WEEKLY EPIDEMIOLOGICAL REPORT

A publication of the Epidemiology Unit
Ministry of Health

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WEER

Avian influenza A(H7N9)

Background

Avian influenza A H7 viruses are a group of influenza viruses that normally circulate among birds. The avian influenza A(H7N9) virus is one subgroup among the larger group of H7 viruses. Although some H7 viruses (H7N2, H7N3 and H7N7) have occasionally been found to infect humans, no human infections with H7N9 viruses have been reported until recent reports from China in March 2013. On 31 March 2013, public health authorities of China reported three cases of laboratory-confirmed human infection with avian influenza A(H7N9) virus.

In Apri 2013, the Ministry of Agriculture of China reported to the World Organization of Animal Health (OIE) the detection of low-pathogenic avian influenza A(H7N9)in a pigeon sampled at an agricultural wholesale market in the Shanghai municipality; this being the first H7N9 reported in birds in Asia since 2011.

Most patients initially developed an influenza-like illness (ILI) that subsequently progressed to respiratory distress syndrome resulting in hospitalization. The case fatality proportion reached approximately 25% (a provisional value, as all the details are not yet available).

Epidemiology

The first case was an 87 year old male patient who reported onset of influenza like symptoms on 19 February 2013. Second and third cases had illness onset dates of 27 February and 15 March respectively. By 29 May 2013, approximately 2months after the initial report, the number of laboratory confirmed H7N9 infections reached 132 with 37 deaths in China.

The median age was 61years with a predominance of males (2.4:1 male to female ratio). In contrast, previous infections with subtype H7 avian influenza viruses have generally been mild and associated with conjunctivitis. Investigations of H7N9 cases have so far revealed that except for four confirmed clusters of two or more cases that were in close contact, the patients did not appear to have known exposure to each other. However, most patients had a history of recent exposure to poultry, generally at live bird markets.

Surveillance for ILI among people in close contact with laboratory-confirmed H7N9 cases indicated that infected individuals are not a likely source of infection. These preliminary studies suggested that despite numerous cases of H7N9 virus infection associated with poultry exposure, there is no evidence of sustained onwards virus transmission to other people.

The agent

A nucleotide sequence alignment comparison of genes indicated that viruses isolated from different sources were very similar to each other and shared greatest identity with genes of avian influenza viruses that circulated recently in China. The HA genes had highest levels of sequence identity (95%) with H7N3 viruses detected recently in ducks at live bird markets in Eastern China. The NA genes were highly similar (96% identity) to N9 NA genes from viruses circulating recently in domestic ducks in China and Korea but featured a distinctive 15 nucleotide deletion beginning at position 215.

The remaining viral genes had greatest identity (99%) with A (H9N2) poultry viruses that have been in circulation in China since 1994. These findings indicate that H7N9 viruses from human cases were most closely related to a previously unidentified avian influenza virus with genes derived from several potential parental strains. A review of the literature indicated that human infections with H7N9 viruses have not been reported previously.

Similarly, H7N9 viruses were not detected in animals from China before the start of this outbreak. The nucleotide sequences of the genes from viruses that isolated from birds were nearly identical to each other and to genes of viruses isolated from human infections. The percent identity was 99% or greater for the majority of the genes. Simultaneous detection of nearly identical H7N9 viruses in peri-domestic birds and people in the same city suggested that human infections could be linked to exposure to birds.

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Clinical Features

Clinical Features in patients with confirmed H7N9 infection at hospital admission include high fever, non-productive as well as productive cough, shortness of breath, dyspnoea, hypoxia and evidence of lower respiratory tract disease with opacities, consolidation and infiltrates noted on chest imaging. Leukocyte counts have been normal or low, with leukopoenia, lymphopoenia and moderate thrombocytopenia in some cases.

Complications of H7N9 virus infection have included septic shock, respiratory failure, acute respiratory distress syndrome, refractory hypoxemia, acute renal dysfunction, multiple organ dysfunction, rhabdomyolysis, encephalopathy and bacterial and fungal infections such as ventilator-associated pneumonia and blood-stream infection (sometimes by multi-drug resistant bacteria).

The median time from onset to hospital admission is approximately 4.5 days, and a high proportion of patients with confirmed H7N9 infection have been admitted to intensive care. The median time from illness onset to death is approximately 11 days, ranging from 7 to 20 days. A small number of clinically mild H7N9 virus infections with uncomplicated influenza (febrile upper respiratory tract illness) have been identified in children and adults. A recent study on hospitalized patients with pneumonia suggests that systemic high-dose steroid use may result in increased risk of prolonged viral replication and shedding providing a favourable condition to the emergence of antiviral resistance.

Laboratory diagnosis

Clinical specimens from the first three cases of H7N9 virus infection were initially reported as testing positive for influenza A viral RNA, but "unsubtypable" by the real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) test routinely used by public health laboratories.

Further real-time RT-PCR tests and sequence analysis of these clinical specimens at the China National Influenza Center in Beijing revealed that the HA belonged to the H7 subtype and the NA to the N9 subtype.

This and similar assays have been developed, validated and made available to public health laboratories. Chinese Center for Disease Control and Prevention in Beijing (China CDC), Centers for Disease Control and Prevention, United States of America and the National Institute for Infectious Diseases, Japan, have also developed and shared H7N9 specific PCR reagents.

The WHO Global Influenza Surveillance and Response System (GISRS) laboratories and partner laboratories have developed both haemagglutination-inhibition and micro neutralization laboratory protocols to detect specific H7N9 virus antibodies in human sera.

Laboratory biosafety

Biosafety guidance for work with H7N9 viruses in the laboratory should be based on existing frameworks and guidelines, such as applying the risk group classification in the WHO Laboratory biosafety manual and considering the bio-risk management approach provided in CENCWA 15793. Only laboratories that meet the appropriate biosafety level and conform to available bio-risk management standards (e.g. CWA 15793) should consider working with these viruses, with relevant national authority oversight.

Final responsibility for the identification and implementation of appropriate risk assessment, mitigation, and containment measures for work with H7N9 viruses lies with individual countries and facilities. Accordingly, regulations may vary from country to country, and decisions should be taken in light of currently available knowledge, context and applicable national requirements.

Antiviral therapy

Based on the sequence of the M2 protein, H7N9 viruses are predicted to be resistant to adamantane antiviral drugs which are therefore not recommended for use. In accordance with the NA (neuraminidase) sequencing data this virus is susceptible to neuraminidase inhibitor antiviral drugs oseltamivir and zanamivir.

The potential severity of H7N9 associated illness warrants recommending that all confirmed cases, probable cases, andH7N9 cases under investigation receive antiviral treatment with a neuraminidase inhibitor drug as early as possible.

Vaccines

The WHO GISRS laboratories, public health research centres and the private sector are actively engaged in a global effort to develop H7N9 vaccines with a view to performing clinical trials to ascertain immunogenicity and establish the optimal vaccination regimen and dose. Ongoing work to develop candidate vaccine viruses based on the HA and NA genes has been successful and several candidate vaccine viruses have recently been made available to interested vaccine manufacturers. A parallel effort to develop candidate live attenuated influenza vaccine (LAIV) viruses has been initiated by joint efforts from public and private sectors .

Infection in animals

Natural infections with H7N9 viruses in chicken, ducks and other birds are asymptomatic and elicit an immune response that can be detected serologically. The virus replicates in the respiratory and digestive tracts and is transmitted by droplets or contact (direct or indirect). Preliminary experimental infections of chicken by the intranasal or intravenous route were also asymptomatic.

Because the H7N9 virus does not cause disease in poultry, sampling asymptomatic animals was necessary to detect the virus in respiratory/cloacal swabs or specific antibodies in serum by laboratory testing.

Within six weeks of the initial case report, testing of tens of thousands of samples from poultry and their environment has resulted in the identification of 51 H7N9 virus isolates from several provinces in China, and most of the specimen were from live poultry markets

It is important to note that some low pathogenic H7 viruses can evolve into highly pathogenic avian influenza viruses, as had been observed in other countries.

Natural infection of swine with subtype avian influenza A(H7N2) viruses has been reported previously in Korea, prompting animal health authorities of China to perform surveillance in swine. Several thousands of respiratory and serological samples were collected from swine farms and swine slaughter houses and all were negative for H7N9 virus.

Source-Overview of the emergence and characteristics of the avian influenza A(H7N9)virus

Available from

http://www.who.int/influenza/human_animal_interface/influenza_h7n9/WHO_H7N9_review_31May13.pdf

Compiled by Dr. Madhava Gunasekera of the Epidemiology Unit

Table 4: Selected notifiable diseases reported by Medical Officers of Health 24th – 30th August 2013 (35th Week)

RDHS	Dengue Fever		Dysentery		Encephaliti		E Fever		F Poisoning		Leptospiros		T Fever		V Hepatitis		H Rabies		Chickenpox		Meningitis		Leishmaniasis		WRCD %	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**T***	**C****
Colombo	132	6987	0	152	0	15	2	105	4	44	1	148	0	6	0	62	0	1	7	303	4	42	0	0	**85**	**15**
Gampaha	85	2635	7	154	2	13	1	39	0	26	12	267	1	14	4	148	0	0	0	119	3	75	0	5	**100**	**0**
Kalutara	37	1276	5	133	0	17	1	64	9	23	5	282	0	2	0	17	0	0	0	196	0	53	0	0	**85**	**15**
Kandy	24	1370	2	109	1	10	0	16	0	7	2	57	0	86	0	70	0	0	2	97	1	11	1	3	**74**	**26**
Matale	5	356	0	76	0	4	2	22	2	5	0	49	0	4	0	33	0	0	1	39	0	29	0	8	**54**	**46**
NuwaraEliya	8	192	2	124	0	2	0	9	0	4	0	21	2	56	0	19	0	0	7	86	0	11	0	0	**69**	**31**
Galle	21	646	3	84	6	18	0	3	0	79	0	159	1	41	0	10	0	1	7	240	1	42	0	0	**84**	**16**
Hambantota	7	250	0	37	0	3	1	12	0	30	0	152	0	54	2	77	0	0	2	82	4	42	0	222	**67**	**33**
Matara	5	369	0	64	1	10	1	21	0	27	3	122	4	66	2	129	0	2	1	202	4	60	5	68	**100**	**0**
Jaffna	4	544	14	193	0	7	3	285	2	86	0	7	0	326	0	14	0	1	1	123	0	49	0	0	**75**	**25**
Kilinochchi	3	48	0	19	0	0	0	10	0	5	0	9	0	16	0	0	0	0	0	2	0	7	1	8	**75**	**25**
Mannar	2	59	7	47	0	1	0	57	11	25	2	13	0	18	0	2	0	0	0	11	0	5	0	1	**100**	**0**
Vavuniya	0	58	0	35	0	12	0	8	1	14	0	49	0	2	0	3	0	2	0	20	1	28	0	7	**50**	**50**
Mullaitivu	1	99	0	12	0	2	0	7	0	34	0	36	0	6	0	1	0	2	0	8	0	4	0	12	**20**	**80**
Batticaloa	6	471	8	220	1	5	0	3	0	15	0	30	0	2	0	10	0	3	1	37	0	7	0	0	**79**	**21**
Ampara	1	130	4	92	0	0	0	4	0	7	0	29	0	1	1	4	0	0	3	66	0	14	0	2	**57**	**43**
Trincomalee	2	177	1	51	0	3	0	5	0	1	1	58	0	10	0	3	0	1	0	33	0	4	1	27	**75**	**25**
Kurunegala	26	2341	4	131	2	32	2	35	0	21	13	240	1	31	1	42	0	1	5	282	1	92	1	36	**81**	**19**
Puttalam	11	744	2	55	0	7	0	15	0	35	4	32	0	12	0	5	0	0	0	65	2	28	0	7	**69**	**31**
Anuradhapura	4	412	3	72	0	13	0	3	0	30	1	293	0	18	1	18	0	1	3	140	0	82	12	306	**68**	**32**
Polonnaruwa	2	321	1	52	0	1	0	14	0	61	0	143	0	3	0	24	0	1	0	110	0	16	2	122	**57**	**43**
Badulla	15	394	1	141	0	3	0	14	0	8	1	45	2	65	0	39	0	0	2	97	1	52	0	5	**82**	**18**
Monaragala	2	188	4	89	0	4	0	19	0	20	1	188	3	48	1	70	0	1	0	39	0	20	1	10	**64**	**36**
Ratnapura	23	1456	5	283	0	82	0	35	0	16	3	273	0	47	4	244	0	1	2	123	0	64	0	8	**72**	**28**
Kegalle	12	880	2	97	2	13	3	22	2	11	5	147	0	63	5	174	0	0	4	243	3	93	0	0	**91**	**9**
Kalmune	3	485	3	123	0	2	0	3	2	98	0	8	0	2	0	4	0	0	3	71	0	8	0	1	**77**	**23**
SRI LANKA	**441**	**22888**	**78**	**2645**	**15**	**279**	**16**	**830**	**33**	**732**	**54**	**2857**	**14**	**999**	**21**	**1222**	**00**	**18**	**51**	**2834**	**25**	**938**	**24**	**858**	**76**	**24**

Source: Weekly Returns of Communicable Diseases (WRCD).

***T=**Timeliness refers to returns received on or before 30th August , 2013 Total number of reporting units 339. Number of reporting units data provided for the current week:257 C** Completeness

A = Cases reported during the current week. **B** = Cumulative cases for the year.**H Rabies***= Human Rabies, **E Fever***=Enteric Fever, **F Poison*** =Food Poisoning, **T Fever***=Typhus Fever, **V Hepatitis***=Viral Hepatitis

Table 1: Vaccine-Preventable Diseases & AFP

24th – 30th August 2013 (35th Week)

Disease	No. of Cases by Province									Number of cases during current week in 2013	Number of cases during same week in 2012	Total number of cases to date in 2013	Total number of cases to date in 2012	Difference between the number of cases to date in 2013 & 2012
	W	C	S	N	E	NW	NC	U	Sab					
AFP*	00	01	01	00	00	00	01	00	00	03	02	61	54	+ 12.9 %
Diphtheria	00	00	00	00	00	00	00	00	00	-	-	-	-	-
Mumps	05	03	01	05	06	05	03	03	02	33	48	1121	3374	- 66.7 %
Measles	45	04	24	00	03	03	03	06	31	119	02	2446	41	+ 5865.8 %
Rubella	00	00	00	00	01	00	00	00	00	01	-	22	-	-
CRS**	00	00	00	00	00	00	00	00	00	00	-	06	-	-
Tetanus	01	01	00	00	00	00	00	00	00	02	00	16	08	+ 100.0 %
Neonatal Tetanus	00	00	00	00	00	00	00	00	00	00	-	00	-	-
Japanese Encephalitis	01	00	00	00	00	00	00	00	00	01	-	66	-	-
Whooping Cough	02	00	00	00	01	00	00	00	00	03	03	57	67	+ 14.9 %
Tuberculosis	64	00	20	04	08	39	18	00	01	154	180	5792	6085	- 04.8 %

Key to Table 1 & 2

Provinces: **W**: Western, **C**: Central, **S**: Southern, **N**: North, **E**: East, **NC**: North Central, **NW**: North Western, **U**: Uva, **Sab**: Sabaragamuwa.

RDHS Divisions: **CB**: Colombo, **GM**: Gampaha, **KL**: Kalutara, **KD**: Kandy, **ML**: Matale, **NE**: Nuwara Eliya, **GL**: Galle, **HB**: Hambantota, **MT**: Matara, **JF**: Jaffna, **KN**: Killinochchi, **MN**: Mannar, **VA**: Vavuniya, **MU**: Mullaitivu, **BT**: Batticaloa, **AM**: Ampara, **TR**: Trincomalee, **KM**: Kalmunai, **KR**: Kurunegala, **PU**: Puttalam, **AP**: Anuradhapura, **PO**: Polonnaruwa, **BD**: Badulla, **MO**: Moneragala, **RP**: Ratnapura, **KG**: Kegalle.

Data Sources:

Weekly Return of Communicable Diseases: Diphtheria, Measles, Tetanus, Neonatal Tetanus, Whooping Cough, Chickenpox, Meningitis, Mumps., Rubella, CRS,

Special Surveillance: AFP* (Acute Flaccid Paralysis), Japanese Encephalitis

CRS =**Congenital Rubella Syndrome

AFP and all clinically confirmed Vaccine Preventable Diseases except Tuberculosis and Mumps should be investigated by the MOH

Dengue Prevention and Control Health Messages

Thoroughly clean the water collecting tanks bird baths, vases and other utensils once a week to prevent dengue mosquito breeding.

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Comments and contributions for publication in the WER Sri Lanka are welcome. However, the editor reserves the right to accept or reject items for publication. All correspondence should be mailed to The Editor, WER Sri Lanka, Epidemiological Unit, P.O. Box 1567, Colombo or sent by E-mail to **chepid@sltnet.lk. Prior approval should be obtained from the Epidemiology Unit before publishing data in this publication**

ON STATE SERVICE

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