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A Literature Review Report On H5N1 Virus [Avian Influenza] And Their Symptoms And Treatment.

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ABSTRACT

H5N1 [AVIAN FLU] is a type of influenza virus that causes a highly infectious, severe respiratory disease in birds called avian influenza (or "bird flu"). Human cases of H5N1 avian influenza occur occasionally, but it is difficult to transmit the infection from person to person. It is a highly pathogenic avian influenza {HPAI}. When people do become infected, the mortality rate is about 60%.

INFLUENZA [bird flu], A subtype H5N1 has represented a growing alarm since its recent identification in Asia. Previously thought to infect only wild birds and poultry, H5N1 has now infected humans, cats, pigs and other mammals in an ongoing outbreak, often with a fatal outcome. In order to evaluate the risk factors for human infection with influenza virus H5N1, here we summarize 53 case patients confirmed with H5N1 infection during 2006. The review also compares the mortality rate among human cases from late 2003 until 15 June 2006 in different countries. Neither how these viruses are transmitted to humans nor the most effective way to reduce the risk for infection is fully understood. A wide range of serological and molecular methods have substantially aided in the identification of bird flu in humans. Candidate vaccines have been developed, yet are not ready for widespread use. Oseltamivir (brand name: Tamiflu) is the preferred drug for the management of human Influenza-like illness (ILI). Surveillance, mass awareness and pandemic preparedness abiding WHO recommendations are of paramount importance for the prevention of bird flu outbreaks.

KEY WORDS: Avian influenza flu [AIV], Avian flu, Bird flu, H5N1, Oseltamivir.

INTRODUCTION

The purpose of this Overview is to summarize the latest available studies and finding on AVIAN INFLUENZA and hygiene. Based on the information, we discussed the evidence of avian influenza – related risks to human health.

Although the "pandemic H5N1" virus does not exist, it may behave like avian influenza H5N1 virus in many aspects. There are three types of influenza viruses: A, B and C. Influenza A virus can infect humans, birds, pigs, horses and other animals [influenza A can cause pandemic]. Influenza B viruses are usually found only in humans and generally are associated with less severe epidemics than influenza A virus. Influenza C viruses cause mild illness in humans and are not a significant concern of human health. Except Influenza A viruses [IAV], including all avian influenza viruses possess eight separate genomic segments ranging in size between 890-2341 nucleotides.

Influenza viruses are part of Orthomyxoviridae family and are negative sense single-stranded RNA viruses with segmented genomes. Like other RNA viruses, influenza viruses have a fast mutation rate, typically accumulating two to eight substitutions per 1000 sites per year. Segmentation further increases the evolutionary speed of the virus by permitting exchange of genes between virus strains that co-infect cells in the same host, a process known as reassortment. The genome segments of IAV encode ten core polypeptides, including: three subunits of a vital polymerase, a nucleoprotein, three transmembrane proteins [haemagglutinin (HA), neuraminidase (NA), and the M2 ion channel].

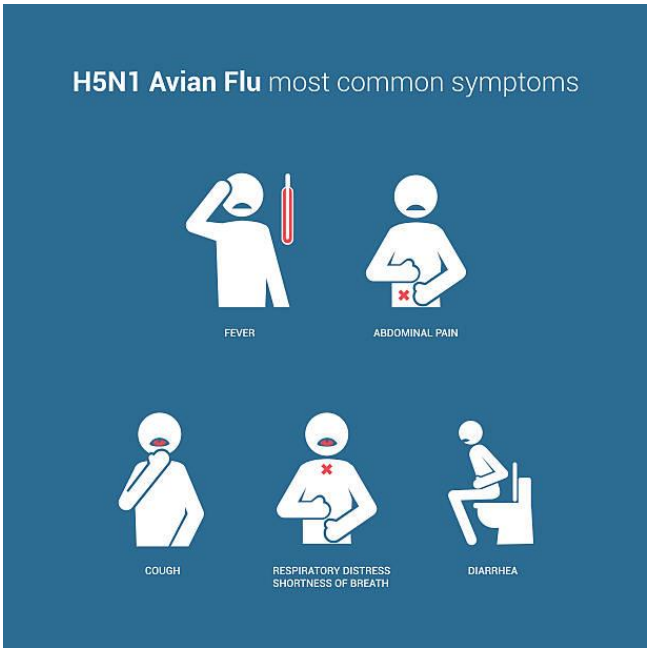
SYMPTOMS AND CAUSES

Symptoms vary from mild to severe, but usually start with normal flu-like symptoms, including:

- Runny nose
- Cough
- Sore throat
- High grade Fever (over 100.4°F or 38°C)
- Headache
- Muscle ache
- Conjunctivitis
- Malaise
- Diarrhoea
- Vomiting
- Respiratory difficulties
- Lethargy
- Twisted neck
- Sudden death without clinical signs

The causes of the avian influenza are as follows:

- You can become infected if you breathe in the virus that is present in droplets or dust. You can also be infected by touching something infected and then touching your eyes, nose or mouth.
- Bird flu has been passed from people who were infected to people who had no contact with infected birds, but this has been rare.
- You can't get bird flu from eating properly processed poultry or eats, but you should avoid eating anything that has raw poultry or blood as an ingredient.



DIAGNOSTIC TESTS FOR AVIAN INFLUENZA

SAMPLE COLLECTION

Testing for the presence of AI requires that samples be taken from live birds, dead birds or the environment birds inhabit. Samples are routinely collected from wild birds, domestic flocks, live bird markets and quarantined birds

TESTING PROCESS

Initial AI screening tests are performed by one of more than 45 USDA approved laboratories in the National Animal Health Laboratory Network (NAHLN). In the case of wild bird samples, the U.S. Department of the Interior's National Wildlife Health Centre also performs initial screening tests. These labs will determine if AI virus is present and whether it is an H5 or H7 subtype. Because of the potential for H5 or H7 subtypes to mutate into highly pathogenic strains, those samples are forwarded to USDA's National Veterinary Services Laboratories (NVSL) for confirmatory testing. NVSL then conducts additional screening tests and confirmatory tests, with research assistance from USDA's Southeast Poultry Research Lab. This USDA laboratory in Ames, Iowa, is the only AI reference laboratory in the United States recognized by the World Organization for Animal Health, known as the OIE. Although there is a network of laboratories across the nation approved to conduct AI screening tests, confirmatory testing in the United States is conducted only at NVSL.

STAGES OF USDA TESTING

I. Rapid screening tests A series of AI rapid screening tests are performed that cannot differentiate between HPAI and LPAI viruses. Varieties of this test can screen for the presence of all strains of AI virus, specifically for H5 or H7 subtypes and the N1 subtype. NVSL conducts the following rapid screening tests:

1) Matrix test – used to screen for AI viruses

2) H5 test – used to screen for H5 subtype

3) H7 test – used to screen for H7 subtype

4) N1 test – used to screen for N1 subtype

Serological Tests:

These are serum or egg yolk tests that check for the presence of Avian Influenza antibodies. Antibodies are substances produced by the birds in response to exposure to the viruses. They are generally detected 10 days and thereafter in the serum or egg yolk of the birds. The serum antibodies do not differentiate which AI viruses the birds were exposed to, but detect antibodies from all the group A Influenza virus.

When a serological test is POSITIVE, it means that sometime in the PAST, the bird had been exposed to the Avian Influenza virus. The birds often are no longer shedding actual virus, as the antibodies produced help the animals rid themselves of the infection. However, this does not mean the entire flock has cleared the virus or that the virus is gone from the environment.

Two serological tests approved for monitoring for Avian Influenza exposure by the National Poultry Improvement Plan are the Agar Gel Immunodiffusion test (AGID) and the Avian Influenza Enzyme Linked Immunosorbent Assay (ELISA). Both tests are SCREENING TESTS ONLY!! Finding a positive AGID or ELISA result on serum samples is merely a cue that further confirmatory testing is needed. Occasional false reactions (both positive and negative) have been known to occur with any screening test. The advantage of the AGID and ELISA tests is that the results may be available in 24 hours (AGID test) or within a few hours (ELISA tests). They are also very inexpensive to run.

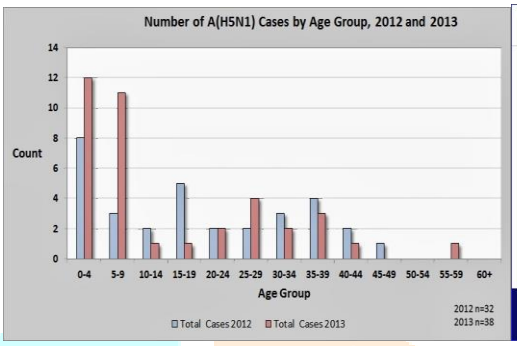
Virus Detection Tests:

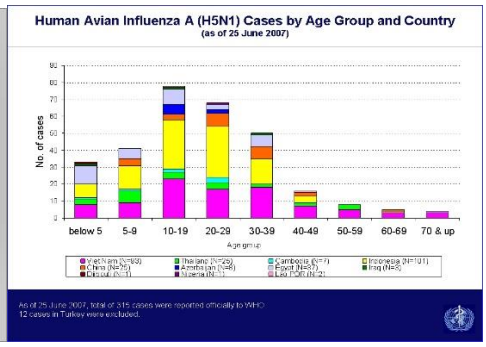
Antigen detection ELISA test kits are available for rapid bird-side testing for Avian Influenza. Oropharyngeal swabs are collected from birds, mixed with specific fluid reagents in a test tube and then a test strip is inserted in the tubes. Results are available in 15 minutes as positive or negative. The tests are fairly specific but not as sensitive das some tests. Large amounts of virus are needed in the sample for the test to turn positive. This means there is a fairly narrow window of time when the test will detect AI virus (within the first week of infection generally). A positive result is considered significant, but false negatives are possible if the amount of virus shed is very low. The advantage is the convenience of bird-side testing. The disadvantage is the expense. This test is also considered a screening tool. If a positive result is detected, more confirmatory tests will be needed.

Molecular tests (rRt-PCR tests): The polymerase chain reaction (PCR) assay is a rapid and sensitive method for detecting the genetic material of influenza viruses. These tests can identify if the virus is present in the sampled material and also the sub-types of the virus (H 5, H7). They do not differentiate whether the virus is highly pathogenic or low pathogenic. For that, live chicken testing or genetic sequencing are necessary. The advantage of these tests is their quick turn-around time (one day or less) and high sensitivity. The disadvantage is the expensive equipment needed, and highly trained technicians. Only certain laboratories (NAHLN or National Animal Health Laboratory Network) are approved to run this test and standardized training, methods and equipment are needed.

MORTALITY RATE (from 2007-2013)

The average mortality rate was found to be 60%





OUT BREAKS OF AVIAN FLU IN RECENT HISTORY

There have been outbreaks of versions of bird flu all over the world. Some forms have a mortality rate that exceeds 50%. Recent outbreaks have happened in China and Russia. Previous pandemics related to bird flu include the following outbreaks.

- The 1918 pandemic (the Spanish flu) resulted in 50 million people dying throughout the world was later linked to an H1N1 influenza virus that came from birds. The number of deaths in the U.S. was about 675,000.
- The 1957-1958 pandemic was caused by the H2N2 virus, which originated from a bird influenza virus. This pandemic was called the Asian flu, as Singapore and Hong Kong were the first places to report infections. It killed 1.1 million people globally. Deaths in the U.S. totaled 116,000 people.
- In 1968, the H3N2 flu virus caused a pandemic that killed 1 million people throughout the world. It was particularly serious for people over the age of 65. In the U.S, about 100,000 people died.
- In 2009, the H1N1pdm09 virus, a novel H1N1 virus, was found in the U.S. This pandemic claimed an estimated 151,700 to 575,400 lives throughout the world in the first year it was in circulation. The numbers for the U.S. during the first year amounted to an estimated 12,469 deaths. The difference with this virus is that it caused more severe illness and death among people younger than 65 years old.
- In January 2015**,** an HPAI H5N1 virus was identified in a sample taken from a US wild bird in 2014. This virus resulted from reassortment of the Asian lineage H5 viruses with an N1 NA from North American wild birds. No human infections with this reassortment HPAI H5N1 virus were reported.
- As of May 2019, 861 human cases of H5N1 virus infection and 455 deaths had been reported from 17 countries since November 2003.

RISK FACTORS

H5N1 has the ability to survive for extended periods of time. Birds infected with H5N1 continue to release the virus in faeces and saliva for as long as 10 days. Touching contaminated surfaces can spread the infection.

You may have a greater risk of contracting H5N1 if you are:

- a poultry farmer
- a traveller visiting affected areas
- exposed to infected birds
- someone who eats undercooked poultry or eggs
- a healthcare worker caring for infected patients
- a household member of an infected person

EPIDEMIOLOGY

Low-pathogenicity avian influenza (LPAI) viruses are distributed worldwide and are recovered frequently from clinically normal shorebirds (Charadriiformes) and migrating waterfowl (Anseriformes). Occasionally, LPAI viruses are recovered from pet birds and ratites. The viruses may be present in village or backyard poultry flocks and in other birds sold through live poultry markets. In the US and Europe, most commercially raised poultry is free of AI viruses.

Highly pathogenic avian influenza (HPAI) viruses arise from the mutation of some H5 and H7 LPAI viruses. Stamping-out programs have been successfully used to quickly eliminate HPAI viruses; however, some resource-limited areas may use vaccines and management strategies with the aim of control rather than elimination.

AI viruses are transmitted between individual birds by ingestion or inhalation. Spread between farms results from breaches in biosecurity practices, principally by the movement of infected poultry or contaminated faeces and respiratory secretions on fomites such as equipment or clothing. Airborne dissemination between farms may be important over limited distances.

In limited cases, the Eurasian H5-strain HPAI virus has been transmitted by wild birds, and this limited transmission has been associated since 2005 with five transcontinental movements, with more frequent transmission from wild birds to poultry since 2020. Dispersion by wild birds has not been typical of other HPAI viruses. Other HPAI strains and all LPAI strains have minimal potential to infect dogs and cats.

Sporadic natural and experimental infections due to Eurasian H5 HPAI viruses have been reported in cats and dogs, as well as in wild mammals such as red foxes. Such experimental infections occurred after aerosol or respiratory exposure, ingestion of infected chickens or wild birds, or close contact exposure. Potentially, domestic pets could serve as a transmission vector between farms; however, the ability of other AI viruses, including other HPAI strains, to infect pets is unknown. Laboratory mammals have been experimentally infected with Eurasian H5 HPAI viruses, including pigs, ferrets, rats, rabbits, guinea pigs, mice, mink, and nonhuman primates. Cases of Eurasian H5N1 HPAI have been reported also in farmed mink, wild sea lions, wild sea otters, and harbour seals.

TREATMENT

Evidence suggests that some **antiviral drugs**, notably *neuraminidase inhibitor* (oseltamivir, zanamivir), can reduce the duration of viral replication and improve prospects of survival, however ongoing clinical studies are needed. Emergence of oseltamivir resistance has been reported.

- In suspected and confirmed cases, neuraminidase inhibitors should be prescribed as soon as possible (ideally, within 48 hours following symptom onset) to maximize therapeutic benefits. However, given the significant mortality currently associated with A(H5) and A(H7N9) subtype virus infections and evidence of prolonged viral replication in these diseases, administration of the drug should also be considered in patients presenting later in the course of illness.
- Treatment is recommended for a minimum of 5 days, but can be extended until there is satisfactory clinical improvement.
- Corticosteroids should not be used routinely, unless indicated for other reasons (eg: asthma and other specific conditions); as it has been associated with prolonged viral clearance, immunosuppression leading to bacterial or fungal superinfection.
- Most recent A(H5) and A(H7N9) viruses are **resistant** to adamantane antiviral drugs (e.g amantadine and rimantadine) and are therefore not recommended for monotherapy.
- Presence of co-infection with bacterial pathogens can be encountered in critically ill patients

IMMUNOLOGICAL RESPONSE CRITERIA

Immunogenicity response criteria for pandemic influenza vaccine licensure.

Parameter	US (FDA) acceptance criteria	European (CHMP) acceptance criteria
Geometric mean HI titer	No standard	No standard
Mean geometric increase (ratio day 42 GMT/day 0 GMT)	No standard	>2.5%
Seroconversion (HI) rate or significant increase in titer	Lower limit of 95% CI >40%	>40%
Microneutralization assay titer	No standard	No standard
Seroprotection rate (HI titer ≥40)	Lower limit of 95% CI >70%	>70%

Immunogenicity profiles of recombinant avian H5N1 vaccine candidates with and without adjuvants.

Manufacturer (trade name/designation)	Vaccine antigen	HA dose (µg)	Seroconversion without adjuvant (%)	Seroconversion with adjuvant (%)
Protein Sciences (Panblok, UMN-0501)	rHA (A/Hong Kong/156/1997)	90	52†	
		45	28	
		15	17	
	rHA (A/Vietnam/1203/2004)	45	22	8 (alum)
		15	17	16 (alum)
		5		20 (alum)
	rHA (A/Indonesia/05/2005)	135	32	
		45	15	82 (GLA-SE)
		15		75 (GLA-SE)
		7.5		66 (GLA-SE)
		3.8		72 (GLA-SE)
Fraunhofer (HAI-05)	rHA (A/Indonesia/05/2005)	90	10	5

VACCINES FOR AVIAN FLU

Till September 2021, there is no specific vaccine approved for the Avian flu H5N1 virus for humans. However, there have been efforts to develop vaccines for this strain of avian flu due to its potential to cause severe illness and its ability to spread from birds to humans.

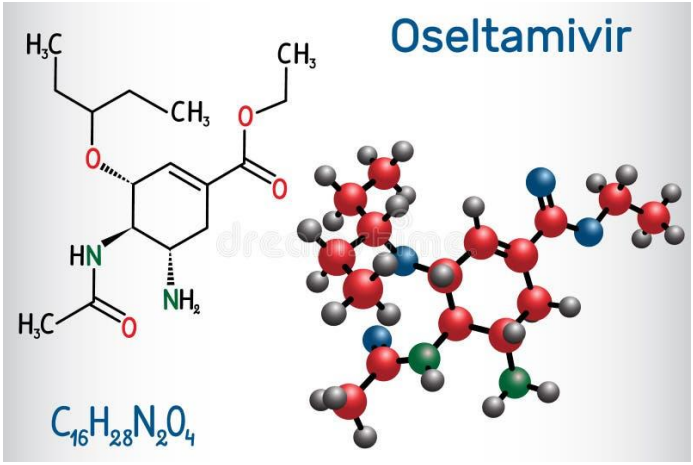
In case of an outbreak or pandemic involving the H5N1 virus, public health authorities may recommend the use of influenza vaccines that target other strains of the influenza virus. These vaccines may offer some cross-protection or reduce the severity of illness in individuals infected with H5N1.

Whereas, some **antiviral drugs,** notably *neuraminidase inhibitor* (oseltamivir, zanamivir), can reduce the duration of viral replication and improve prospects of survival from the viruses.

OSELTAMIVIR

Oseltamivir, sold under the brand name **Tamiflu**, is an antiviral medication used to treat and prevent influenza A and influenza B, viruses that cause the flu. Many medical organizations recommend it in people who have complications or are at high risk of complications within 48 hours of first symptoms of infection. They recommend it to prevent infection in those at high risk, but not the general population. The Centres for disease control and Prevention (CDC) recommends that clinicians use their discretion to treat those at lower risk who present within 48 hours of first symptoms of infection. It is taken by mouth, either as a pill or liquid.

Recommendations regarding oseltamivir are controversial as are criticisms of the recommendations. A 2014 Cochrane review concluded that oseltamivir does not reduce hospitalizations, and that there is no evidence of reduction in complications of influenza. Two meta-analyses have concluded that benefits in those who are otherwise healthy do not outweigh its risks. They also found little evidence regarding whether treatment changes the risk of hospitalization or death at risk conditions.



As of 2013, H274Y and N294S mutations that confer resistance to oseltamivir have been identified in a few H5N1 isolates from infected patients treated with oseltamivir, and have emerged spontaneously in Egypt.

SIDE EFFECTS

Tamiflu may cause serious side effects including:

- sudden confusion,
- tremors or shaking,
- unusual behaviour, and
- hallucinations

Common side effects of Tamiflu include:

- nausea,
- vomiting,
- diarrhoea,
- dizziness,
- headache,
- Nosebleed,
- eye redness or discomfort,
- sleep problems (insomnia), or
- cough or other respiratory problems.
- The flu itself or Tamiflu may rarely cause serious mental/mood changes. This may be more likely in children. Tell your doctor of any signs of unusual behaviour, including confusion, agitation, or self-injury

Most Frequent Adverse Events in Studies in Naturally Acquired Influenza in Subjects 13 Years of Age and Older.

	Treatment				Prophylaxis			
Adverse Event[a]	**Placebo N=716**		**TAMIFLU 75 mg twice daily N=724**		**Placebo/ No Prophylaxis[b] N=1688**		**TAMIFLU 75 mg once daily N=1790**	
Nausea (without vomiting)	40	(6%)	72	(10%)	56	(3%)	129	(7%)
Vomiting	21	(3%)	68	(9%)	16	(1%)	39	(2%)
Diarrhea	70	(10%)	48	(7%)	40	(2%)	50	(3%)
Bronchitis	15	(2%)	17	(2%)	22	(1%)	15	(1%)
Abdominal pain	16	(2%)	16	(2%)	25	(1%)	37	(2%)
Dizziness	25	(3%)	15	(2%)	21	(1%)	24	(1%)
Headache	14	(2%)	13	(2%)	306	(18%)	326	(18%)
Cough	12	(2%)	9	(1%)	119	(7%)	94	(5%)
Insomnia	6	(1%)	8	(1%)	15	(1%)	22	(1%)
Vertigo	4	(1%)	7	(1%)	4	(<1%)	4	(<1%)
Fatigue	7	(1%)	7	(1%)	163	(10%)	139	(8%)

DOSAGE AND ADMINISTRATION

• Adults and adolescents (≥13 years): 75 mg twice daily for 5 days

• Paediatric patients (≥1 year): Based on weight twice daily for 5 days

• Renally impaired patients (creatinine clearance 10-30 mL/min): Reduce to 75 mg once daily for 5 days (2.4)

CONTRAINDICATIONS

TAMIFLU is contraindicated in patients with known serious hypersensitivity to oseltamivir or any component of the product. Severe allergic reactions have included anaphylaxis and serious skin reactions including toxic epidermal necrolysis, Stevens-Johnson Syndrome, and erythema multiforme.

PHARMAKOKINETICS

ABSORPTION AND BIOAVAILABILITY

Oseltamivir is readily absorbed from the gastrointestinal tract after oral administration of oseltamivir phosphate and is extensively converted predominantly by hepatic esters to oseltamivir carboxylate. At least 75% of oral dose reaches the systemic circulation as oseltamivir carboxylate. Exposure to oseltamivir is less than 5% of the total exposure after oral dosing.

DISTRIBUTION

The volume of distribution (VSS) of oseltamivir carboxylate, following intravenous administration in 24 subjects, ranged between 23 and 26 litres. The binding of oseltamivir carboxylate to human plasma protein is low (3%). The binding of oseltamivir to human plasma protein is 42%, which is insufficient to cause significant displacement-based drug interactions.

METABOLISM

Oseltamivir is extensively converted to oseltamivir carboxylate by esterases located predominantly in the liver. Neither oseltamivir nor oseltamivir carboxylate is a substrate for, or inhibitor of, cytochrome P450 isoforms.

ELIMINATION

Absorbed oseltamivir is primarily (>90%) eliminated by conversion to oseltamivir carboxylate. Plasma concentrations of oseltamivir declined with a half-life of 1 to 3 hours in most subjects after oral administration. Oseltamivir carboxylate is not further metabolized and is eliminated in the urine. Plasma concentrations of oseltamivir carboxylate declined with a half-life of 6 to 10 hours in most subjects after oral administration. Oseltamivir carboxylate is eliminated entirely (>99%) by renal excretion. Renal clearance (18.8 L/h) exceeds glomerular filtration rate (7.5 L/h), indicating that tubular secretion occurs in addition to glomerular filtration. Less than 20% of an oral radiolabelled dose is eliminated in faeces.

PHARMACODYNAMICS

- **In vitro studies**

In vitro antiviral assays (plaque reduction, virus yield, or cytopathic effect) of influenza viruses of active oseltamivir were mainly performed using Meden-Darby canine kidney (MDCK) cells. Active oseltamivir inhibited in vitro the influenza neuraminidases with Ki and IC50 values in the nanomolar range (0.06 – 1 ng/ml), but had little or no activity against other neuraminidases from other sources (human liver, rat liver or uterus or two bacterial and parainfluenza and Newcastle disease neuraminidases). Clinical isolates and laboratory strains of A-type virus seem to be more sensitive than B-type viruses to active oseltamivir. Ki value for a resistant mutant enzyme was >27000x above the value obtained for a wild type enzyme.

- **In vivo studies**

In vivo studies used highly virulent viruses to infect mice. Effects of lethal intranasal doses of mouseadapted influenza A (H1N1, H3N2) and B were inhibited dose-dependently. Other animal models tested in vivo were ferrets and chickens. In ferrets, symptoms of disease caused by clinical isolates (A/H1N1 or A/H3N2 or B)

were slightly relieved by oseltamivir doses that give the exposure comparable to that observed in clinical trials. Chickens infected by a highly pathogenic avian influenza A virus (H7N7) and treated with 10 or 100 mg/kg oseltamivir (Ro 64-0796) had lower virus titres and a slightly improved survival in the high dose group only.

WHO(World Health Organisation) REPORT on Avian flu

Influenza infection in otherwise healthy (OWH) adults and adolescents is usually a self-limiting condition that is not associated with a high risk of secondary complications. However, in children, elderly, pregnant, chronically ill, and immunocompromised populations, influenza infection can be associated with substantial morbidity and mortality.

Since its first approval (in September 1999 in Switzerland), oseltamivir has been widely used throughout the world for the treatment of influenza infections. In a pooled analysis of all influenza-positive adults and adolescents (N = 2413) enrolled into treatment studies, use of oseltamivir 75 mg twice daily for 5 days reduced the median duration of influenza illness by approximately 1 day, from 5.2 days (95 % confidence interval [CI] 4.9, 5 5.5 days) in the placebo group to 4.2 days (95 % CI 4.0, 4.4 days; p ≤0.0001) in the oseltamivir group (Nicholson et al. 2000, Treanor et al. 2000). In a meta-analysis that included only patients with laboratory confirmed infection, the reduction in time to resolution of symptoms was more pronounced (97.5 hours for oseltamivir versus 122.7 hours for placebo, reduction of 25.2 hours, 95% CI: 36.2, 16·0 hours) (Dobson et al. 2015). In addition, a random effects meta-analysis of observational studies of oseltamivir treatment based on studies that provided adjusted effect measures found that oseltamivir may reduce mortality (odds ratio [OR]=0.23, 95% CI: 0.13, 0.43), hospitalization (OR=0.75, 95% CI: 0.66, 0.89), and duration of symptoms (33 hours [95% CI: 21, 45 hours]) compared with no treatment.

FUTURE RESEARCH DIRECTIONS

The virus that may one day bring about a new influenza pandemic does not yet exist. In the absence of virus-specific information, studies of existing potential precursors, such as the avian influenza virus H5N1, and related subtypes can shed light on potential risk factors and thus aid decision makers in planning and preparedness activities. With respect to water, sanitation and hygiene, little is known about the specific risk factors posed by H5N1 avian influenza for the human population. There is a paucity of information on the presence and stability of the H5N1 virus in water and sewage. Further, the site(s) of infection and the route(s) of transmission of H5N1 avian influenza virus that presently causes disease in some birds and, in rare instances, humans are likely to change in future pandemic strains. When H5N1 cases in humans arise, the focus is often on collection of specimen samples for case management and epidemiological data to trace the origin of disease. Opportunities for environmental sample collection that could help fill the knowledge gaps described in this report are often overlooked. Additional data on the survival of the H5N1 virus in water and sewage under field conditions would improve exposure assessment. Quantitative estimates of the range of influenza virus concentrations in bird faeces and in waters in which birds have congregated would provide better information on the potential viral loads that could be shed into the environment. From this, virus concentration could be estimated based on dilution factors of faeces in water resources. Thus, there is a need for environmental sampling protocols that can provide investigators with well documented, representative samples while recognizing the time-constrained, resource-limited conditions faced by the field team. More information is needed about the inactivation of avian influenza H5N1 viruses in water and in avian waste. Specifically, information on the means and methods for effective disinfection at all levels of water and wastewater treatment (household, healthcare settings, community systems). In the event a new strain of virus with efficient human-to-human transmission emerges, the window of opportunity to intervene could

be very small. Rapid response and effective infection control in healthcare and community settings will require a number of public health intervention strategies. While standard precautions and good hygiene practice have been developed for seasonal human influenza, these need to be underpinned by virus-specific research on the efficacy and effectiveness of barrier and behavioural approaches to infection control.

CONCLUSION

The recent epidemics caused by the avian influenza A virus in Asia, in particular those caused by the H5N1 subtype, have demonstrated the capacity of this agent to cause serious illness in humans, without any recombination between human and avian viruses or any intermediate mammalian host, such as the pig. This alerts us to the fact that any influenza A subtype can cross the interspecies barrier and become a latent pandemic strain. Human beings themselves can function as intermediate hosts, in which avian viruses recombine with human viruses. This can result in a virus with a new surface glycoprotein and a constellation of genes that facilitate the rapid transmission of the virus to susceptible populations. We cannot rule out the possibility of mild or asymptomatic infection in persons exposed to infected birds or humans. In some senses, the dynamics of human influenza in humans and avian influenza in birds are similar—both can be thought of as stratified into layers with different connectivity: age for humans—with locally moving children and long-range moving adults; and domestic and wild species for birds—with domestic birds moving via trades by long-range migration. However, unlike human IAV, where reassortment between the few dominant subtypes is rare, reassortment is a common feature for avian IAVs, especially in wild bird populations. Consequently, avian IAVs are far more diverse and more easily generate novel strains than the more specialized human viruses. Looking to the future, we should expect the emergence of more HPAI strains. Experience teaches that this has previously occurred somewhere in the world approximately once or twice per decade; and the fundamental driver of leaving H5 and H7 LPAI viruses uncontrolled in a host-dense environment until de novo mutation into HPAI forms occurs has not been removed.

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