PUBLIC HEALTH
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STREAM 1
Background document

REDUCING RISK

Reducing the risk of emergence of pandemic influenza

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Introduction

This document summarizes what is known about the factors that influence how influenza viruses with pandemic potential emerge from the animal reservoir. In recent years research and observational activities have expanded in the field of zoonotic influenza. But avian influenza viruses have been disproportionately emphasized compared with other animal influenza viruses because of the international focus on the H5N1 epizootic. Thus, many of the data reported here refer to knowledge generated from avian influenza viruses.

Background

Influenza viruses have segmented, negative sense, single-strand RNA genomes and are placed in the family Orthomyxoviridae. The Orthomyxoviridae family now consists of five genera; only viruses of the Influenzavirus A genus are discussed here. Influenza A viruses are further divided into subtypes based on the antigenic relationships of the surface glycoproteins, haemagglutinin (HA) and neuraminidase (NA). 16 HA subtypes have been recognized (H1-H16) and nine NA subtypes (N1-N9). Each virus has one HA and one NA antigen, apparently in any combination. All influenza A subtypes in most possible combinations have been isolated from avian species. Of the many HA/NA subtype combinations, only those of the H1N1, H2N2, and H3N2 subtypes have been shown to form stable lineages in humans.

Factors associated with the emergence of influenza viruses with zoonotic or pandemic potential

It has been known for some time that the human pandemic viruses of 1957 and 1968 appeared to arise by reassortment between viruses circulating in the human population and avian influenza viruses (1-3). However, because of the apparent barriers to human influenza viruses infecting birds, and apparent barriers to avian influenza viruses infecting humans, it was most often suggested that pigs, which can often be infected by both human and avian viruses, acted as "mixing vessels." By this mechanism, reassortment between human and avian influenza viruses could occur in pigs concurrently infected with dual strains. Subsequently, a new strain could emerge that possessed the necessary gene(s) from the virus of human origin to allow replication and spread in the human population, and that also had an antigenically different haemagglutinin surface glycoprotein, which would allow the immunologic memory of the human population to be circumvented. This swine mixing-vessel theory has yet to be proven for the pandemic viruses of 1957 and 1968, but it appears to have been the mechanism by which the human pandemic (H1N1) 2009 virus emerged.

The other mechanism by which the generation of a pandemic virus may occur is through progressive adaptation of a virus entirely of animal origin. Studies on the genome of the H1N1 "Spanish" influenza virus, which affected humans at the beginning of the 20th century, have resulted in the speculation that this virus was entirely of avian origin (4), thus suggesting that a virus containing all 8 segments of avian origin was able to establish itself in the human population. Other theories on the genesis of the 1918 pandemic virus, however, include the possibility of recombination (5) and that this pandemic emerged as the result of reassortment between at least two viruses already circulating in mammalian species (6).

Another insufficiently explored idea is the role of genetic heterogeneity in the human host. In all the outbreaks of H5N1 viruses in humans, 1997 and 2003-2009, suspected human-to-human

transmissions have predominately occurred within family groups. Within these family clusters, transmission has been shown to occur primarily between genetically, not matrimonially, related contacts (7-9). Whether or not these family clusters were the result of limited human-to-human transmissions or infections from a common source, the strong bias towards infection of genetically related individuals favors a genetic basis for susceptibility. In humans, major histocompatibility complex (MHC) class I or II genotype has been associated with an increased influenza A virus-specific cytotoxic T cell precursor frequency and a better antibody response to influenza vaccine, respectively (10,11). In mice, the *Mx1* gene, one of the first described disease susceptibility genes (12), confers increased resistance to infection with influenza A virus. Apart from these examples, little is known of other host genes and their polymorphisms involved in modulating influenza A virus infection. It is possible to speculate that inter-host variations in areas such as receptor expression and innate immunity could be involved.

Host range

Influenza A viruses have been shown to infect birds and mammals. Viruses of avian origin have become adapted to new hosts and then have undergone sustained transmission in several animal species, such as pigs, humans, horses, dogs and poultry[1]. On most occasions, avian viruses have caused sporadic outbreaks that were self limiting in the alternate host populations, e.g., infections of humans, cats, mustelids and sea mammals. There appear to be no fixed rules governing the evolution, transmission, perpetuation, or spread of influenza A viruses in susceptible hosts. One of the main factors that influence susceptibility to infection appears to be the receptor conformation and distribution of types of receptors on the host cells.
Receptor specificity is considered a key factor that affects the species barrier (infectivity and pathogenicity) and pandemic potential of avian influenza viruses. The viral HA protein specifically binds to host cell sialic acid (SA) receptors in either Neu5Ac-α2,3-Gal (SA2,3) or Neu5Ac-α2,6-Gal (SA2,6) linkage. Birds, horses, sea mammals, dogs, cats, mice, and monkeys express predominantly SA2,3 receptors in the upper respiratory tract, while humans, pigs, and ferrets express predominantly SA2,6 receptors. In general, viruses tend to preferentially bind the type of receptor predominantly expressed in the upper airways of their typical host, so that avian viruses typically bind SA2,3 receptors and human viruses typically bind SA2,6 receptors. However, this association is not absolute. Recent studies (e.g., experimental infections in airway epithelial cell cultures and animal models, lectin-binding studies) show that the distribution of receptor type also varies by tissue location, including at different levels of the respiratory tract, as well as by cell type and species. Data are not yet available on differential receptor distribution among races or breeds or among individuals within a host species.

Despite these uncertainties, a SA2,6 receptor binding preference is considered essential for an influenza virus to be easily transmissible to or among humans. Although some H5N1 viruses have acquired the capacity to bind to some SA2,6 receptors, clearly these changes have so far been insufficient to allow easy transmission to or among humans. Studies of pandemic (H1N1) 2009 virus (13) examining the tissue binding of CA/04 HA indicate that it exhibits a binding pattern correlated with the predominant distribution of SA2,6 receptors and is not consistent with an SA2,3 binding preference.

[1] The World Organisation for Animal Health defines poultry as all birds reared in captivity for the production of commodities.

Influenza in birds

Influenza viruses have been shown to infect a great variety of birds (14-18), including free-living birds, captive caged birds, domestic ducks, chickens, turkeys, ostriches, pigeons, quail, and other domestic poultry. Influenza A viruses cause two different clinical conditions in birds, highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI). The latter, a clinically mild disease, may be caused by all 16 subtypes of avian influenza. In contrast, HPAI is caused only by certain viruses of H5 and H7 subtypes and is a severe disease with a fatal outcome in many avian species. The low pathogenicity viruses are commonly found in healthy free-living birds, predominantly waterfowl and shorebirds.

Before the ongoing H5N1 epizootic, HPAI had only once affected wild birds significantly (19). It appeared, therefore, that HPAI was a disease of domesticated birds, and that wild birds usually harboured only the low pathogenic form of these viruses. The unprecedented panzootic situation has now resulted in both the establishment of endemic HPAI in poultry in some countries as well as the transmission of infections with HPAI H5N1 from domestic poultry to naïve populations of wild birds (20,21).

Avian influenza infections of mammals

Pigs

Swine influenza viruses originate from avian or human influenza viruses that become established in pigs, through progressive adaptation or by reassortment with other swine, avian, or human influenza viruses. Pigs play a crucial role in influenza ecology and epidemiology, primarily because of their dual susceptibility to human and avian viruses. They possess both SA2,3 and SA2,6 receptors in their upper airways, and are therefore considered a potential mixing vessel for influenza viruses, from which reassortants may emerge.

The introduction of avian influenza viruses to pigs followed by limited circulation in pigs and subsequently other species is not an uncommon occurrence. Kida et al. (22) demonstrated experimentally that pigs were susceptible to infection by at least one virus representative of each of the subtypes from H1 to H13, and serological evidence has been obtained of infections of pigs with viruses of H4, H5 and H9 subtypes (23). An independent introduction of H1N1 virus from birds to pigs occurred in Europe in 1979 (24). This virus became established in pigs and was subsequently transmitted to turkeys (25,26). In addition, the introduction of classical swine H1N1 influenza viruses to turkeys from infected pigs has been reported to occur regularly in the USA, and in some cases, influenza-like illness in pigs has been followed immediately by disease signs in turkeys (27-29). Genetic studies of H1N1 viruses from turkeys in the USA has revealed a high degree of genetic exchange and reassortment of influenza A viruses of turkeys and pigs (30). A similar introduction occurred in Asia in the early 1990s; these viruses are genetically distinct from the viruses in Europe (31). H9N2 viruses were introduced into pigs in South-East Asia (32). With reference to the introduction of zoonotic avian influenza to pigs, during the HPAI H7N7 epidemic in The Netherlands in 2003, 13 pig herds on farms with infected poultry were shown to have antibodies to H7 subtype, although no virus was detected (33,34). In Canada, however, avian viruses of H3N3 and H4N6 subtypes have been isolated from pigs (35,36). But despite the occurrence of infections with various subtypes, the only subtypes to have become truly established in pig populations and readily transmissible from pig to pig and herd to herd are H1N1, H3N2, and the reassortant H1N2. Genotype analysis of different isolates of these subtypes,

however, suggests that they can be the result of various reassortments of viruses from different progenitor host species (pig, human, and avian) (37).

There have been sporadic unpublished reports of natural infections in pigs with the panzootic HPAI H5N1 viruses (38), and three experimental infections have been carried out with a total of 8 of these viruses. Six of these have replicated in pigs, although clinical signs were mild or inapparent and shedding levels were not high. In none of the experiments was pig-to-pig transmission observed (39-41).

The complicated epidemiology of swine influenza has received intense review, particularly since the identification of the virus associated with pandemic (H1N1) 2009 influenza (37,42). As of September 2009, the existing epidemiological pattern of swine influenza had not changed in response to the human pandemic, although sporadic documented instances of pandemic H1N1 2009 virus infecting pigs from different parts of the world have been reported. Swine influenza viruses have occasionally been transmitted to humans, with at least 50 documented cases representing all swine influenza virus subtypes (43,44).

Horses

Although there have been isolated reports of evidence of infection of horses with viruses of subtypes H1N1, H2N2 and H3N2 (45), enzootic influenza infections of horses have been restricted essentially to H7N7 and H3N8 subtypes of influenza A. These viruses form distinct and established lineages in phylogenetic studies. However, H3N8 viruses isolated from severe epidemics in horses occurring in the Jilin and Heilongjiang Provinces in the north-east of the People's Republic of China in 1989 and 1990 were antigenically and genetically distinguishable from other equine H3N8 viruses. Guo et al. (46) concluded that this virus was of recent avian origin and had probably spread directly to horses without reassortment. Despite these epidemics, H3N8 does not appear to have become established in the horse population. There is no evidence that panzootic HPAI H5N1 has naturally infected horses. There have been no confirmed cases of transmission of equine influenza viruses to humans, although there is some preliminary serologic evidence of human exposure (G. Gray, personal communication). One explanation may be the avian-like receptor profile (SA2,3) of horse respiratory tract cells (47).

Marine mammals

During 1979 and 1980, approximately 500 deaths (about 20% of the population) occurred in harbour seals (*Phoca vitulina*) around the Cape Cod peninsula in the USA as a result of acute haemorrhagic pneumonia. Influenza A viruses of H7N7 subtype were isolated repeatedly from the lungs or brains of dead seals (48). The virus infecting the seals was shown to be closely related both antigenically and genetically to avian influenza viruses (49) and appeared to represent direct transmission to the seals without reassortment.

In 1983 further deaths (2% to 4% of the population) occurred in harbour seals on the New England coast of the USA and an influenza A virus of subtype H4N5 was isolated. Once again, all eight genes of this virus were demonstrably of avian origin (50). From surveillance of seals on the Cape Cod peninsula, Callan et al. (51) reported isolates of two influenza A viruses of H4N6 subtype collected in 1991 and three of H3N3 subtype in 1992, all from seals found dead with apparent viral pneumonia. Antigenic and genetic characterization revealed that these too were avian viruses that had entered the seal population. Two viruses of H13N2 and H13N9 subtypes

were isolated from a single beached pilot whale. Genetic analysis indicated that the viruses were closely related to H13 avian influenza viruses in gulls, and believe to have originated directly from gulls (52,53).

Mustelids

Ferrets are susceptible to a variety of animal and human influenza viruses, and are a common research model for susceptibility and transmissibility of human seasonal and pandemic influenza virus. Recently, there have been media reports of a few cases of pandemic (H1N1) 2009 infection in pet ferrets in the USA, apparently transmitted to the animals from their owners (54).

In October 1984 outbreaks of respiratory disease affected approximately 100,000 minks on 33 farms situated in close proximity along a coastal region of southern Sweden, with 100% morbidity and 3% mortality (55). Influenza A viruses of H10N4 subtype were isolated from the minks. Genetic analysis indicated that the viruses were of avian origin and were very closely related to a virus of the same subtype isolated from chickens and a feral duck in England in 1985 (56). Recently, Denmark reported farmed minks infected with H3N2 virus (57). Earlier experimental infections had already suggested that minks were susceptible to infection with various subtypes of avian influenza viruses (58).

A panzootic H5N1 HPAI virus was isolated from an ill wild stone marten (*Martes foina*) in Germany on 2 March 2006, a time when there had been numerous reports of H5N1 virus in wild birds in the area where the marten was found (WHO http://www.who.int/csr/don/2006_03_09a/en/index.html). To date, no transmission of influenza viruses to humans from mustelids has been documented.

Felids

Studies by Hinshaw et al. (59) demonstrated the ability of LPAI viruses to infect and replicate in cats without showing clinical signs. However, during the 2003 – 2004 HPAI H5N1 outbreaks in Asia, there were occasional reports of fatal H5N1 virus infections in domestic cats and zoo felids after they had been fed virus-infected chickens (60-62). Mortality in cats caused by a clade II Qinghai lake lineage virus was also reported in Iraq (63). In experimental studies, cats excreted virus and developed lung pathology after intratracheal inoculation with H5N1 virus or after feeding on H5N1 virus-infected chickens (64). In addition, the virus was transmitted from infected to sentinel cats. Thus, cats may become infected with avian influenza after consumption of fresh infective poultry meat and may spread the virus to other cats.

Dogs

Dogs were believed to be resistant to avian influenza infection until a case of H5N1 in Thailand. A fatal infection was caused most probably by ingestion of an infected duck carcass. H5N1 was recovered from lung, liver, and kidney tissue and from urine specimens (65). Subclinical disease and viral shedding were subsequently reported in beagles experimentally infected with panzootic H5N1 (66).

Spillover of equine H3N8 influenza virus to dogs has been reported in the USA. Infection has spread from the southeastern states westwards, infecting racing greyhounds across the country (67). There have been no reports of spread of influenza viruses from dogs to humans.

Viral determinants of zoonotic infectivity and pathogenicity in humans

The four critical steps of the viral life cycle for influenza viruses are (1) virus binding, fusion, and entry (mediated by the haemagglutinin/HA protein, as described above); (2) transcription and replication (mediated by the PB1, PB2, PA, and NP proteins); (3) modulation of innate immune responses (mediated by the NS1 protein); and (4) virus particle release (mediated by the neuraminidase/NA protein). Changes to the proteins mediating these steps therefore affect the infectivity, pathogenicity, and transmissibility of zoonotic influenza viruses in animals and people.

There are extensive data describing specific genomic mutations and protein changes that are associated with and potentially influence characteristics of avian, human, and other animal influenza viruses. However, based on expert opinion, it is currently not possible to predict what specific combination or constellation of mutations would be required to transform an animal influenza virus into a zoonotic influenza virus or then into a pandemic virus. It is also not possible to predict, for example, whether panzootic H5N1 virus would retain its high lethality if it were to become easily transmissible among humans. The pandemic (H1N1) 2009 virus does not contain the postulated molecular motifs thought to be associated with pandemic potential based on the knowledge gained from human seasonal, previous pandemic, and H5N1 research, underscoring the need for additional research in this area.

The HA protein plays a central role in the pathogenicity of influenza viruses. Systemic infections may develop when the HA contains a polybasic cleavage site (as seen in the panzootic H5N1 viruses), which may be cleaved by ubiquitous proteases present in virtually every cell of the host. This is a key feature of increased pathogenicity in birds. Systemic infections may also develop when HA receptors that are able to bind a specific virus are present in a wide variety of host tissues. It has been suggested that although the presence of few SA2,3 receptors in the human upper respiratory tract may limit direct zoonotic transmission of avian influenza viruses (as mentioned above), the higher concentration of SA2,3 type receptors in the human lower respiratory tract may increase the pathogenicity of avian influenza viruses in human lungs. Further, it was noted that cats and dogs differ in receptor expression from pigs and ferrets in a pattern that is not consistent with the pathophysiology of their respective H5N1 virus infections, indicating that susceptibility and pathogenicity do not result solely from receptor specificity of the HA protein. The role of other viral components (such as the NA) should be further studied. Receptor physiology is an area in great need of future research, an opinion that has received further support in the context of the current pandemic virus. Further studies using natural glycan arrays and mass spectroscopy in various species would help to unravel the complicated questions of receptor specificity of viruses, receptor structure and distribution in different tissues and species, and how receptors modulate virus transmissibility and pathogenicity. The importance of collecting appropriate specimens from human H5N1 cases, pandemic (H1N1) 2009 cases, and other cases associated with zoonotic influenza viruses for evaluation of receptors is clear.

Mutations in the other seven influenza genes also influence host range and other characteristics of zoonotic influenza viruses. Mutations in the PB2 gene (including E627K and D701N) may influence the optimal temperature of polymerase activity and interaction with host cell factors, and thus the replication rate in the mammalian upper airway (68). Changes in the NS1 and PB1-F2 genes are thought to influence the host immune response to avian influenza viruses. Moreover, it has been postulated that the severe human infections seen with panzootic H5N1 may be

associated with cytokine disregulation (i.e., severe pneumonia and multiple organ failure), also potentially modulated by the NS1 and PB1-F2 genes (69,70).

External determinants influencing susceptibility of animal populations

Animal populations may have varying susceptibility to influenza virus infections. Apart from proposed natural resistance of certain species (e.g., pigeons), other factors may enhance or reduce the susceptibility of animal populations. Natural infection with a strain of influenza viruses of the same subtype as one circulating in the population may induce an adequate immune response in individuals to prevent the establishment of infection in a given population. Similarly, particularly in avian species, the administration of vaccine containing a seed virus of the same H subtype as the field virus has been shown to increase resistance (71).

Animal populations experiencing pathogen-related immunosuppression (such as infectious bursal disease and hemorrhagic enteritis) may exhibit exacerbated clinical signs (72). Along the same lines, animal populations experiencing poor welfare due to improper husbandry methods, malnutrition, ecto- and endoparasitic infestation or other concurrent conditions may result in greater susceptibility.

Epidemiologic risk factors for interspecies transmission of influenza viruses between animals

The interactions between host, pathogen and environment have long been recognized as the foundations of both animal and human infectious disease epidemiology. Interspecies transmission is undoubtedly favored by continued contact between susceptible animal populations from different species. Young animals are generally more susceptible to infection owing to lack of acquired immunity, and mixing of young animals from different species is often observed in wildlife (e.g., along migratory bird routes, wild bird markets) or domesticated animals as a result of "backyard" farming or marketing practices (e.g., live bird markets, barn sales, shows).

Influenza viruses of aquatic birds replicate in the digestive tract and are transmitted by fecal-oral contamination whereas viruses adapted to mammalian species replicate in the respiratory tract and are readily transmitted by airborne droplets (73-75). The environmental factors that affect these distinct modes of influenza transmission are clearly very diverse and may range from the conditions of natural habitats to those of manmade intensive production or marketing facilities. Drainage of wetlands and lagoons, and lack of clean water and feed supplies may increase fecal contamination of feed and facilitate fecal-oral transmission of influenza viruses across species. Likewise, environmental factors, such as favorable temperature and humidity, enhance the airborne transmission of avian influenza (76-79). High animal population density, particularly in closed buildings lacking effective air circulation, may affect air quality (e.g., particulate matter, ammonia, etc.). This, in turn, may result in physiologic or pathologic respiratory tract changes that could facilitate infection with influenza viruses with a marginal infectivity for a nonstandard host species. In summary, multifactorial and complex interactions between species and their environment may modulate the ability of the virus to switch hosts.

Transmission of animal influenza viruses to humans and human exposure risks

The modes of transmission of animal influenza viruses from animals or contaminated environments to humans and the factors contributing to this exposure and infection are not well understood. Further, risk behaviours and activities differ among countries, settings, and specific animals and viruses involved. It has also become clear from analysis of data on zoonotic H5N1 that although direct contact with infected poultry is certainly a risk factor (80-82) indirect exposure to apparently healthy birds also poses potential risks (83); for many cases exposure remains unknown (84). Close contact with animals, such as through household poultry rearing, home slaughter and preparation of poultry (80,85), handling cockfighting birds (86), and commercial pig farming, increases risk for zoonotic HPAI H5N1 infection and swine influenza viruses, respectively. A case has also been reported in which a veterinarian tending to poultry flocks infected with H7N7 became ill and died (87). Additional risks proposed for infection with HPAI H5N1 include swimming in (presumably contaminated) ponds (86,88) and contact with poultry-origin fertilizer (89). However, exposure to animal influenzas through live animal markets (90,91) and county fairs is less easily explained, especially when no contact with animals is reported. It is also difficult to explain why certain individuals become infected when others engaging in the same activities in the same settings do not.

The main risk factor for zoonotic infection with swine influenza viruses is occupational exposure to infected commercial herds (43,92,93), as well as household herds, and animals in county fairs and animal shows (44,94). One study of workers in the USA with direct exposure to pigs found the highest antibody seroprevalence to swine influenza viruses among farmers, followed by veterinarians and then slaughterhouse workers (43). As with H5N1 infections of humans, the total number of human cases of infection with a swine influenza virus who require medical attention is small given the number of swine workers and other in close contact with swine worldwide. Many swine influenza virus infections in people likely go undetected; however, it is difficult to determine seroprevalence due to cross-reactivity between human and swine viruses in the hemagglutination inhibition (HI) assay and the fact that recent human seasonal influenza exposure or vaccination can boost antibody titers to swine influenza viruses (92).

Live animal markets

Live animal markets likely contribute to both animal and public health influenza risk (90,95). Multiple influenza subtypes, including H5N1, H9N2, and H6N1, have been obtained from birds in live animal markets in Asia. Isolation rates and virus subtypes differ by species of poultry and location, with more frequent virus recovery from aquatic poultry (ducks and geese) than chickens, and higher isolation rates during the winter. Studies show that live animal markets can maintain, amplify, and allow dissemination of avian influenza viruses to farms and are a source of human infection and therefore a useful site for targeted surveillance(96). In an affected country, virus concentration is generally low at the farm or household level, increases at wholesale markets, and is further amplified and sustained at live animal markets, where virus may be disseminated back to farms and households (96).

Husbandry methods and vaccination of animals

Poultry and pigs are reared worldwide in intensive, semi-intensive, rural, or household settings. To a lesser extent they are reared for hobby purposes or as pets. Farm animals and their commodities are also traded at local (by peddlers, at live animal markets and at fairs and shows)

and commercial levels. The type of farming, the hygienic and biosecurity standards, and the extent of contact of infected animals with humans greatly influence the occurrence of episodes of transmission of influenza viruses to humans. Proper vaccination of poultry and swine has been shown to result in increased resistance to infection and, if infection does occur, to reduce shedding levels and thus the environmental load of virus (97-102).

Surveillance

Extensive surveillance for avian influenza infections in wild birds and poultry has been carried out since 2005. This surveillance has yielded a plethora of newly characterized viruses from wild and domesticated birds in both developed and developing countries, allowing decision makers and international organizations a greater understanding of the complex global ecology and epidemiology of these viruses. In contrast, little influenza surveillance in pigs is conducted globally. For the sake of comparison, 32446 individual avian influenza virus gene sequences (of which 6231 are HA) are available in publicly accessible databases while only 4242 individual swine influenza gene sequences (of which 836 are HA) are currently available. In addition, full-length sequences and whole genome sequencing are largely underrepresented when compared with partial gene sequences and submission of incomplete genomes.

There are increasing reports of non-traditional influenza infections in humans and animals, for example, as mentioned above, pandemic H1N1 in turkeys in Canada and Chile, H3N2 in a mink in Denmark, additional human cases of SIV infection in the USA and Canada, and panzootic H5N1 in a myriad of species in many regions of the world. It is unlikely that these increased reports are due to increased numbers of events, but are more likely the result of increased surveillance associated with panzootic H5N1 and pandemic H1N1.

Reporting in animals

Internationally, avian influenza infections need be officially reported only in their notifiable forms (103), i.e., H5 and H7 subtype viruses identified in poultry, or any highly pathogenic avian influenza virus, although outbreaks of potentially zoonotic influenzas are reportable to the World Organisation for Animal Health when they meet the reporting indication for an "emerging disease." The detection and compulsory reporting of these viruses often result in the imposition of restrictive measures and have trade implications. Swine influenza in pig herds is not currently a disease listed by the World Organisation for Animal Health, and thus is not reportable at the international level.

Strategies to enhance information sharing

Sharing of epidemiologic and virologic information across multi-disciplinary fields, including animal health (both wildlife and domestic), human health, public health, and basic science research is essential to accelerate the progression of knowledge for both animal and human health. The sharing of genetic information, through the deposition of relevant sequences in publicly accessible databases, yields valuable data and is easy to accomplish. Awareness of the importance of sharing has increased, resulting in greater availability of information. Sharing of other data, including epidemiological information, is much more complex and difficult to achieve, requiring additional resources especially for the harmonized collection of information.

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