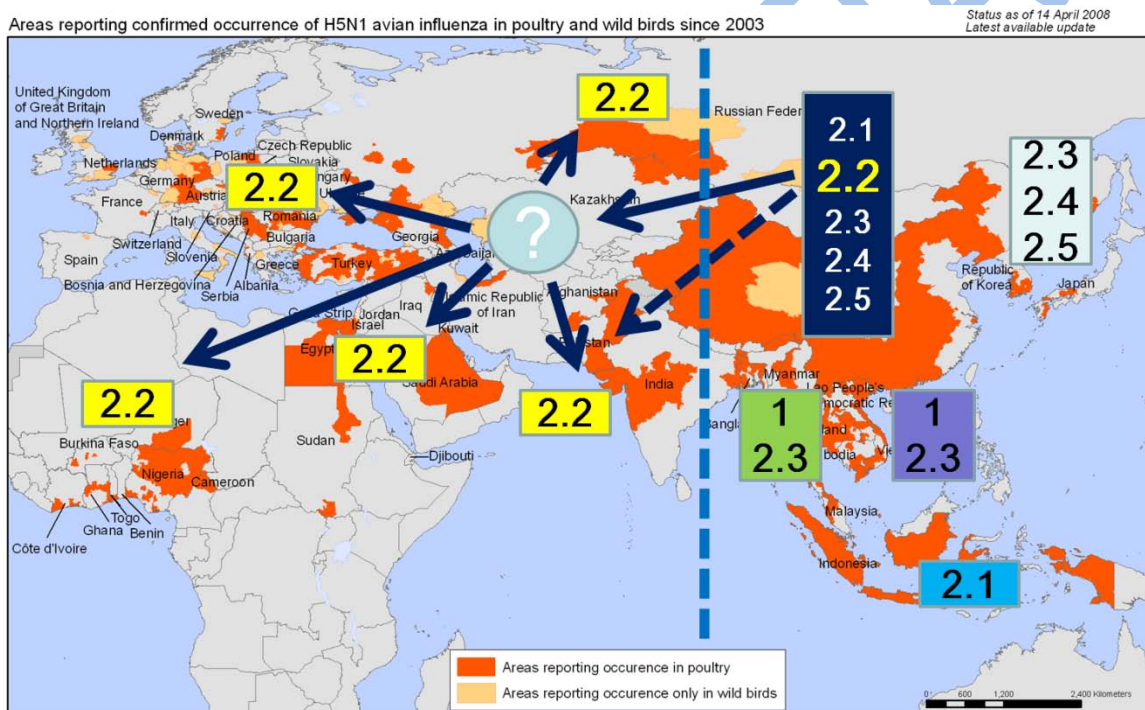


Figure 5: Annual Transition of Dominant Clades in China, Thailand, and Viet Nam



Enlarging the geographic perspective, a different kind of diversity emerges. Figure 6 reveals some of the global dispersion of H5N1, clearly suggesting a bird pandemic if not a human one. Despite having infected so many countries, however, the genetic variability of these outbreaks is much narrower than in East and Southeast Asia. Indeed, all tested outbreaks west of Bangladesh are drawn from a single clade group (2.2). This suggests a few salient policy insights. Firstly, mutagenic risk in these areas may be much more limited, perhaps justifying more intensive use of multilateral resources in areas with more diverse clade records. Second, policy coordination between countries with like virus variants might also be recommended, since advances against a given clade can be expected to generalize more readily. Finally, limited variability may suggest less risk of endemicity, although this inference should be supported by detailed ecological analysis.

Figure 6: International Dispersion of H5N1 Clades



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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.

Data Source: World Organisation for Animal Health (OIE) and national governments
Map Production: Public Health Mapping and GIS
World Health Organization

Classifying Country Conditions

The combined effects of viral evolution and spatial dispersion now present a more heterogeneous global landscape of H5N1 disease risk, and policies toward both livestock sector defense and pandemic aversion must adapt to this reality. To facilitate more effective policy design, we propose a classification scheme for functional differences in national disease incidence.

Category	Definition
0	No prior or existing H5N1 incidence
1	Prior outbreaks, but no current outbreaks or discernable reservoir risk
2	Current, recurrent, or proximate (<6 month) outbreaks
3	Apparently endemic – persistent localized recurrence with discernable reservoir potential
4	Apparently endemic and actively mutagenic – appearance of novel local clades

According to this classification, policy orientation toward livestock sector defense can be stratified into preventative/proactive (C0, C1) and active (C2-4) regimes. The former would emphasize surveillance, transboundary risk management, and limited commitments to contingent response. In the second group, more extensive commitments are needed to respond to and contain current outbreaks, possibly including multilateral coordination to limit transboundary spillovers. For localities experiencing multiple clades, the notation Ck.n.m can denote both the risk category (k=0-4), n denotes the number of active clades, and m the number of total clades recorded. This information conveys general risk as well as risk history.

For the two highest categories (C3-4), intensive measures need to be targeted toward containment and eradication of persistent reservoirs. In this context, rigorous assessments are needed to determine if and how to combat endemic strains and conditions that facilitate them. Without these investments, risks of both re-infection and mutagenic contagion will lead to very high present-value social costs. Again, multilateral commitments may be justified to avert or limit these risks.

Category 4 countries are a special regional and global priority for coordinated policy support. Because they represent the most dynamic mutagenic conditions, all countries have an interest in supporting containment and eradication efforts within C4 countries. Conversely, C4 countries have special responsibilities to make full use of multilateral resources, sustain constructive and open policy dialogue, and maintain standards for timely information sharing.

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