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Special Topic **Review**

H5N1 avian influenza in China

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H5N1 highly pathogenic avian influenza virus was first detected in a goose in Guangdong Province of China in 1996. Multiple genotypes of H5N1 viruses have been identified from apparently healthy waterfowl since 1999. In the years 2004–2008, over 100 outbreaks in domestic poultry occurred in 23 provinces and caused severe economic damage to the poultry industry in China. Beginning from 2004, a culling plus vaccination strategy has been implemented for the control of epidemics. Since then, over 35420000 poultry have been depopulated, and over 55 billion doses of the different vaccines have been used to control the outbreaks. Although it is logistically impossible to vaccinate every single bird in China due to the large poultry population and the complicated rearing styles, there is no doubt that the increased vaccination coverage has resulted in decreased disease epidemic and environmental virus loading. The experience in China suggests that vaccination has played an important role in the protection of poultry from H5N1 virus infection, the reduction of virus load in the environment, and the prevention of H5N1 virus transmission from poultry to humans.

avian influenza, H5N1, control, China

In the past few years, there have been many significant outbreaks of H5N1 avian influenza involving multiple farm flocks in more than 20 provinces in China. The H5N1 viruses affected millions of domestic poultry, including chickens, ducks, and geese, as well as thousands of migratory wild birds[1]. In 2004, the Chinese government decided to use a culling plus vaccination combined strategy to control avian influenza virus infection. Several vaccines, including inactivated and live virus vectored vaccines, have been developed and successfully applied in the field. Here, we will present the epidemiology, vaccines and vaccination, and the control policy and experience of H5N1 avian influenza in China.

1 The current situation of the poultry production in China

China is one of the largest countries for poultry production in the world, with the production of domestic poultry totaling 15 billion in 2007, accounting for 20% of the global poultry production. Among the 15.2 billion poultry, over 60% are bred in small scale farms or in backyards. China is home to an even larger population of waterfowl, encompassing approximately 70% of the world total. The majority of the waterfowl are ducks that are distributed in the provinces of southern China, and these ducks are raised in the open field rich in lakes and rivers. During breeding season, the ducks may migrate from one province to another over hundreds of miles. This special breeding style enables domestic waterfowls to contact both wild waterfowls and other domestic animals, such as chickens and pigs, allowing the waterfowl to play an important role as an intermediate host in the transfer of influenza from wild birds to domestic animals. Waterfowl migration also serves to spread influenza from one place to another, which poses huge difficulties for the control of avian influenza in China.

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2 Surveillance of avian influenza virus

Active surveillance of avian influenza virus has been performed on a regular basis since 1994, when an H9N2 influenza virus was first detected in Guangdong province[2]. H9N2 is the most prevalent influenza A subtype[3], but several other subtypes including H1, H3, H4, H6, H7[4,5], H9 and H14, have been identified from chickens, ducks and geese.

In 1996, an infectious disease with high mortality (40%) was observed in an outdoor rearing goose farm in Guangdong province. Influenza A viruses were isolated from the samples in embryonated chicken eggs and were identified as being an H5N1 subtype by hemagglutination inhibition (HI) and neuraminidase inhibition tests with a panel of antisera provided by the Office International Des E´ pizooties (OIE) Reference Laboratory (Veterinary Laboratory Agency, Surrey, U.K.)[4,6,7]. Although the viruses exhibited different virulence in chickens[8], one of the viruses is highly pathogenic for chickens based on the OIE standard, which was designated as A/goose/Guangdong/1/96 (GS/GD/1/96), with an intravenous injection index (IVPI) value greater than 1.2. This virus contains a series of basic amino acids (-RRKKR-) inserted at the cleavage site of the hemagglutinin (HA) protein that is characteristic of influenza viruses that are highly pathogenic in chickens. This is the first documented H5N1 highly pathogenic avian influenza virus isolation in Mainland China. Since 1999, H5N1 viruses have been repeatedly isolated from apparently healthy waterfowl, mainly ducks, in southern China[9]. In 2001 and 2003, two H5N1 viruses were isolated from pigs in Fujian Province during routine surveillance[10].

3 Outbreaks of H5N1 avian influenza in China

3.1 Outbreaks in 2004

Starting from the end of 2003, H5N1 avian influenza virus has caused outbreaks in domestic poultry in several countries in southeast Asia (OIE WBS), including Vietnam, Thailand, South Kerea, Japan, Combodia, and Indonesia. On January 27, 2004, an H5N1 highly pathogenic virus caused an outbreak in domestic ducks in Guangxi Zhuang Autonomous Region, and then 49 outbreaks occurred within the next month. Multiple species of birds were affected during these outbreaks, including chickens, ducks, geese, quails, and turkeys, and infection of wild zoo birds was also detected in some areas. Although outbreaks were detected in 16 provinces, 41 cases (83% of the total) occurred in the southern provinces or autonomous region of China, including Yunnan, Guangxi, Guangdong, Hubei, Hunan, Jiangxi, Zhejiang, Anhui, and Shanghai. The origin of the epidemic was not established. However, the epidemiological data gathered allowed for the identification of risk factors in the affected farms and markets. The primarily risk factors were the presence of the mixed species and the rearing of the birds in the open field. Five months after the large scale outbreaks in the 16 provinces were controlled, a new outbreak was detected in a backyard chicken farm in Anhui province. In 2004, about 143000 birds were infected, and over 9 million birds in the threatened area were depopulated to control the epidemic of H5N1 avian influenza (Table 1).

3.2 Outbreak in 2005

On June 7, 2005, eleven months after the 2004 outbreak in Anhui province, a goose sample from Xinjiang Uigur Autonomous Region was identified as containing highly pathogenic H5N1 avian influenza virus. The outbreak occurred in a small-scale (<2000 birds), open-field rearing goose farm. To control this outbreak, 79000 poultry in the threatened area were depopulated. On June 20, two weeks after this outbreak, H5N1 highly pathogenic virus infection was again confirmed in another backyard farm that owned a small amount of ducks and geese (<200 birds) in Xinjiang Uigur Autonomous Region. About 149000 poultry in the surrounding area were killed to control the spread of the disease. These two farms were located in two different cities that are 500 miles away from one to another, and yet the two viruses were simliar though multiple mutations were detected in all of the genes. This suggested that the H5N1 avian influenza viruses that caused the outbreaks in these two farms was originated from the same source, but that the virus that caused the second outbreak was not directly spread from the first one (unpublished data). On August 10, H5N1 highly pathogenic virus infection in a backyard farm (<200 birds) in Tibet was confirmed.

Starting from October 19, a total of 28 outbreaks were detected in domestic poultry in ten provinces or autonomous region, including Xinjiang, Inner Mongolia, Liaoning, Shanxi, Ningxia, Hunan, Hubei, Yunann, Jiangxi, and Sichuan. All of the outbreaks in southern

Table 1 H5N1 avian influenza outbreaks in China in 2004−2008

Province/ autonomous region	2004			2005			2006			2007			2008		
	Out-breaks	Birds infected	Birds slaughtered	Out-breaks	Birds infected	Birds slaughtered	Out-breaks	Birds infected	Birds slaughtered	Out-breaks	Birds infected	Birds slaughtered	Out-breaks	Birds infected	Birds slaughtered
Anhui	5	26461	569707	2	1350	294000	1	13	200						
Gansu	1	400	91543												
Guangdong	9	6877	613560							1	9830	153000	2	3987	320500
Guangxi	2	880	754005												
Guizhou							1	16000	42000				1	3993	238000
Henan	1	1500	20810												
Hubei	10	18347	747570	3	8844	37800									
Hunan	5	5961	659701	2	1001	136800	1	1805	217000	1	12484	53000			
Inner Mongolia				3	3022	118100	1	985	8990						
Jilin	1	49	936												
Jiangxi	3	10301	1370752	1	3100	332500									
Liaoning				4	125010	19958500									
Ningxia				1	294	99400	2	51300	653930						
Qinghai				1[a]		16000	1[a]								
Shanghai	1	1500	365000												
Shaanxi[b]	2	2296	138549												
Shanxi[c]				1	8103	67800	2	17600	1657745						
Sichuan				1	1800	12900									
Tianjin	1	236	288244												
Tibet	1	425	36188	1	133	78800	1[a]			1	680	7000	3	1400	30400
Xinjiang	1	4058	15605	11	7954	1365600	2	3245	357413	1	4850	35000			
Yunnan	7	65093	3304997	1	2500	53000									
Zhejiang	1	550	67789												
Total	50	144934	9044956	32	163111	22571200	12	90948	2937278	4	27844	248000	6	9380	588900

a: The outbreaks were detected in wildbirds. b: The province with the capital city in Xi'an. c: The province with the capital city in Taiyuan.

China occurred in small-scale, backyard farms (<2000 birds) with mixed species of chickens and ducks or geese. The outbreak that occurred in the Liaoning province of northern China was confirmed on November 9, which was at least two weeks after the disease was initially noticed in the field. The delayed disease report in this case resulted in the wide spread of the virus. The infections of 39 farms in two cities were confirmed and 125010 chickens died. To again control the spread of the disease, 19958500 chickens were depopulated.

3.3 Outbreaks in 2006

In 2006, there were 10 outbreaks detected in seven provinces (Table 1). The first outbreak occurred in Yunnan province, which resulted in the death of 16000 quail. In the threatened area, 42000 poultry were killed to prevent the spread of the disease. Five outbreaks occurred in small-scale, backyard chicken or duck farms in Hunan, Anhui, Xinjiang and Inner Mongolia. The birds in these farms were not vaccinated, though 100% vaccination of the domestic poultry was encouraged and required by the Chinese government starting at the end of 2005. The four outbreaks in Shanxi provinces and Ningxia Uigur Autonomous Region however, occurred in the vaccinated chicken layers.

In February 2006, respiratory disease and decreased egg production were noticed in some layer farms in Shanxi province, and about 10%−20% mortality was also recorded in some flocks. Most importantly, the chickens in these farms had been vaccinated with the H5 inactivated vaccines and had average HI antibody titers of >8lg2. Samples were sent to the National Avian Influenza Reference Laboratory for disease diagnosis. An H5N1 influenza virus was isolated, but this strain reacted poorly with the antisera raised against GS/GD/1/96 virus-based antigen. Sequence analysis indicated that this H5N1 virus, A/chicken/Shanxi/2/06 (CK/SX/06), was also genetically quite different from the H5N1 viruses isolated from other locations. This suggested that a new genotype of H5N1 avian influenza virus had been introduced into the chickens in northern China, though its origin was still unclear. To control the outbreaks caused by the CK/SX/06 virus, over 2311000 poultry were depopulated in Shanxi Province and Ningxia Autonomous Region (Table 1). In August 2006, six months after the detection of this variant, a new inactivated vaccine was developed by using a recombinant H5N1/PR8 reassortant virus bearing the modified HA and NA genes from the CK/SX/06 virus. The vaccine was applied in the selected provinces in northern China to control the CK/ SX/06-like viruses.

3.4 Outbreaks in 2007−2008

In 2007 and 2008, 4 and 6 outbreaks, respectively, were detected in Guizhou, Guangdong, Hunan, Tibet and Xinjiang autonomous region To control these outbreaks, total 836900 birds were slaughtered (Table 1).

3.5 Outbreaks of H5N1 avian influenza in wild birds in 2005−2006

Wild aquatic birds harbor all 16 HA and all nine neuraminidase (NA) subtypes of influenza A virus and therefore serve as the natural reservoir for this pathogen. Although influenza viruses in wild aquatic birds are occasionally transmitted to avian (e.g., chickens and turkeys) and mammalian (e.g., humans, pigs, horses, minks, whales, and seals) species, where they may produce outbreaks of severe disease, they persist in evolutionary equilibrium (stasis) in their natural reservoir and do not generally cause disease in wild waterfowl[11]. Highly pathogenic H5N1 viruses do not appear to have entered the wild-bird populations to any appreciable extent until late April to June 2005, when a large outbreak of H5N1 infection occurred in Qinghai Lake in western China[1,12], a major breeding site for migratory birds whose flyways extend to Southeast Asia, India, Siberia, Australia, and New Zealand[13].

The islets and wetlands of Qinghai Lake, located in western China, are part of a protected natural reserve for wild birds. More than 100000 wild birds, representing 189 species, spend the spring and summer at this reserve every year. Since the end of April 2005, bar-headed geese (*Anser indicus*) arriving at Qinghai Lake from southern Asia have shown signs of disease, including tremor and torticollis. On May 4, 2005, two bar-headed geese were found dead in the wetlands of Qinghai Lake, and 105 geese were reported dead on the following day [1]. On May 13, a total of 437 dead birds were collected. The species identified extended to great black-headed gulls (*Larus ichthyaetus*) and brown-headed gulls (*Larus brunnicephalus*), whose habitats on the lake overlap closely with those of bar-headed geese. Disease signs and death were observed among ruddy shelducks (*Tadorna ferruginea*) beginning on May 13, with 90 and 12 dead shelducks collected on May 24 and May 25, respectively. A limited number of dead great cormorants

(*Phalacrocorax carbo*), gathered on two islets located 2 miles away from concentrations of bar-headed geese and gulls, was first observed on May 16, and a large number of these birds were found dead on the dates of May 24−26 and June 1[1]. Altogether, 6184 dead gulls, geese, great cormorants, and ruddy shelducks were found from May 4 to June 29, with bar-headed geese accounting for more than half of this total. A limited number of whooper swans (*Cygnus cygnus*), black-headed cranes (*Grus nigricollis*), and pochards (*Aythya ferina*) also died during this outbreak.

The epidemiologic information indicated stepwise introduction of the virus into different avian species in the lake. Our sequence analyses revealed that four genotypes of H5N1 influenza viruses contributed to the outbreak and that at least three genotypes of H5N1 viruses were circulating among bar-headed geese, while the viruses isolated from great black-headed gulls, brown-headed gulls, great cormorants, and whooper swans were similar to each other and belonged to only one of the genotypes found in bar-headed geese[1]. These data suggested that bar-headed geese infected elsewhere were the species that brought the virus to Qinghai Lake, presumably via the East Asian-Australian flyway or the Central Asian-Indian flyway.

Subsequent to the outbreak in Qinghai Lake from April to June 2005, H5N1 viruses have continued to cause outbreaks in Asia, Europe, and Africa (WHO report, http://www.who.int). We sequenced the entire genomes of several H5N1 viruses isolated from wild birds in Mongolia in August of 2005, and viral genomes isolated from chickens during major outbreaks in the Liaoning Province and Inner Mongolia autonomous region in October and November 2005, respectively. Phylogenetic analyses of these viruses and a virus isolated from a wild bird in Russia in August of 2005 showed that these viruses belonged to genotype C[1]. Moreover, all of these viruses possessed a Lys at amino acid position 627 in the PB2 protein. This same genotype caused the outbreaks in wild birds in Qinghai and Tibet in 2006 and resulted in the deaths of 3461 wild birds.

4 Phylogenetic analyses of the H5N1 avian influenza viruses in China

The H5N1 viruses identified from different dates and locations over last 10 years are quite different phylogenetically. The HA genes of most H5N1 viruses that were isolated before 2005 belong to a GS/GD/96-like virus, and all of the isolates had a series of basic amino acids at the cleavage site of HA (-RRKKR-) that is characteristic of influenza viruses that are highly pathogenic in chickens. The viruses could be divided into different forks in the phylogenic tree. The NA genes of the H5N1 viruses isolated in China could be divided into two sub-lineages. The NA genes in one sub-lineage derived from GSGD/1/96 encode a 20 amino acid deletion in the NA stalk (residues 49–68), whereas the NA gene of GS/GD/96 itself does not. This NA stalk deletion is distinct from, but overlaps with the 19 amino acid deletion found in the HK/97 viruses and the viruses that were detected from eggs of Vietnam waterfowls in 2005 [14,15].

The phylogenetic trees of the PB2, PB1, PA and NP genes of the H5N1 viruses are very similar. They could be further divided into several sub-lineages. The genes between different lineages shared less than 90% homology, and the genes among different sub-lineages shared about 90%−95% homology. The M genes of the H5N1 viruses are relatively reserved, though they also formed multiple forks in the phylogenetic tree. The NS genes of the viruses were separated into two alleles. Some viruses and GS/GD/1/96 were included in the *A* allele, whereas the remainder, including the human HK/97 viruses, were in the *B* allele, which was further divided into two branches. The deduced NS amino acid sequence of the viruses in one branch in the *B* allele had a 15 nucleotide deletion resulting in a 5 amino acid (position 80–84) deletion in the NS protein. Many H5N1 genotypes have been described in previous reports[9,16−18].

During evolution in the nature, H5N1 avian influenza viruses have not only formed multiple phylogenetic genotypes, but have also exhibited great diversity in their biological properties. Detailed analysis of these viruses will provide insights towards the genetic basis of host range, antigenicity, and virulence of H5N1 viruses [8,19]

5 Control of H5 HPAIV in China

5.1 The policy for the highly pathogenic avian influenza control in China

A culling plus vaccination mixed strategy was used for the control of outbreaks of highly pathogenic avian influenza in China. After the final confirmation of a highly pathogenic H5N1 avian influenza infection, all of the

poultry within a 3 kilometer radius should be depopulated. Disinfection and movement control are implemented for 21 days after the poultry depopulation. Any existing live bird market within a 10 kilometer radius will be shut down for at least 21 days. All of the domestic poultry in the buffer zone of a 3−8 kilometer ring will be vaccinated immediately. Samples will be taken from the buffer zone for the detection of influenza virus, and negative results are necessary for the retraction of the movement control. The government pays for the vaccines, vaccination implementation and the compensation for the slaughtered poultry.

In 2004, only the birds in the buffer zone were required to be vaccinated. The epidemiological investigation indicated that all of the outbreaks in 2005 occurred in farms that did not vaccinate or vaccinated with unqualified vaccines. Therefore, by the end of the 2005, the government provided financial support for 100% vaccination coverage in domestic poultry.

5.2 H5 avian influenza vaccines developed and used in China

The vaccine development for the H5 avian influenza has been supported by the government since the detection of the highly pathogenic H5N1 virus GS/GD/96 in 1996. During the last ten years, we have successfully developed several inactivated vaccines using naturally isolated low pathogenic H5N2 virus or the use of artificially generated low pathogenic high growth reassortant virus by reverse genetics as seed viruses[20,21]. Two kinds of live virus-vectored vaccines using the fowlpox virus and Newcastle disease virus as backbone were also developed in China[22,23]. Most recently, we have generated an HA gene codon optimized DNA vaccine that is very immunogenic and provides solid HI and NT antibody responses and completely protects chickens against highly pathogenic H5N1 avian influenza virus challenge. Intramuscular injection of two doses of 10 μg of the plasmid induced a very good immune response and the duration of protective immunity lasted for more than 50 weeks[24].

5.3 Inactivated vaccines

An inactivated oil-emulsified vaccine has been developed using an H5N2 low pathogenic virus, A/Turky/England/N-28/73 (kindly provided by Dr. Danis Alexander), as a seed virus. The vaccine was approved to be used in August 2003 in Guangdong province in the chickens that were exported to Hong Kong and Macao. This vaccine was fully evaluated by the Chinese Veterinary Drug Evaluation Committee and got certified by the end of 2003. After the H5N1 outbreak in 2004, this vaccine was licensed to nine companies that have Good Manufacture Practice (GMP) facilities and the experience to produce egg cultured vaccines. In total, 2.5 billion doses of H5N2 inactivated vaccine were used in the district where H5N1 outbreaks occurred in 2004.

The H5N2 vaccines played an important role for the rapid control of the H5N1 outbreaks in China in 2004. However, this vaccine is not an ideal one. First, the vaccine seed virus exhibited antigenic diversity with the prevalent H5N1 strains in China at the time, Second, the seed virus could not grow to high titers in egg, which severely impaired vaccine production. To solve these problems, we generated a reassortant virus using plasmid based reverse genetics[25−27], which contained the HA and NA genes from the GS/GD/1/96 virus and the internal genes from the high growth A/Puerto Rico/8/34 (PR8) virus. The multiple basic amino acids (-RRRKKR-) in the cleavage site of the HA protein that are associated with virulence in H5 avian influenza viruses were changed into -RETR-, a characteristic of low pathogenic avian influenza viruses[28,29]. The reassortant virus, Re-1, is completely attenuated in chicken embryos and chickens[20]. It does not kill eggs within 72 hours after inoculation and grows to a titer higher than 11log2. Most importantly, the Re-1 virus contains the HA and NA genes of GS/GD/1/96 virus, which antigenically matches well with the H5N1 viruses that circulated in China[9]. This H5N1 inactivated vaccine induced higher HI antibody responses and longer lasting protective immunity in chickens compared with the H5N2 vaccines, and had been shown to be effective in ducks and geese [20]. This vaccine was approved to be used in the field by the end of 2004, and up to the present date, over 10 billion doses of the Re-1 vaccine have been used in China, Vietnam, Mongolia and Egypt.

In early 2006, an H5N1 avian influenza virus was isolated from a chicken flock that had been vaccinated with the H5 inactivated vaccines. The disease in those flocks was recorded as a decrease in egg production and a mortality range of 10%−20%. The viruses, represented by CK/SX/06, exhibited huge antigenic drift from the viruses that were isolated in China previously. Though 187,000 poultry were depopulated to control the spread of this new virus after its first detection in February, the virus was re-isolated in June from Shanxi province and

Ningxia autonomous region. We found that the inactivated H5 vaccines used in China only provided 80% protection to the variant strain in a laboratory challenge study in specific pathogen free (SPF) chickens, which is quite different from the protective efficacy we reported previously[20] . We therefore developed a new reassortant virus, designated as Re-4, that contained the cleavage site modified HA and NA genes from CK/SX/06 and 6 internal genes from the PR8 virus. This new vaccine was approved for use in Shanxi, Ningxia autonomous region and several of their neighboring provinces in northern China in August.

In May 2008, the Re-1 reassortant virus was replaced as the seed virus used for vaccine production. The new H5N1/PR8 reassortant virus, which derives its HA and NA genes from A/duck/Anhui/1/06 (clade 2.3), was designated as Re-5 (Table 2).

5.4 Live virus vectored vaccines

In addition to the inactivated vaccines, we also developed two kinds of recombinant vaccines using fowlpox virus and Newcastle disease virus (NDV) as vectors[21,23]. After the detection of the GS/GD/96 virus, we started the development of a recombinant fowlpox virus expressing the HA and NA genes of H5N1 virus as a live virus-vectored vaccine. The vaccine efficacy of this recombinant virus was proven in both laboratory and field tests[21,22]. About 0.7 billion doses of the recombinant fowlpox vaccine have been used in poultry in China since 2005. Whole-virus inactivated vaccines and fowlpox virus-based recombinant vaccines have been used as control strategies for highly pathogenic avian influenza in the laboratory and in poultry farms located in different geographic regions in the world[30−33]. However, their high cost of production and the laborious administration of these vaccines are limitations for their wide application in the field.

In 2005, we established a reverse genetics system of NDV (LaSota) and generated several recombinant NDV expressing the avian influenza virus HA genes from several H5N1 viruses representing different phylogenetic lineages of the viruses isolated in China (our unpublished data). These viruses included GS/GD/96, A/duck/Anhui/1/06, and A/bar-headed goose/Qinghai/3/05. Recently, we also generated a recombinant NDV expressing the HA gene of the CK/SX/06 virus. We have demonstrated that the recombinant NDV expressing the various influenza HA genes induced strong HI antibody responses to NDV and to H5 avian influenza viruses in chickens. The recombinant NDV vaccinated chickens were protected from disease signs and death from challenge with highly pathogenic NDV. Most importantly, the vaccinated chickens were completely protected from homologous and heterologous H5N1 virus challenges and displayed no virus shedding, signs of disease, or death[23].

In the beginning of 2006, rLH5-1 was approved for use in chickens as a bivalent, live attenuated vaccine for the control of H5N1 avian influenza and highly pathogenic Newcastle disease. By the end of 2007, a total of 4 billion doses of this vaccine had been applied in chick-

Table 2 Vaccines developed and used for H5N1 avian influenza control in China from 2004 to 2008

Vaccine	Seed virus generated		Doses used in the year [a] (billions)					
	Seed name	HA and/or NA gene donor virus	2004	2005	2006	2007	2008	Total
Inactivated vaccine								
H5N2 subtype	A/turky/England/N-28/73 (H5N2) (N-28)	NA	2.5	4.08	3.6	/	/	10.18
H5N1 subtype	H5N1/PR8 (H5N1) (Re-1)	A/goose/Guangdong/1/1996	0.57	3.3	4.5	9.6	4.6	22.64
	H5N1/PR8 (H5N1) (Re-4)	A/chicken/Shanxi/2/2006	/	/	0.84	0.42	/	1.26
	H5N1/PR8 (H5N1) (Re-5)	A/duck/Anhui/1/2006	/	/	/	/	4.4	4.4
	Re-1/Re-4	NA	/	/	/	2.2	1.5	3.7
	Re-4/Re-5	NA	/	/	/	/	1.5	1.5
Live virus vector vaccine								
Recombinant fowlpox vaccine	rFPF-HA-NA	A/goose/Guangdong/1/1996	/	0.615	/	/	/	0.615
Recombinant NDV vaccine	rLH5-1	A/goose/Guangdong/1/1996	/	/	2.6	1.3	/	3.9
	rLH5-5	A/duck/Anhui/1/2006	/	/	/	/	1.2	1.2

a) a forward slash indicates that the vaccine was not used in that particular year

ens (Table 2). In May 2008, a recombinant NDV virus rLH5-5 with the HA gene derived from A/duck/Anhui/1/06 (clade 2.3) replaced rLH5-1 as the seed virus strain for vaccine production (Table 2).

6 Conclusion

Here, I briefly summarized the epidemiology and control of the H5N1 avian influenza in China in the last 12 years. The epidemic of H5N1 avian influenza in China resulted in the deaths of over 35420000 poultry either by infection or depopulation during 2004−2008, and led to severe economic damage to the poultry industry. China employs the culling plus vaccination strategy to control H5N1 avian influenza, and financial support from the government ensures the implementation of this strategy. Billions of doses of the vaccines have been used in the field and the vaccines are antigenically well matched with the circulating strains. Though the government has required 100% vaccine coverage in domestic poultry since the end of 2005, it is impossible to give the every single bird one or two doses of the vaccine in actual practice as over 70% of the birds are reared in small scale or backyard farms, oftentimes in the open field with ducks and geese. It is clear that the increased vaccination coverage results in decreased disease epidemics. There is no doubt that vaccination has played an important role to protect poultry from H5N1 virus infection, reduce the virus load in the environment, and to prevent the transmission of the H5N1 virus from poultry to human.

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