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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

TECHNICAL REPORT

AVIAN INFLUENZA PORTFOLIO

Collected risk assessments, technical guidance to public health authorities and advice to the general public

Stockholm, June 2006

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The ECDC Avian Influenza Portofolio

This binder collects a number of documents produced

by the ECDC on various aspects of avian influenza.

They can also all be found on tne ECDC web page

http://www.ecdc.eu.int/avian_influenza/Scientific_Technical_Guidance.php

The documents are

Risk assessments

1. The public health risk from highly pathogenic avian influenza viruses emerging in Europe with specific reference to type A/H5N1 (June 2006)

2. Avian influenza A/H5N1 in bathing and drinking water and risks to human health (June 2006)

Advice to EU citizens

3. Health advice for people living in or travelling to countries where the A/H5N1 has been detected (April 2006)

4. ECDC guidelines to minimise the risk of humans acquiring highly pathogenic avian influenza from exposure to infected birds or animals (December 2005)

5. Avian influenza in cats – ECDC advice for avoiding exposure of humans (March 2006)

Technical advice to EU public health authorities

6. Interim guidance for national authorities to produce messages for the public concerning the protection of vulnerable groups (March 2006)

7. Oseltamivir prophylaxis and other actions following suspected exposure of humans to avian influenza type A/H5N1 (May 2006)

8. H5N1 surveillance case definition and documentation (April 2006)

The Public Health Risk from Highly Pathogenic Avian Influenza Viruses Emerging in Europe with Specific Reference to type A/H5N1

Interim ECDC Risk Assessment – Revision 20th May 2006

(previous versions from 19th October 2005 and 5 January 2006)

Preamble

The objective of this revised document is to further determine the risk to human health in Europe from highly pathogenic avian influenza viruses in birds and animals. Specifically the additional risk that arises from the recent emergence and extension of A/H5N1 viruses into the European Union and elsewhere in the world, and the changed biology of the viruses among wild and domestic birds. In addition the document identifies areas requiring additional scientific and public health work both as single pieces of work and for risk monitoring by ECDC and its partners. Given the rapidly developing epidemiology in Europe and elsewhere the document remains an interim assessment, that will be regularly updated. The document should be considered along with other relevant publications concerning Avian Influenza produced by ECDC and other authoritative bodies such as WHO, he European Commission, the FAO, OIE etc. ECDC's collection of documents on H5N1 - the H5N1 Portfolio – is available at /www.ecdc.eu.int/avian_influenza/index.php.

Weekly updates are published in ECDC's Influenza Surveillance and Risk Monitoring summaries at www.ecdc.eu.int/influenza/update_influenza.php

Comments and contributions to the document continue to be welcomed to influenza@ecdc.eu.int

Executive Summary

Outbreaks of highly pathogenic avian influenza (HPAI) viruses in domestic poultry have been increasing since the late 1990s and have affected poultry in Europe as elsewhere.

Essentially there are two forms of risk to human health from these viruses:

- direct infection of humans with the avian virus
- the emergence of a new pandemic strain of type A influenza.

The human health impact of HPAI epizootics was very small, and almost unnoticed, until 1997. Infections were generally minor and usually self-limiting. The appearance of A/H5N1 in Asia, changed this perspective when infection of humans with a high mortality rate was detected during an outbreak in Hong Kong in 1997 after a pause until around 2003 this pattern of infection has continued as huge epizootics extended across the domestic poultry populations of South East Asia. However considering the massive exposure in Asia from one HPAI type (A/H5N1) there have been very few human infections resulting from HPAI. In the over 200 reported human infections since 2004 mortality is around 57%.

Compared to before 2003 there have been some significant changes in the behaviour of the H5N1 viruses in birds. One strain has stabilised and has been spreading more easily through a range of bird species and this is the strain that has spread to the EU. In some countries outside the European Union that strain could become endemic in some domestic birds as it has seemingly done in certain wild species. In the Asia-Pacific region, Indonesia is currently the most active site of H5N1 transmission but, in general, reported activity appears reduced compared to similar periods of 2004 and 2005.

In contrast in Africa, the Middle East and South Asia there is some evidence of significant levels of infection in domestic poultry. There has to be caution here as surveillance is weak. Equally weak are the veterinary services which mean that the prospects for control may be bleak in the short term.

Mild and asymptomatic human H5N1 infection seems to be rare and the indications are that transmissibility of A/H5N1 to humans is still very low even for those directly exposed. Most infections continue to be acquired from exposures to high doses of virus from sick domestic poultry in household settings. There is no evidence of transmission to humans from casual contact with infected wild birds. The clinical picture continues to be unusual for HPAIs in humans in that infections are usually severe and often affect not just the respiratory system. Though human outbreaks and cases have been occurring in settings where it has proved difficult to mount proper investigations and studies, there is no evidence of any recent significant change in the behaviour of the virus in humans. Human to human transmission occurs but there is no evidence that it has become more efficient, cluster size has not increased and the case fatality rate of human infection has remained extraordinarily high for a human influenza. There is thus, as yet no evidence that the viruses have become any better adapted to humans than they were nearly a decade ago. The few humans who are infected do so only when exposed to high doses or virus and are likely to become very ill. They are unlikely to be a major

infection risk to their families and those providing care. However normal infection precautions must be taken and antivirals given to those most exposed, usually other household members. A notable feature has been the focus of infections in other family members which could indicate some genetic susceptibility.

Surveillance for human cases may be becoming harder where poultry immunization is widely but inevitably imperfectly practiced as the marker of local poultry deaths for human case detection is being lost. Declines in the number of sporadic human cases in some countries should therefore be interpreted cautiously. It is also unclear as yet if massive immunization poultry programmes increase or decrease the overall human population exposure to H5N1 viruses.

Despite the seeming lack of adaptation of H5N1 viruses a major caveat is the ability of influenza viruses to change, recombine, adapt and generally confound those attempting to control them. Though no H5 virus is known to have adapted to humans in the past it would be unwise to assume they cannot do so. Exposure of humans to H5N1 viruses must have increased considerably recently, for example in Africa. This does not necessarily change the pandemic potential of H5N1 viruses. However if through genetic recombination with human influenza or mutation the viruses can achieve any potential then they now must be more likely to do so sooner than when human exposure to H5N1 viruses was uncommon and localized.

The pattern of infection and disease seen in Asia for A/H5N1 may not be seen elsewhere and therefore close clinical and laboratory surveillance for and of human cases in Europe will be vital. That said, the Asian pattern of A/H5N1 has to be expected for planning purposes: a group of influenza viruses of birds, poorly adapted to humans whom they find hard to infect except at high doses. They are dangerous as they are highly pathogenic in those few humans that do become infected, but then they generally do not transmit on to other humans.

In the European Union, where surveillance for HPAI in wild-life is strong, this has detected steady extension of the virus in wild birds, including non-migratory species, and some domestic poultry. This peaked in early 2006 seemingly following migrations and numbers have declined but not fallen to zero. The risk of reintroduction through further migrations is significant though very difficult to predict.

The direct risk to the health of people in Europe from A/H5N1 is very low, but not zero. Human outbreaks in Turkey, Iraq, Azerbaijan, Egypt and elsewhere have indicated the potential of infection of humans from sick domestic poultry and probably also wild birds. The risk is mostly concentrated in one human group, those with domestic or pet poultry. Such groups exist in most European countries and they need to be informed of the risk and how to protect themselves. These pose particular challenges in terms of protection and risk communication as some of these groups are poor, marginalized or simply difficult to reach. There are occupational groups at lower and mostly theoretical risk who should take precautions. For those people who have no contact with domestic or wild birds or their products the risk must be almost non existent.

Monitoring human H5N1 infections and other emerging influenza viruses is of crucial importance as probably it's only in the early phases of emergence of a pandemic that there is any hope of containment. Though such emergence could take place in the European Union that seems unlikely. Though there are places not far beyond the borders of Europe where this could occur as well as in Asia and Africa.

ECDC and its partners will continue to monitor the risk from H5N1 and other HPAIs actively. A surveillance system for human cases A/H5N1, compatible to that already in use by WHO elsewhere has been developed and adopted as part of surveillance of human influenza. In addition some specific pieces of work on immunisation with seasonal vaccines are recommended. Most crucial will be continuing and developing close working of those responsible for animal and human health at all levels, proper risk communication and dissemination of factual scientific data to the public including those few people at risk of infection.

It does not follow from any of the above that the next pandemic will necessarily be due to H5N1 or another HPAI. Equally since it is not fully understood how pandemics arise it does not follow that the risk of a pandemic is actually any higher now than it was say a decade ago. Though there is more H5N1 in circulation it does not follow that there has been an overall increase worldwide of the influenza viruses (of all H types) whose genetic material has pandemic potential.

Though there has been no increase in the pandemic potential of H5N1 the likelihood that it might achieve any inherent potential in the near future may have risen. There are many good reasons why the momentum of pandemic preparations in EU countries and preparations for possible outbreaks of H5N1 in birds and some human cases should continue and intensify. One implication for those determining policy is that if they are convinced that preparation should be made for a pandemic based on an H5N1 virus there are now reasons for speeding up those preparations.

New considerations since January

- It has become apparent that a strain of the H5N1 viruses has been able to affect a wide range of birds' species and has adapted well to certain migratory birds being able to travel widely with them extending its geographical range. These viru ses have shown considerable stability over time.
- The range of these H5N1 viruses has greatly extended from being mostly confined to East and South East Asia to Europe including wild birds in the EU, the Middle East and parts of Africa and South Asia.
- Should the stability of the current H5N1 strains be maintained, Europe will have to adjust to add A/H5N1 influenza as one of endemic or occasionally appearing zoonotic infections. With H5N1 infec tions being in wild birds in all of Europe that risk will inevitably seem closer to home to EU citizens.
- Many more people worldwide are going to come into contact with H5N1. This will be less so in Europe than elsewhere because poultry in the EU are mostly segregated from humans.
- Though this does not mean any change in the pandemic potential of H5N1, if such potential exists at all it must now be more likely to become evident sooner rather than later.
- Certain other animal species notably cats can become infected naturally and in artificial conditions may occasionally transmit on the infection to other cats though no human infections have resulted.

Unchanged considerations

- There has been no indication of a significant change of behaviour of H5N1 viruses in humans. They currently remain "a group of influenza viruses of birds, poorly adapted to humans whom they find hard to infect except at high doses. They are dangerous as they are highly pathogenic in those few humans that do become infected, but then they generally do not transmit on to other humans."
- Control of infection in poultry along with risk communication to those at risk and prompt re sponse (case finding and management) to human cases remain the cornerstones of strategies for protecting human health from H5N1 viruses.
- Human to human transmission occurs but remains uncommon and there has been no increase in cluster size where human cases have occurred.
- A few human cases have been detected in most countries where outbreaks in domestic poultry have occurred.
- The groups at risk in Europe are the same as before with the most important group being people with domestic poultry.
- There is no risk of catching H5N1 from eating food that has been prepared properly.

1. Background – the Zoonotic Potential of Avian Influenza

Influenza is an infectious disease of certain animals including humans with mostly respiratory characteristics. It is a zoonosis, that is an infection originally of animals which has extended to infect humans.[1] It is caused by RNA viruses of the family Orthomyxoviridae. These viruses are unstable in their structure and are continuously evolving.* Some of the viruses are well adapted to humans which have become their hosts and are regarded as human influenza viruses.** While the human infection and resulting disease caused can be mild or even asymptomatic it can also be severe and sometimes lethal for all age groups. It can extend beyond the respiratory system and is especially dangerous in the elderly and those with underlying chronic medical conditions. The most significant sudden impacts of influenza viruses on humans are those arising from the influenza A pandemic strains. These are novel or re-emerging viruses to which a large proportion of the human population have little immunity. They are thought to emerge through genetic recombination of human viruses or through recombination of human and animal viruses or perhaps changes in an animal virus and its adaptation to humans.[2] When pandemics emerge they quickly sweep world-wide before settling down to dominate the less severe seasonal influenza epidemics seen each winter. Since 1918 three strains have arisen causing major pandemics each resulting in millions of deaths. These were: H1N1 (1918) with an estimated forty million deaths world wide***, H2N2 (1957) and H3N2 (1968) both with estimated deaths of between one and four million. A lesser pandemic occurred in 1977 when an H1N1 strain emerged without major mortality and only partially replaced the H3N2 strain so that at present both H1N1 and H3N2 strains circulate currently along with less pathogenic influenza B strains.[2]

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* Influenza A viruses are classically characterized according to the serologic reaction to the surface glycoproteins into sixteen hemagglutinin subtypes (H1-16) and nine neuraminidase subtypes (N1-9). Not all potential combinations exist and of the 16 H types known, only subtypes H1, H2, H3, H5, H7, H9 and H10 seem capable of infecting humans.

** The families of influenza A viruses that are well adapted to humans are mostly in the subtypes H1, H2 and H3.

*** The 1918 pandemic is considered exceptional in its high pathogencity and it particularly affecting young adults.

The natural reservoir of influenza A strains is a diverse pool of viruses among aquatic wild bird populations, so called avian influenza (AI) viruses. These viruses are well adapted to many aquatic bird species, less so to other bird species while most are not at all adapted to humans and other mammals.[1] Adaptation means the viruses' ability to infect a host, reproduce and be transmitted onto fresh hosts. The AI viruses are divided on the basis of their impact on birds into those of high and low pathogenicity avian influenza (hence HPAI and LPAI) mostly on the basis of their biological characteristics. Highly pathogenic avian influenza (HPAI) viruses are those that when injected into chickens cause a high mortality (over 75%). All are H5 or H7 influenza

A subtypes and an alternative criteria not requiring biological testing is any H5 or H7 virus with a haemaglutinin proteolytic cleavage site compatible with an HPAI virus.[3§]

2. Risk to Human Health from Avian Influenza Viruses - Principles

Essentially there are two mechanisms of risks to the physical health of humans from avian influenza viruses, Direct or indirect[‡] infection causing disease and sometimes death.[4]

Pandemic Potential from the potential for the emergence of new pandemic strains either directly from avian viruses, or from their recombination of their genetic material (RNA) with RNA from human or other animal viruses.[2]

To realise any inherent genetic potential to cause a pandemic an influenza virus has to have three attributes. It has to be able to infect humans, to produce disease and most crucially to be efficiently transmitted from one human to another. Whilst HPAI infections as a whole carry a somewhat higher risk of producing infection in humans through direct or indirect infection it does not follow that because avian influenza is 'highly pathogenic' for birds that it has any greater risk of forming or contributing to a pandemic virus for humans.

§ On occasions in the last decade HPAI viruses have arisen that have a cleavage site that has not been seen before. Hence, the in vivo pathogenicity index is still necessary to judge an AI virus highly pathogenic if it has a cleavage site that has never been associated before with HPAI.

‡ Indirect meaning from the environment of fomites whereby live virus is deposited and survives for a short while. E.g. on hands, a towel or another surface and then is transferred to a human e.g. by shaking hands or sharing towels.

3. The History and Development of Highly Pathogenic Avian Influenza

3.1 Infections among Animals

Between 1959 and 2005 twenty-four HPAI epizootics (epidemics in animals) have been documented worldwide. These are all due to the A/H5 and A/H7 groups with types A/H5/N1-N3, N8, N9 and A/H7/N1, N3, N4, N7 respectively.[4,5] Many million birds have died in these epizootics either directly from the infection or from culling undertaken to control the infection. Outbreaks have sometime been due to the introduction of HPAI from wild birds. Equally some low pathogenicity A/H5 and A/H7 strains have mutated to become HPAI viruses following circulation among domestic poultry.[6]

Since 2000 there have been more and larger outbreaks of HPAI in poultry.[4,5] The reason for this is unknown and the subject of speculation. Both large and small outbreaks have taken place in Europe. Notable very large outbreaks have occurred in densely populated commercial bird populations such as in Italy in 1999 (type A/H7N1)[7], the Netherlands, Belgium and Germany in 2003 (type A/H7N7) and Canada in 2004 (H7N3).[8,9,10,11]

3.2 Human Infections due to Avian Influenza

The first documented human infection with an avian influenza (A/H7N7) goes back to 1959.[4] Cases occur in association with both large and small outbreaks in birds but not all animal influenza infections in humans have come from birds. For example in the late 1970s some workers dealing with infections in seals developed eye infections (conjunctivitis).[12] However infected birds seem to have been the major source of risk to humans.4 There have been human infections with both low pathogenicity and high pathogenicity strains. Human infections with LPAI are recorded only occasionally but these have all been with minor self-limiting illnesses so it may be that they are under-recognised. For example there was one infection of a woman in the UK in 1996 receiving an eye infection from her domestic poultry which had mixed with wild birds and in 2006 a single case in a person seemingly exposed occupationally.[13,14] No LPAI virus has been reported connected with severe disease or death in a human.[4] In contrast the HPAI outbreaks in birds have resulted in at least 217 human cases and 123 deaths (a case fatality rate near 57%)*. Apart from a single fatality attributed to A/H7N7 virus strain during the Netherlands / Belgium / German outbreak all the deaths and most of the severe disease have been due to A/H5N1 (Figure1).[4,5,15] Mild human infections have been

* A/H5N1 data infections meeting WHO criteria as of 19 May 2006 http://www.who.int/csr/disease/avian_influenza/country/cases_table_2006_05_19/en/index.html

reported in a number of outbreaks, for example in Italy and Western Canada.[7,9,16] In the Netherlands, during the epizootic of HPAI with a different virus (A/H7N7), up to 64% of persons exposed to the virus showed a serological response consistent with infection.[17]

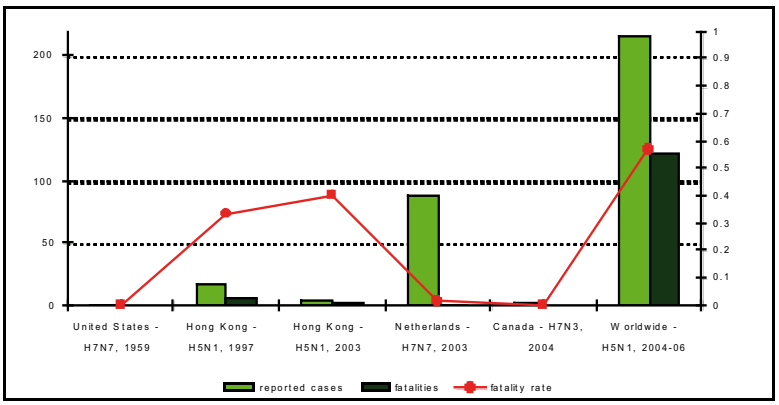

Figure 1. Reported human cases of infection and deaths with HPAI virus strains, 1959 – 2006.

4. A/H5N1 - an unusual HPAI*

4.1 The Emergence of H5N1

In 1997 a series of poultry outbreaks of highly pathogenic avian influenza occurred in Hong Kong. An A/H5N1 strain was isolated both from chicken and humans (18 human cases, 6 fatalities). This included the first human to human transmission and the first occupational infection of a health care worker.[18,19,20,21] The outbreak was contained by the rapid culling of infected and at risk poultry and biosecurity measures. The virus strain is thought to have been circulating in Mainland China before 1997.[4,22,23]

These A/H5N1 viruses are a group of evolving viruses forming distinct strains some of which have achieved a degree of genetic stability. They have an ability to infect a surprisingly wide range of bird and even some animal species (for example the cat family with some cat-to-cat transmission in artificial circumstances).[22,24,25] This ability to transmit from mammal to mammal has raised concern of public health officials.[26]

The A/H5N1 viruses were not detected again until they reappeared in Hong Kong in February 2003 in humans (5 cases, 2 fatalities).[23] The infection was again controlled in poultry through vigorous culling, biosecurity measures and poultry vaccination. However this was the prelude to a vast expansion of the infection in the poultry populations in the Far East in Vietnam, Thailand, Cambodia and Indonesia and beyond.[23] The drivers for this rapid dissemination are unclear but commercial movements of chicks, birds and their products are as likely as dissemination through wild birds. By the end of 2005, over 140 human cases with a fatality rate close to 50% had been reported to the World Health Organization (WHO) from five counties.[23] It was on this basis of this spread and the possibility of A/H5N1 further adapting to humans that WHO raised its global influenza alert to Pre-Pandemic Alert Phase 3 in 2005.[27§] To date that further adaptation has not been observed, specifically clusters of human H5N1 infection have not expanded in size as would be the case if there had been increases in human to human transmission.[28] However the potential may remain. It is thought by some that a particular risk of pandemic emergence arises through recombination with circulating well-adapted (human) viruses through dual infections in humans and other mammals to produce a pandemic strain.[29,30]

By early 2005 H5N1 was causing special concern because it was becoming widely distributed in East and South East Asia.[23] The next major development, the dissemination of a particularly stable strain well adapted to birds beyond East and South East Asia seems to have started from an important natural event in China. This was at Qinghai Lake in West Central China where in April 2005 there was a large die-off of wild birds affecting an unusually diverse range of bird species.[23,31] Subsequent bird outbreaks across Asia, Europe and Africa have mostly been of the same strain as that observed at Qinghai, an unusual genetic stability for an avian influenza. When compared to earlier strains the virus has shown no diminution in its pathogenicity for chickens or humans.[23,32,33,34,35] The same virus then started to be seen in well migratory and non-migratory wildfowl and showed some indication of being somewhat more persistent in the environment though peer-review publications confirming this latter point have yet to appear.[36] Hence it became apparent in late 2005 that some H5N1 viruses could travel long distances quickly with wild birds as the vectors.[23,37]

Single cases or outbreaks in wild birds were subsequently detected in early 2006 in many European countries where wild bird surveillance was already in

* The on-going history of A/H5N1 in animals and humans is well described in tabular form in the WHO Time Line available at http://www.who.int/csr/disease/avian_influenza/timeline.pdf

§ In 2004 WHO changed its Pandemic Scale to a Six Point measure with three Pre-Pandemic Phases. Phase Three is when a novel influenza A virus has appeared can infect humans and cause disease, occasionally transmits from human to humans but has yet to show efficient person to person transmission.

place.[23,38] Outbreaks were also detected in Middle Eastern, African and South Asian countries.[23] In these settings wild bird surveillance is unusual and so detection has usually taken place when either a domestic or commercial flock has been affected or when human deaths occur.[23]

The emphasis on wild birds does not mean that they have been the only source of dissemination though nobody could deny their role.[29,39,40] There are other important routes of local spread, notably through commercial practices and poor biosecurity (e.g. movements of infected poultry and people and vehicles with contaminated fomites). Control of these latter factors are crucial for protection of animals and humans at the local level.[29,40]

4.2 Increased Human Exposure to H5N1 2005-6 – the Implications

The range of the stable strain of H5N1 has extended considerably in 2005-6. Outbreaks in domestic poultry have expanded in some Regions where veterinary services are weaker than in the European Union. Therefore in those places the likelihood of control of the infection is low and the numbers of people potentially exposed to H5N1 though domestic flocks has increased dramatically. That is in the Middle East, Africa and South Asia. This means that there will be more people who are at direct risk of H5N1 infection.30 Equally there are many more governments that are needing to prepare for this eventuality. Though there may not have been any change in the pandemic potential the likelihood of any potential manifesting in the near future must have increased. This will be discussed in Section 5.

4.3 Poultry Immunisation to protect against H5N1

At least three countries, China, Indonesia and Viet Nam are undertaking large-scale poultry vaccination programs against H5N1, seemingly as medium term strategies and with the objective of reducing disease and the need for culling in poultry. The impact of these strategies on human risk of infection and disease is unclear. If poultry immunization is efficient and well monitored it could reduce the population burden of H5N1 in poultry and hence the risk for humans.[40] Equally however if it leads to the silent circulation of H5N1 in poultry it could actually increase the threat to humans in those countries and the risk of co-infection with other influenzas. The closely studied programme in Viet Nam is perhaps most likely to reveal which of these alternatives is realized. One unintended effect of these programmes is that they may make surveillance for single cases and small clusters of human H5N1 more difficult. Outbreaks in poultry can become 'silent' and the marker of die-offs of domestic flocks could be lost when deciding which human pneumonias to investigate. Falling numbers of reported human cases in countries practicing large scale poultry immunization may therefore be misleading.

4.4 The Extension of A/H5N1 into Europe

H5N1 extended into Europe in wild birds in early 2006 (Figure 2) with outbreaks or single cases in 13 out of 25 EU countries. Prior to 2006 large scale wild bird surveillance and surveys had produced results that were entirely negative for H5N1. The outbreaks have been instructive. Almost all the H5N1 that has been seen in the European Union has been in wild birds with only a handful of outbreaks in commercial poultry.38 This reflects generally high levels of biosecurity in the European Union in the commercial sectors. The presentations have sometimes been subtle with relatively few bird deaths, notable odd neurological behaviours and no striking die-off of poultry. This raises the possibility that the virus could spread to other areas and not be immediately apparent. Die-offs in commercial flocks due to HPAI are unlikely to go unnoticed in Europe. However it is acknowledged that more could be known about the presence of HPAI in the wild bird population and especially migratory birds.[41] Commercial flocks of poultry in the European Union are on the whole more separated from wild birds than those in Asia and Africa and so are less likely to act as sentinels. After the pulse of H5N1 in the early spring of 2006 numbers of H5N1 wild bird cases are diminishing but has not gone away as shown by outbreaks in commercial and domestic poultry along the Danube (Romania) and in the Baltic (Denmark) (Figure 2). The threat may return later through further migrations. There is agreement that controlling H5N1 in wild birds is impossible and should the stability of the current H5N1 strains be maintained Europe may simply have to adjust to add A/H5N1 influenza as one of endemic or occasionally appearing zoonotic infections. Guidelines to that effect for human health have been developed by ECDC.[42]

4.5 Human A/H5N1 Cases - An Unusual Clinical and Epidemiological Profile

The only multi-country review of the clinical pattern of A/H5N1 in humans to date found that the infection and disease pattern differed significantly from any other human infections with HPAI.30 Whilst it is certain that human cases have gone unrecognised and unreported, serological studies around cases to date have failed to identify mild or asymptomatic cases.30 These serological studies have been criticized for being small scale and incompletely published. Also it has been suggested that the methods applied may only have the ability to

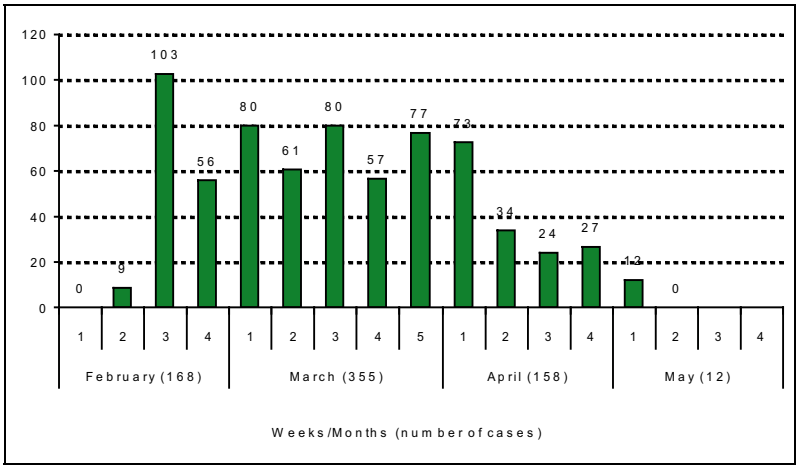

Figure 2. Highly Pathogenic Avian Influenza (H5N1) reported in the European Union through the Animal Disease Notification System February to May 2006

Source DG Sanco; http://europa.eu.int/comm/food/animal/diseases/adns/index_en.htm

detect serological responses in heavily ill hospitalized patients. However these findings are consistent with other results indicating that the H5N1 viruses are yet poorly adapted to humans.[23, 28]

A/H5N1 viruses do not transmit easily from birds to humans but when they do infect humans they cause severe disease.30 It seems even less able to transmit on from human to human, which is typical of other poorly adapted zoonoses. [43,44,45] This combination of high pathogenicity and only occasional person to person transmission has changed little since the first observed infections in Hong Kong in 1997.[19,20,23]

4.6 Human Risk Groups and Risks of Transmission in Europe

See Table - Human Risk Groups in Europe (Annex 1)

While the routes of entry of H5N1 into humans remain poorly understood epidemiological data and the principles that follow from H5N1 being a virus as yet poorly adapted to humans indicate that the chances of humans becoming infected with an HPAI virus are small.[23] Equally the opportunity for transmission are confined to specific circumstances.

Human exposure to AI viruses occurs through contact with infected tissues, excretions, and secretions of infected birds, especially faeces and respiratory secretions.[30] The avian influenza viruses could seemingly be transmitted through various media: inhalation of contaminated dust, inhalation of fine water droplets, aerosols, hand-to-mucous membrane transfer of infected faeces or respiratory secretions and theoretically, mucous membrane exposure through consumption of raw or undercooked blood, organs or meat.30 In general however, human cases have been principally related to close direct contact with high doses of virus from live or dead infected poultry or occasionally wild birds.46 Transmission probability is thought to be linked both to virus and host factors. Current efforts (genomic approaches, animal models, recombination approaches) are being undertaken in order to determine which characteristics allow viruses to infect humans.30 However even though many millions of people in East and South East Asia have been directly exposed to H5N1 virus, only a very small percentage of them have become infected or ill.

Determining the exact routes of human infection and their risk factors has been beset with problems. Detailed field investigations have been rare and those with serological support even rarer.30,46,47 Also in most cases there are multiple exposures and it is very difficult to determine if a person was infected by direct exposure to poultry, fomites, contaminated food or person to person transmission. There are a few case reports with seemingly reported unusual transmission (e.g. associated with bathing or consuming uncooked blood).30,48 However further investigations of these have usually revealed multiple exposure and not evidence that the water or food was actually contaminated (R. Brown, WHO Vietnam, personal communication). Almost all of the A/H5N1 cases in Asia have been most closely associated with direct exposure to live or dead infected poultry.30 Some cases suggest exposure only to raw poultry products. The handling and consumption of raw or undercooked products could be a source of human infection. This suggests there may be a need for a model for enteric transmission and mucous membrane exposure in addition to the usual respiratory models.

It has been suggested that these findings could have implications for Europe from environmental exposure to humans for example where wild migratory birds gather, for example at and around lakes. Certainly some studies of environmental contamination with HPAI where people and wild birds co-exist would be justifiable and risk assessments have been undertaken or are underway.49,50 However it needs to be remembered that H5N1 remains poorly adapted to humans and that the greater risk for human infection (Table - Risk Group 1) is direct exposure to poultry raised or kept outdoors and those who have direct close contact with wild birds.46 Poultry are highly susceptible to A/H5N1 Asian viruses and the expressed

virus load grows to very high titres making the probability of exposure, infection and amplification and human infections greater through contact with outdoor-reared domestic poultry than indoor commercial or industrial poultry where biosecurity and worker protection is generally higher. There are also those who may theoretically be at risk though exposure (Table – Risk Group 2) but among whom clinical infections have been very rare even in the Far East where exposure has been considerable.[23,30]

Three striking epidemiological features of human A/H5N1 infections have been

- how few infections have taken place considering the massive exposure to humans,
- the focus of infections in small household clusters involving family members
- the almost total absence of infections among those controlling the disease or caring for infected persons.

It has been suggested that a genetic susceptibility may partially explain some of these observations. Some comments have been made that children are more at risk (though the age structure of the human cases in the Far East is close to that of the population living in close proximity with poultry). This contrasts with the experience with the other HPAIs where those working to control the disease have been more at risk.[14,15,16,17]

This has implications for Europe as there is a risk, albeit very small to those who live closely with poultry and will probably not be so used to biosecurity considerations as those in the commercial farming sector – so called 'Sector 4' poultry owners, those with backyard or hobby poultry. This is especially so where those poultry may mix with migratory wild birds.

4.7 Risk to humans from Wild Birds

The experience from Azerbaijan indicate that there are rare circumstances where wild birds can pose a risk, for example if people attempt to handle and defeather sick or dead birds without taking precautions.[46] The public will be concerned but they need only follow simple measures already specified by European authorities and WHO such as not handling birds found dead and avoiding unnecessary contact with live birds when A/H5N1 has been shown to be present in a country. [42,46]

Finally however for the vast majority of people in Europe who do not have any of the above contact there can be hardly any risk at all of acquiring H5N1 infection while it remains in its present poorly adapted form.

Since unlike Asia, Africa and the Middle East most of the European Union's poultry flocks are segregated from humans the population risk is low. Those working to control outbreaks of H5N1 are an obvious risk group. Good guidance for protection of this group already exists from the ECDC and also from other international and national sources in Europe and elsewhere.[51,52,53]

4.8 Risk from Food

Acquisition through food is a theoretical risk and has been demonstrated in the field and experimentally with tigers acquiring infection in Thailand from eating raw chicken and artificially infected cats.[24,25] However since cooking destroys the virus it should only be people consuming raw poultry products that would be at risk in Europe and there is already standard guidance to avoid such products including eggs.[54]

4.9 Identifying and Communicating with the Groups at Highest Risk

Because of the potential entry of the virus from migratory birds away from commercial flocks, the humans more at risk may be those with small flocks and a few backyard poultry (chickens, turkeys, ducks etc) and they also require guidance based on what has already been developed by WHO and UNICEF.[55,56] It is especially important to establish where there are such groups in Europe who are living with more intimate contact with domestic poultry and perhaps near migration sites. These groups can be hard to define and reach (e.g. families in poor circumstances without access to electronic communication). Those most at risk may be women who care for domestic poultry and children who play with them. However the extremely low transmissibility of A/H5N1 to people living like this observed in Asia is reassuring.

4.10 Preventing infection of Humans by H5N1 Viruses.

There is no single strategy that will uniformly prevent human infection with HPAI viruses though the most important strategy is control in poultry, the most likely way that people will be exposed. Three approaches seem sensible and have been supported internationally by WHO, OIE and FAO [29,40]

i. Control the infection in birds which people will come into contact with – usually domestic poultry.

ii. Community mobilisation and education to reduce risk of human exposure to infected birds

iii. Case finding, surveillance, laboratory confirmation, treatment, patient isolation and infection control
Bearing in mind he people at highest risk are those living with other cases of H5N1 and after that people living intimately with domestic poultry

Most people in Europe will not be at risk (Table Risk Groups) though the potential widespread dissemination in the environment means that certain sensible precautions should be taken universally, most of these are around good general hygiene and should be being applied already and that is the basis of ECDC's advice to people living where H5N1 has been found.[42] The little risk that exists is mostly in groups that come into direct contact with birds. These groups need to take certain special precautions.

4.11 The importance of small household clusters – Person to Person Transmission

One paradox arising from the human data is that while the risk of H5N1 in any individual is very low once a case appears the risk of cases other household members rises considerably. There have been many small household clusters in China, South East Asia, Turkey, Iraq and Azerbaijan. Hence the emphasis on case finding and then early treatment of other household members in public health guidance.[57]

This observation has been misinterpreted as implying there is more person to person transmission than appreciated. The cause of these small clusters is unclear. They include shared exposure, some genetic susceptibility as well as person to person transmission. Occasional transmissions to very close contacts have been seen since 1997 but remain rare.[23,30] Those who have become infected were generally blood relatives providing care at home. Apart from one case there have been no onward transmissions to those providing care in a health setting and taking normal precautions.[23] Probably the most important observation is that the clusters are no bigger now in 2006 than they were in 1997 in contrast to what would have occurred should the virus have adapted to humans and become more transmissible.[23,28] It that occurs it which would be an indication that the world was entering WHO's Phase 4 or Phase 5 of a pandemic at which point there would probably only be a single opportunity to contain the pandemic through early containment.[58]

5. The Potential for generation of a pandemic strain from H5N1.

A/H5N1 viruses have been circulating with occasional human exposures for nearly a decade. While the infection can infect and cause disease no change in behaviour of the virus in humans have been detected (in stark contrast to all the changes in birds) and no pandemic strain has appeared.[23] There must be some restriction on widespread transmission in humans of the H5N1 virus since the AI virus strains that infect humans seems to be limited to a restricted genotype and there have been few infections, even though millions of exposures and very close contact is required to infect other humans. Hence most evidence indicates a difficult adaptation process for A/H5N1 viruses among humans.

An enduring concern is that a "normal" seasonal flu virus will infect an H5N1-infected human, the two viruses will recombine and a new efficient H5N1 strain will emerge.[2,59] Equally there might be recombination with another animal influenza or the H5N1 could simply mutate to form a pandemic strain.[2] Previously it was thought that due to the low number of H5N1 infected humans, this would be statistically unlikely though the risk might increase as the epizootic continues. Given that normal human influenza has been circulating world wide, including in Asia, the extension of A/H5N1 to birds in Europe, Africa and South Asia must have increased the numbers of people potentially exposed to H5N1 and human influenzas. At the same time it is unknown whether poultry immunization in the Far East will decrease or increase human exposure.

The reduced amounts of contacts between infected birds and humans in European countries compared to elsewhere makes it unlikely that Europe will be the starting point for an H5N1 pandemic though there are countries on the edge of the European Union to the East and South where those conditions exist and where WHO's Early Containment Strategy might be needed.[58]

The extension of range does not mean that there has been any change in the pandemic potential of H5N1 itself.[30] However the increased exposure of humans to H5N1 means that if this virus does have pandemic potential that potential must be more likely to be expressed in the near future than it was previously. Conversely if H5N1 shows no ability to adapt better to humans despite such exposure confidence is likely to increase that its genetic pandemic potential is low. One implication for those determining policy is that if they are convinced that preparation should be made for a pandemic based on an H5N1 virus there are now good reasons for speeding up those preparations.

It does not follow from any of the above that the next pandemic will necessarily be due to H5N1 or another HPAI. Equally since it is not fully understood how pandemics arise it does not follow that the risk of a pandemic is actually any higher now than it was say a decade ago. Though there is more H5N1 in circulation it does not follow that there has been an overall increase worldwide of the influenza viruses (of all H types) whose genetic material has pandemic potential.

However certainly there is absolutely no room for

complacency. The first pandemic of the 20th century is thought to have emerged at least in part from an avian influenza either in Europe or North America.[60] It has been suggested that other mammals may act as the 'vessel' for dual infection and recombination.[2]

There are reasons for recommending extending seasonal influenza vaccination to wider groups. It has been suggested to include those involved in control measures when seasonal influenza is circulating. This is already a standard recommendation by one of WHO's Regions.[53] The case for immunisation of the wider number of people in Europe who live with domestic poultry either in commercial farms or with just a few chickens in the backyard is a much more difficult decision and requires a measured scientific public health view. A major consideration will be the difficulty of identifying those at risk. It probably will be preferable to further expand the use of seasonal vaccinations in the general population at least in the risk groups as recommended by WHO's Executive Board.[61] Given the need to expand European capacity for production of influenza vaccine there are other reasons why this will be desirable.

There are two crucial caveats to end this section. Firstly the ability of influenza viruses to adapt, change and surprise is well established. Just because the A/H5N1 viruses have been behaving in one way in Asia up to now that does not mean they cannot and will not and so become a greater threat to human health. Secondly it is important in this section to acknowledge that in focusing so much on HPAI in general and A/H5N1 in particular the next pandemic infection may actually arise from a low pathogenic strain, or the already human adapted A/H2N2 virus that caused a previous pandemic because almost no community immunity exists against this virus anymore.

6. Final Considerations

6.1 The Need for Close Co-operation of Veterinary and Human Health Services

Much of the reduction of risk to humans from A/H5N1 will depend on the outcomes of veterinary control programs and how safely they are conducted.[29,40] While it would be difficult to justify large-scale public health expenditures in preventing a few sporadic human cases, it is justifiable to support expenditures to solve the problem in animals with such potentially significant public health implications as development of a pandemic. Increasing cooperation between the veterinary and human health agencies within Europe will be a crucial component to control avian influenza. Unified national and local planning is an imperative and is already part of the assessment exercises that ECDC, the European Commission and WHO Europe is assisting national authorities in making. Especially important will be unified approaches to any outbreaks of human H5N1 in the EU including vulnerable accession and candidate countries notably Romania.

6.2 The Importance of Risk Communication

Though strictly outside the remit of this paper it is impossible to ignore the evident confusion in the minds of the public between avian, seasonal and pandemic influenza. The perception of risk can be massive while as demonstrated above the actual risk to the individual from Avian Influenza is extremely low, even if they are exposed to infected poultry. Partially this confusion is understandable since avian influenza can lead onto pandemic influenza and the two issues are commonly tackled together in publications. However this is leading to disproportionate anxiety and needs to be addressed. Otherwise when the pandemic of 'bird flu' fails to materialize the case for preparing for the next pandemic will be undermined. Equally there will be unwarranted and disproportionate anxiety in the minds of the public and fear of harmless birds, both wild and domestic.

6.3 Adapting to H5N1

Though there is no sign that H5N1 is adapting to humans Europe needs to adapt to H5N1. The detection of H5N1 in wild birds in many European Union Countries and the seeming stability of the virus suggest that countries may need to adjust to this being added to the current list of zoonoses present in animals that occasionally infect humans.

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Annex 1.

Table: Who is at risk of getting "Bird Flu" - Highly pathogenic H5N1 avian influenza?

Broadly speaking there are two types of Risk Groups:

Group 1 - Low but Real Risk

The risk of infection is almost entirely confined to the small numbers of people who have close and intense contact with sick H5N1 infected domestic poultry (chickens, ducks etc) or their droppings or sometimes wild birds. For example through having sick and H5N1 infected poultry in the house. Human cases have almost entirely been in this category.

In these circumstances children may be at higher risk than adults. This probably represents behavioral rather than constitutional susceptibility. In these setting children being more play with or look after poultry and are less likely to practice good persona hygiene than adults.

People traveling to countries where H5N1 is prevalent can sometimes enter this category if they are staying with families with domestic poultry.

The people who are at highest risk of acquiring H5N1 are the very small number of people living in the same household as cases of H5N1 in humans. It is thought that this is through shared exposure. Though person to person transmission also occasionally happens. This is why early identification of human cases and early treatment of them and their household contacts is crucial.

Group 2 Theoretical Risk – Precautions Required

There are also those at theoretical risk who may be exposed to the virus and should take appropriate precautions. This includes the following where H5N1 may be present:

- Health care workers caring for those with H5N1 infection though there have been no cases in this group for nearly a decade the risk is there and preventive measures should be taken. A related group are those working in laboratories with H5N1 viruses
- Veterinarian and people involved in controlling outbreaks in birds (culling)
- People who work on industrial poultry farms,
- People who may have close contact with infected wild birds e.g. some ornithologists and hunters,
- People who deal with sewage which is contaminated with H5N1

For the majority of people who have no contacts with domestic or wild birds or their droppings, the risk of acquiring H5N1 is almost non existent.

Table 1. Who is at risk of getting "Bird Flu" - Highly pathogenic H5N1 avian influenza?

"a group of influenza viruses of birds, poorly adapted to humans whom they find hard to infect except at high doses. They are dangerous as they are highly pathogenic in those few humans that do become infected, but then they generally do not transmit on to other humans."

From ECDC Revised Risk Assessment May 2006

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- People who deal with sewage which is contaminated with H5N1

Current maps showing where H5N1 has been found recently are available for the EU at http://europa.eu.int/comm/food/animal/diseases/adns/map/europe.htm and for the rest of the world through http://disasters.jrc.it/AvianFlu/

For both Groups 1 and 2 there is probably greater risk of catching other potentially serious infections from birds – examples include campylobacter and salmonella infections. Standard hygienic precaution to protect against these infections will protect against H5N1.

For the majority of people who have no contacts with domestic or wild birds or their droppings, the risk of acquiring H5N1 is almost non existent.

Version May 20th 2006 (This table is available on the ECDC web site at http://www.ecdc.eu.int/avian_influenza/Human_H5N1_Bird_Flu_Risk.pdf)

1. Summary

Avian influenza type A/H5N1 is an animal influenza virus poorly adapted to humans. That is it does not infect humans easily, certainly not at low dose exposure. Those humans at risk in Europe are those with close direct contact with ill infected birds and bird products (mostly domestic poultry).

Some wild birds with the H5N1 virus have been found in Europe, mostly these are waterfowl (swans, ducks, geese etc). Though the numbers of birds being found with infection has of late declined greatly concern has been expressed that wildfowl defecating live virus into or around water sources and recreational waters might be a health hazard for humans who are bathing in the waters, or drinking tap or bottled drinking water originally derived from those sources.

Presence of a virus does not equal risk to human health, especially with a virus that does not infect humans easily. There is only scanty and circumstantial evidence that H5N1, or any other viruses than are poorly adapted to humans can be acquired by humans through drinking or bathing in water. The appearance of H5N1 in some wild birds in Europe is not considered by ECDC to increase any residual risks to health from drinking waters in Europe. Current standard practice in providing tap or bottled drinking water through centralized water-supply undertakings in Europe and pre-existing European Union directives if enacted will protect against pathogens that could come through drinking water. Somewhat more vulnerable are the private wells or private water sources in single-family houses and summer cottages but even then the risk from H5N1 is almost non-existent because of the poor adaptation of the virus to humans. The risk to human health in those waters is from other pathogens better adapted to humans, not H5N1.

Concerning bathing there is in ECDC's expert view no additional risk to human health from the occasional presence of H5N1 in the environment from wild birds. Again this is because of the poor adaptation of the virus to humans and the dilution effects in large bodies of water. Current standards like those of the EU European Bathing Water Directives (1976 and 2006) if enacted will assist in making bathing in non-treated waters safer but through reducing the risk of other human pathogens (such as salmonella and campylobacter) not through further reducing the risk from H5N1 since these are already close to zero.

Hence the conclusion of ECDC is that there is no additional risk to health from drinking water or bathing in Europe since the emergence of avian influenza A/H5N1 in birds in Europe. This view is consistent with other risk assessments undertaken by national authorities in Europe.

These views are interim would need to be rapidly reviewed and a more precautionary approach taken if convincing evidence emerged that H5N1 had adapting better to humans.

Some work is recommended by ECDC. This includes that guidance might usefully be prepared on what action to take over bathing recommendations when there are abnormal numbers of dead birds reported in bathing waters. Though ECDC does not see any scientific case for suspending bathing should the deaths be attributed to H5N1. This guidance would best be prepared by the European Commission to ensure that it is consistent with other relevant guidance on bathing and responding to cases of H5N1 in animals. Some research should be undertaken to investigate possible infection human health risks from bird faeces in or around bathing areas and beaches. This would be to detect pathogens that are better adapted to humans than H5N1.

2. Scientific and Public Health Considerations

Hazard Identification

Influenza type A/H5N1 at present is a highly pathogenic avian influenza (HPAI) that only occasionally infects humans, though then with serious effect. Hence it has been characterized as "a bird flu virus, poorly adapted to humans for whom it is not very infectious, but highly pathogenic in those few humans it infects, though then it generally does not transmit on to others"[1] The scientific knowledge of precisely how it behaves with humans, how infection is acquired, how it enters the body and who is at risk of infection remains incomplete.[2]

The virus has changed significantly in its behavior in birds since it was first observed in the 1990s with the establishment of one relatively unchanging variant.[3,4,5] It has been stated that this variant is somewhat more persistent in the environment[4,5] The fact that that live and dead H5N1 infected waterfowl have been found in some European countries earlier this year (see DG Sanco map[6]) has led to concerns in Europe that the virus might possibly be acquired from bathing in open water or drinking water sourced from open water. The concern about bathing may be especially felt in countries where lake and sea bathing are common in the warmer months of the year. Reports of H5N1 in birds in Europe declined steeply in April and May (Figure). Occasional infected birds are still being detected and ECDC was asked to undertake this risk assessment by member states and the Commission.

Figure. Highly Pathogenic Avian Influenza (H5N1) in birds reported in the European Union through the Animal Disease Notification System February to mid May 2006 Source DG Sanco http://europa.eu.int/comm/food/animal/diseases/adns/index_en.htm

The Scientific Evidence

Presence of the virus in the environment does not equal risk to humans, especially with a virus that is poorly adapted to humans and mostly seems to transmits where there is intense and close exposure.[1,7] There are a limited number of case reports where it is suggested that humans with H5N1 infections in Asia may have acquired their infection from bathing or swimming in water (Van Tam J, HPA Personal Communication). For example one fatal case in Vietnam was reported to have perhaps been infected through this route having seemingly had no other bird exposure than regular swimming in a canal inhabited by ducks.[8,9]

However investigations of these cases have generally been incomplete.[10] Enquiries with relevant authorities in the Western Pacific Region of WHO indicate that in all of these few cases swimming was not the only possible exposures, that it was not documented whether or not the water was contaminated with H5N1 and that such risk behaviors are common and so are likely to be reported in case investigations by chance alone (Brown R, WHO Viet Nam personal communication). Hence, it cannot be concluded that this was the route of transmission in these cases. On a precautionary basis WHO issued guidance in late 2004 for SE Asia indicating that potable (drinking) water supplies for human use should not be drawn from open ponds used by domestic ducks and used untreated and should be stored in ways that prevent contact with ducks. However WHO did not identify bathing in water as a risk to health where H5N1 might be in waterfowl.[11]

There are no prior data suggesting that other avian influenzas have ever been acquired by humans through drinking or swimming. This is unlike other viruses known to be occasionally transmitted to humans by this route (hepatitis A & E and certain human enteroviruses).

Even though the current H5N1 virus may be more persistent in the environment than its predecessors that does not mean that risk of human acquisition has increased. Even if the virus was well adapted to humans, which it is not, the virus would be very much diluted in the water. Also for water going for drinking supplies the processes of treatment required would inactivate the virus.[12] There is also some evidence from the recent outbreaks that birds with H5N1 infection do not express virus so well in their faeces as in their respiratory tract. This is different from other avian influenza viruses (Beer M, Fredrich Loefller Institute, Personal Communication). There may be a higher concentration of virus in duck faeces itself and this deserves further investigation.

Infections that Humans Do Acquire from Water

People do acquire infections from bathing in or drinking impure water especially if located near contaminating sewage water sources. However these are infections that are better adapted to humans than H5N1 is at present.[13,14] Both gastrointestinal infections and acute febrile respiratory infections have been shown to be associated with swimming in sea water contaminated with faecal pollution as indexed by relatively harmless faecal indicator bacteria. Worldwide most of the infections are occurring in resource-poor settings but infections from bathing and drinking water also take place in the most well-resourced countries.[13,14] However with some notable exceptions, such as leptospirosis most of these are infections where the origin of the organism is an infection in another human not an animal. A universal feature is that these all infections are well adapted to humans. For example one important pathogen that is probably acquired from exposure to or drinking impure water is

campylobacter. However unlike H5N1 it is well adapted to both human and animal hosts.[15]

ECDC's specialists and those experts it has consulted cannot as yet identify any case reports of an animal viral infection that is poorly adapted to humans that have been acquired by a human from bathing in or drinking water. There are many examples of human viruses (e.g. norovirus from one toddler to another in paddling pools) and some viruses that are well adapted to both humans and animals (Hepatitis E), but not viruses that are almost entirely animal viruses.[13]

It is possible that, with high doses of virus the species barrier could be breached. That is what is thought to have happened in the cases where humans have been infected with H5N1 through close and intimate contact with domestic poultry.[2]

However when introduced into bathing water H5N1 will be diluted far too much for any transmission risk to humans.[16] There is concern that in some waterfowl faeces viruses could remain concentrated. When exposure takes place to bird faeces then good personal hygiene should be practiced (washing hands, cleaning feet and shoes etc). Children will need particular instruction in these practices.[17]

Potential Hazards from Drinking Water

Providing safe potable (drinking) water for the population is the goal of all countries. If there is concern here, it is of a low risk of spread of infection to commercial and domestic poultry flocks through this route, not to humans.[16] The risk assessment undertaken by the Netherlands assumed a low virus infectivity to humans found that the average daily infection risk for humans by consumption of contaminated drinking water was estimated to be close to zero ($2x10^{-12}$). Risk was reduced by effective drinking water treatment, and the risk from surface water recreation scarcely any higher (10^{-8}).[16]

Comparison with Other Risk Assessments

This risk assessment's conclusions are consistent with others that have been conducted in Europe to date. These have concluded that the current treatment and disinfection mechanisms will eliminate any risk to human health from H5N1 in its current form.[16,18] Where water-supply undertakings provide ground water without treatment, there may be enhanced risk as there could be for consumers of inadequately treated private water supplies. Again, however, the currently 'unadapted' form of the H5N1 virus presents a minimal threat to humans. The real risk from drinking such water is from other pathogens which are adapted to humans and may be acquired from these water sources. The risks of these is minimized by the application of the relevant European Directives.[19,20]

Hazards from Bathing and Swimming in Untreated Water

Bathing, diving and swimming in untreated waters in lakes, estuaries and the seaside can be hazardous to humans with one of the hazards being acquiring infections.[21] This has been recognized for many years at an EU level and is one of the prime reasons for the 1976 Bathing Water Directive.[22] In February this year the EU Parliament adopted a new directive with a view to steadily improving the safety of bathing waters in Europe, replacing the earlier 1976 Directive. The aims of both Directives was to reduce the potential infection risk from bathing in Europe's surface waters.[23,24] At one extreme it is clearly hazardous to bathe or dive in what is effectively sewage or heavily polluted waters.[25,26,27] Equally, however, it would seem unreasonable to insist that all bathing waters achieve that same standards as apply in commercial indoor swimming pools which are commonly chemically disinfected. Important components envisaged in the new Directive are the monitoring and classification of bathing water quality and management. Management measures include, among others, timely and adequate measures to be taken in unexpected situations that have, or could reasonably be expected to have, an adverse impact on bathing water quality and bather's health. In this case, a temporary bathing prohibition may be put in place.

Enactment of the standards in the 1976 Bathing Water Directive improves protection against significant threats from pathogens that are well adapted to humans. These include human viruses, protozoan parasites and bacteria such as E. Coli O157 and Campylobacter.13 Some of the non-viral pathogens will be animal derived. Therefore for these reasons alone the 1976 and 2006 Directives deserve strong support and proper enactment by all EU countries. However it cannot be stated that the Directives will further reduce the risk from H5N1 in bathing waters since that is close to zero already.

Comparison with Other Risk Assessments

Such an analysis is consistent with the conclusions of the three published national risk assessments in Europe,[16,18,28] Namely that the individual additional risk from H5N1 to individuals bathing in recreational waters in Europe is negligible.[29]

Responding to Bird Deaths

An important question is what to do when H5N1 is detected in wildbirds in Europe and specifically they are found in lakes where people bathe.[6,30] Or even what to do when birds are found dead in water? There would be advantages to having standard EU guidance on this. An ECDC scientific panel has suggested that where there are abnormal numbers of dead birds they should be

reported and investigated as recommended by the European Commission but that recreational swimming should be suspended in that water until tests are completed.[31] This would be equivalent to dealing with a suspected acute escape of sewage and is well in line with the existing and new bathing directives. However given the lack of risk from H5N1 there would in ECDC's view be no real scientific reason for such suspension of bathing and little justification of testing for H5N1 in the water, which is not easy technically (M.Beer, Robert Loeffler Institute, Personal Communication). Also the numbers of H5N1 infected birds detected though surveillance has declined steeply in April and May (Figure). ECDC notes that the country that is most affected in the EU (Germany) is generally not suspending water bathing where birds have died from H5N1. ECDC would support suggestions from its Panel that additional research is needed. One issue is to look at the infection risks from human pathogens bird faeces that are found in and around bathing and recreational water and may be encountered by children in particular.

General Hygiene Considerations

Bathing in untreated water in lakes and the sea can carry infection risks for humans, though not from H5N1. Care should be taken that people are aware of these risks and particularly that hands are washed after bathing before eating or drinking. Also it is important that food hygiene be well practiced as standards may slip when eating food in recreational settings. When exposure takes place to bird faeces then good personal hygiene should be practiced (washing hands, cleaning feet and shoes etc). Children will need particular instruction in these practices.[17]

3. Conclusions and Cautions

This view is interim. It has especially to be so with an influenza because of these viruses ability to change their structure and behaviours. H5N1 has seemingly changed its behavior in birds since its emergence in 1997. However though the evidence is scanty, so far H5N1 has not changed in its behavior towards humans since the first human cases were also observed in 1997.1 Should evidence emerge that the virus was adapting better to humans and so becoming more infectious then a more precautionary view should prevail and swimming might need to be confined to treated waters while further urgent risk assessments were undertaken.

Until more information is gathered recommendations and decisions have to be based on what the current evidence and what experience indicates. That is that this virus (A/H5N1) does not infect humans easily and that the dilution and natural inactivation of the virus in bathing water will further reduce the dose and any infectivity. Also the numbers of H5N1 infected birds detected though surveillance has declined steeply in April and May. Similarly normal treatment of drinking water in Europe can be expected to be effective against H5N1. Hence the ECDC conclusion it that the introduction of H5N1 in European bathing in EU waters will not increase any residual risks of infection from bathing and drinking. ECDC would emphasis the current Bathing Water Directive Standards and the Directives relating to drinking water should be applied but emphasizes that this is to protect against other established threats, mostly human pathogens not against H5N1. The European Commission should consider whether to prepare guidance for Member States on how to respond when bird deaths in water leads to the suspicion that H5N1 may be present, or it is actually confirmed. However this guidance would be to ensure standard responses across Europe (and to prevent the anxiety caused by different responses in different countries) not because there was any additional risk to human health from H5N1.

Some further research should be undertaken. Consideration should be given to undertake investigations into the existence and persistence of the virus around the current outbreaks in birds in Europe. Perhaps of more importance given some public concern about bird faeces at bathing sites there should be investigation as to any microbiological risk from these though this will be mostly looking for microorganisms better adapted to humans, not H5N1.

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Introduction

Influenza type A/H5N1 (bird flu) has infected birds in many countries in Europe and world-wide. For the moment, in the EU, the birds most commonly infected are wild water fowl such as swans and ducks. It has also occasionally infected other animals. It has also infected some other animals (such as cats). As a bird virus it does not easily cross from birds to humans though in a very few instances it has done so, mostly outside Europe.

People that have been infected in other parts of the world had been in close contact with live or dead infected birds, principally domestic poultry.

That makes H5N1 another 'zoonosis'. an animal infection that can also affect humans and animals. There are many other zoonoses already present in Europe, such as salmonella and camplylobacter in cattle and poultry, toxoplasmosis and toxocara in cats and dogs, rabies in foxes and bats, etc.

There are already standard precautions that have to be taken to protect humans from zoonoses. Hence most of actions that need to be taken to protect people and their families against H5N1 are just applying common sense or simple rules of good hygiene. Examples would be not handling sick wild animals and the rules for food hygiene and safe food preparation.

Specific measures are in place to protect in the European Union to protect commercial poultry and to prevent infected birds entering the food chain. In any case, thorough cooking ensures that meat and eggs are free of any virus. Hence the risk to the public of catching the H5N1 virus from live animals or from poultry products is very low. Certainly there is no need to change the food that you eat or travel plans because of H5N1.

In areas of the EU (and many other European countries which follow EU rules) where H5N1 has been detected and is circulating either in wild birds or domestic poultry special veterinary measures are in place. The present document provides general advice for people living in those areas, including poultry owners.

Knowledge about H5N1 is constantly improving. Also the virus is still spreading in wild-life. Equally influenza viruses themselves often change over time and specific influenza viruses appear for a while, and then go away. Hence this guidance will be improved as changes occur. Regular updates on what is know about influenza viruses as they affect human health appear on the ECDC web-sites where there are also links to other relevant web-sites including that of the European Commission.

Twelve Questions and Answers

1. Where is Influenza Type A/H5N1 (bird flu) to be found?

In EU Countries H5N1 has been detected in wild birds in many places. It also has been found occasionally in domestic birds. That does not mean bird flu is in those places for the future. Some of the infected birds have been migrating and anyway birds living in the country may only be infected temporarily. However given the movements of wild birds it is probably best to imagine that H5N1 may, in the future be found in certain wild birds in many if not most EU countries. That is not the position yet but it seems to be the way things are going.

Are all wild birds affected?

No. The H5N1 viruses seem best adapted to water living birds, the wild-fowl ducks, swans etc. However beyond them we are seeing a number of other species affected occasionally so that it is not possible to easily say which birds are and are not affected.

Are other animals affected?

Yes but it is rare. A few animals that will eat birds have become infected including cats that have been out hunting. That is why when there is a proven outbreak in birds those responsible for animal health may recommend people restrict the movement of their domestic cats.

2. Who is at risk?

Please refer to the Table at the end of the Risk Assessment Document.

3. What standard precautions should be taken, concerning wild birds, animals and poultry?

You and your family should follow:

General Hygiene

- Exercise good personal hygiene with frequent hand washing
- Make sure food is prepared hygienically in a clean environment and follow the basic rules of food safety

Specific to H5N1 and other zoonoses

- Remember children are at somewhat higher risk of infection with zoonoses than adults
- Avoid direct contact with live poultry and wild birds unless absolutely necessary (young children in particular should not be allowed to have close contact with poultry or with bird or animal waste)
- Try to avoid direct contact with bird and animal faeces, untreated bird feathers and other animal and bird waste. Where direct contact has been unavoidable (e.g. from walking and bird faeces getting on shoes) sensible hygiene precautions should be taken (e.g cleaning shoes and hand washing).
- Especially avoid handling sick birds or animals or birds found dead
- Generally avoid visiting live animal markets
- When visiting farms children in particular should stay away working areas which includes any area with farm animals
- Where you or your children may have had contact with animals or birds e.g. from caring for pets, when visiting 'children's farms' or going where there may have been bird or other animal faeces make sure you follow basic hygiene rules (see Question 2.)

4. What do I do if I or my family have come into direct contact with poultry, wild birds or other animals or their waste in an area where H5N1 has been detected?

The guidelines are the same as for anywhere areas:

- Wash hands well with soap and water after any contact and
- Remove your shoes outside the house and clean them of all dirt
- Follow the standard rules for food hygiene http://www.who.int/foodsafety/fs_management/No_07_AI_Novo5_en.pdf

In addition

- If you or a family member who has had contact with sick or dead poultry, wild birds or other animals develop a significant temperature (>38°C) and/or a respiratory infection or diarrhoea get advice from a doctor or nurse or visit the nearest health care facility. It is important to mention any significant exposures (e.g. contact with sick poultry or a dead wild bird). The chances of this being H5N1 is very slim but its best to be safe and the illness may be caused by another zoonosis.

5. What is different when H5N1 has been confirmed locally recently in domestic or wild birds or other animals?

When a highly pathogenic bird flu, especially H5N1 has been confirmed locally in poultry, special veterinary emergency rules and procedures come into play, such as preventing movement of domestic birds and increasing surveillance in what are called Protection and Surveillance Zones. Hygiene rules also become tighter, for example to prevent ordinary people accidentally carrying the infection from one farm to another on their shoes or vehicles. If you are in one of these areas the local authorities will let you know what these rules say. After a certain period these rules are then relaxed back to the normal level.

6. What do I do if I encounter sick and dead poultry or wild birds?

Birds die – wild and domestic – and so coming across individual dying or dead birds is quite a common experience. What is unusual is to come across unusually numbers of dying or dead birds or animals which suggests this may be due to a highly pathogenic infection such as H5N1. Similarly for those who have domestic birds if unusually high numbers of their birds die. They should:

- Inform the authorities immediately
- Leave the handling of the animal to experienced personnel

7. What should I do if I am travelling abroad to protect against Bird Flu?

The advice now for people traveling to other countries in the EU and outside is now little different from that staying in their own country. So travellers are reminded of the following standard precautions to avoid avian influenza:

- To avoid contact with live poultry and wild birds
- To avoid visiting live animal markets and poultry farms
- To avoid contact with surfaces contaminated with animal faeces (droppings)
- To avoid handling birds found dead
- Not to eat or handle undercooked or raw poultry, egg or duck dishes
- Exercise good personal hygiene with frequent hand washing
- Do not attempt to bring any live poultry or uncooked poultry products back into the EU from outside

It is not recommended that travellers take with them the neuraminidase inhibitor, Oseltamivir (Tamiflu®) unless they may be exposed to avian influenza through their work e.g. veterinarians working to control HPAI.

There are general and specific hazards to do with traveling abroad and advice should be sought ahead of time. Authoritative sources of advice are obtainable on most EU national public health or surveillance institute web sites.

8. What additional precautions should be taken by "commercial", "backyard" or "hobby" poultry owners?

- Follow the instructions of the local veterinary aut horities to prevent any possible spread of H5N1 virus to your poultry;
- Inform immediately the veterinary authorities in case your poultry become sick;
- Never make use of any sick poultry for the preparation of food and do not use eggs from sick hens;
- Follow very good hygiene practice when you butcher and defeather poultry for consumption within your own family;
- Make especially sure that children and people visiting know how to protect themselves

9. What precautions should be taken in relation to food?

Nothing has changed here. The usual guidance on food safety should be followed. Follow the established rules of food hygiene such as http://www.who.int/foodsafety/fs_management/No_07_AI_Novo5_en.pdf

These include

- Do not eat or handle undercooked or raw poultry or egg dishes
- Poultry should be prepared hygienically and thoroughly cooked to an internal temperature of 70°C or above
- Take care in handling raw eggs and shells
- Wash egg shells in soapy water and wash hands afterwards
- Eggs should be cooked thoroughly

In addition

- Do not use poultry from areas where the virus has been found recently for preparing food for humans and/or animals. Even seemingly healthy-looking poultry of any kind from a bird-flu affected area should not be used for food.

10. How do I protect myself and my family from zoonoses that my domestic animals and pets may be carrying?

Again it comes down to good sense and good hygiene. Always wash hands after handling animals, especially before eating or drinking

- Animal waste (faeces and urine etc) should be seen as potentially hazardous. It is a good idea to wear gloves when handling cat litter etc and certainly to wash hands afterwards
- When animals get sick it's a good idea to consult a vet who can advise you but take special care to exercise good hygiene
- Prohibit children from cuddling or comforting sick animals
- If you see unusual illness that look like an infection (a number of your animals getting sick at once) tell the local authorities that deal with animal health.

11. Cats have been infected with H5N1 – does this mean I or my family are at risk from our animals at home?

Cats can become infected with H5N1 and can infect other cats they are in close contact with them. However the risk of any specific cat catching the virus from a wild bird is very small indeed and we do not know if they can transmit the infection to humans.

Therefore the rules specifically in relation to H5N1 are

- Sick domestic animals that eat meat and might have eaten infected birds (i.e. you in an area where H5N1 has been reported recently) should be treated as a possible infection hazard.
- do not handle the animal unless you have to and then use gloves.

12. Is there any risk from bathing where there are wild birds?

Risk assessments have been undertaken on this by authorities in Europe and these suggest that the risk, if there is any is incredibly small at present because the current form of H5N1 virus is poorly adapted to humans. It also does not survive for very long in water, especially salt water.

There are higher risks of other infections, most of them are from humans not birds or other animals. That is why the European Union has recently adopted a new Bathing Water Directive and most EU countries monitor the quality of water where people bathe in fresh or sea water. http://europa.eu.int/water/water-bathing/report.html

13. Can people catch H5N1 from other people?

Even when people have really been infected with H5N1 the risk of them passing this on seems to be very low. Though person to person transmission has happened it seems to be very are rare. So there is very little risk from people with H5N1 though when cases have occurred it is important that other people in the same household and nearby are quickly investigated to see if they need treatment as they may have also been exposed to the virus.

Summary

The risk for any one person working with infected birds is low, though it seems to vary according to the exact type of highly pathogenic avian influenza (HPAI). HPAI transmission is by direct contact with infected birds or bird products.

Protection is based on the application of the following eight principles:

1. Control infection in birds.
2. Minimise the number of people possibly exposed to the virus as far as possible separating people from the avian viruses and potentially infected birds and animals.
3. Technical measures
4. Organisational measures
5. Proper use of personal protective equipment and adoption of technical and organisational measures for those directly involved in the work with potenti ally infected animals.
6. Proper but controlled limited use of antiviral drugs.
7. Considering seasonal influenza vaccination, especially if seasonal influenza is circulating.
8. Careful surveillance for infection among those potentially exposed.

Each preventive measure should follow a local risk assessment.

Risks for people working with infected birds

The risk of acquiring infection for any one person working with infected birds is low, although it seems to vary according to the exact type of highly pathogenic avian influenza (HPAI). For the most dangerous HPAI, A/H5N1, the infection risk seems to be very low. Although there have recently been huge epidemics of A/H5N1 in birds in southeast Asia there have been surprisingly few human infections, and very few among those engaged in culling (killing) of birds.1,2 Infection protection for workers employed in culling of large chicken flocks in Thailand and Vietnam flocks has often been poor, but no illness due to A/H5N1 has been noted in the many workers involved. Even if there may be sub-clinical cases in humans, present evidence indicates that this should be very rare and that infection with A/H5N1 is generally so severe that it would not be missed.

EU legislation on occupational health and safety

There already exist EU directives for occupational health and safety that contain general principles/measures concerning the prevention of occupational risks and the protection of the workers safety and health[§]. The full and accurate practical implementation of the national legislation transposing the Community directives on health and safety at work is essential to ensure an appropriate protection of workers. The specific obligations of employers (such as risk avoidance, risk assessment, prevention and protection measures, training, information and workers consultation) are clearly specified in the above Community legislation. In particular, Directive 2000/54 on the protection of workers against the risks arising from exposure to biological agents contains more specific provisions on information and notification to the competent authority (Articles 7 and 13), hygiene and individual protection (Art. 8), information and training of workers (Articles 9 and 10), list of exposed workers (Art. 11) and health surveillance (Art 14), as well as special measures for industrial processes, laboratories and animal rooms (Article 16). Strict adherence to the provisions of directive 2000/54/EC shall be closely monitored by Member States.

All prevention measures have to follow a local risk assessment. The employer is responsible for this assessment and for establishing the protective and preventive measures. EU directive 1989/391 states that collective protective measures have priority over individual ones.

Examples of activities with possible direct contact with infected birds and contaminated materials

- Activities in poultry farming with infected birds
- Veterinary examination and post-mortem examina-tion
- Culling of poultry including activities in mobile culling and disposal units
- Carcass disposal facilities

[§] EU Council Directives: 89/391/EEC (on the introduction of measures to encourage improvements in the safety and health of workers at work), 89/686/EEC (on the approximation of the laws of the Member States relating to personal protective equipment), 89/656/EEC (on the minimum health and safety requirements for the use by workers of personal protective equipment at the workplace), 2000/054/EC (on the protection of workers from risks related to exposure to biological agents at work, seventh individual directive within the meaning of Article 16(1) of Directive 1989/391)

- Cleaning and disinfection of contaminated areas
- Sampling
- Activities in diagnostic laboratories
- Other activities where humans are exposed to a confirmed infection in a bird or animal (quarantine staff, owners of small domestic flocks, etc.)

Following a local risk assessment, it may be prudent to include people living close to an infected farm among those potentially exposed to the virus.

Mode of Transmission

When birds are infected by HPAI they shed large amounts of virus with their faeces and also when coughing and sneezing (although some evidence suggests that respiratory spread plays a lesser role for A/H5N1). Viruses are usually not very stable outside a living cell, however in particles of dust or faeces they can survive for days or even weeks depending on strain and ambient factors. HPAI causes primarily conjunctivitis and respiratory disease in humans though more severe disease may follow. Conjunctivae and upper respiratory tract mucosa are therefore the most likely entry routes for AI viruses. Humans usually get infected by HPAI when having close contact to live infected birds, their faeces or other bird body fluids and secretions. Also contact with contaminated surfaces of cages, shed equipment or places where infected birds have been kept and contact with infected dead birds can lead to infections of humans, for example when eyes or nose are rubbed, or feathers get behind goggles.

When handling diseased birds for the purpose of culling wing-flapping and other bird movements and human activities that cause development of dust could increase the risk of transmission.

Handling uncooked meat and blood of infected birds might pose a risk when again these get in contact with eyes or nose. Cooking poultry meat inactivates/kills the virus and renders the meat fully safe.

The Principles of Protection

Guidance has already been developed by WHO Western Pacific Region and a number of individual European countries and this guidance draws on that. Until now there has been no specifically European Guidance.[2-4]

Protection of workers against occupational infection rests on following principles:

1. Control infection in birds quickly and safely

- This is straightforward. The less infection in birds and the quicker they are controlled then the fewer people will be exposed and infected.
- People may mechanically spread infection from one bird flock to another by contaminated hands, shoes or clothes. Conversely, adherence to the appropriate precautions plays an important role in controlling infection. Outbreaks of avian influ enza in poultry are subject to stringent control res laid down in EU legislation[1§].

2. Minimise those exposed separating people from animal infections

- The minimum number of people necessary should be involved in bird culling.
- Farm workers or owners who are not directly involved in culling activities should avoid exposure to known or potential sources of avian influenza virus (i.e. avoiding contact with chickens, ducks and other poultry unless absolutely necessary).
- Other people living on the farm (e.g. family members) should also avoid exposure to known or potential sources of avian influenza virus.
- It may be a good idea to restrict local movement of people into and out of the affected area both to reduce the number of people exposed and to lower the risk of extansion of infection among animals.
- Cleaning and disposal of laundry and disposal of waste should be safe at all stages until the infection risk has been eliminated.

3. Technical measures

When handling birds or contaminated materials (e.g. body parts, tissue, blood, feathers and excretions, including used beddings) attention must be paid to avoiding or minimising the formation of dust or other aerosols. Possible measures are:

- culling the birds by either flooding the animal housing with CO_2 or according to EFSA recommendation by placing the animals in suitable containers including effectively restricted areas of a building, containing inert gas mixtures such as Argon with not more than 2% oxygen5. See also Council Directive 93/119/EC
- moistening the dead birds with fine water mist
- moistening the surfaces for cleaning
- mechanising the carcass collection and disposal
- transporting the dead birds and contaminated materials in tightly closed containers.

4. Organisational measures

All workers in contact with potentially infected birds and materials should be given information and specific training about HPAI infection in humans, its symptoms and the specific preventive and protective measures to be adopted.

§ Council Directive 92/40/EEC on Community measures to control avian influenza

All workers should have access to appropriate personal protective equipment (PPE) and should receive instruction and training in PPE use.

5. Use of Personal Protective Equipment (PPE) for those directly involved in the work

The employer has to provide the following required PPE:

- Impermeable disposable gloves or heavy duty rubber work gloves that can be disinfected should be worn.
- Gloves must be removed promptly after use and safely disposed of, before touching non-contaminated items and environmental surfaces.
- A respiratory protective device (RPD) of at least filter class P2, individually fitted. A power assisted filtering device with a hood (class TH2P or higher) may be easier to work in and can be used as an alternative to a respiratory mask and safety goggles. Note that if any gaseous potentially harmful substances are used another more adequate class of RPD might be needed depending on the substance/situation. This is the minimum standard we recommend, but in absence of such equipment, any protection covering nose and mouth probably has some benefit.
- Protective clothing including headwear which fully covers the hair must be worn; preferably disposable outer garments or coveralls, an impermeable apron or surgical gowns with long cuffed sleeves, plus an impermeable apron.
- Close-fitting protective goggles with side protection should be worn to stop virus contacting the conjunctivae (the mucous membranes of the eyes).
- Disposable protective shoe covers or rubber or polyurethane boots that can be cleaned and disinfected should be used.
- Opportunities for safe cleaning or disposal after use must be available. Disposable PPE should be properly discarded, and non-disposable PPE should be cleaned and disinfected using standard disinfection procedures.
- Hand hygiene measures (hand washing or disinfection) should be performed after removal of PPE.
- Workers should be trained in proper techniques of donning, removing and disposing of PPE, without contaminating themselves. Summary of order of removal of protective attire/equipment:
  · Remove gloves
  · Remove gown
  · Wash/decontaminate hands
  · Remove eye protection
  · Remove mask/respirator
  · Wash/decontaminate hands again

6. Proper but limited use of antiviral drugs

Use of antivirals should be restricted and under medical control in order to

- Minimise the risk of side-effects
- Prevent the development of drug resistance
- Conserve stocks

In countries where no outbreaks of highly pathogenic avian influenza are known or suspected

No prophylaxis for poultry workers is required.

In countries where one or more outbreaks of highly pathogenic avian influenza are known or strongly suspected

All workers exposed to infected birds or poultry (including those birds directly implicated in an outbreak of highly pathogenic avian influenza, and the birds in neighbouring areas being culled as part of the local control measures) should be offered prophylaxis. Those who are retrospectively recognised to have been exposed should receive post-exposure prophylaxis.

Local veterinary and public health authorities should collaborate in the development of a risk assessment, based on the local situation, the type of HPAI and expert advice, to determine which individuals should be considered at risk of exposure.

- Pre-exposure prophylaxis. Unless medically contraindicated, workers should receive 75mg oseltamivir daily for the duration of time during which contact with infected poultry or contaminated surfaces occurs. This should be continued for 7 days following last exposure.
- Oseltamivir is presently not recommended for continuous use during more than 6 weeks. The risk of adverse effects from longer use are not known at present, but Canadian guidelines recommend that persons who have been on 6 weeks continuous oseltamivir prophylaxis discontinue use for a 2-week period prior to re-starting the medication. During this period persons should not work in an environment where they may be exposed to an HPAI.
- Post-exposure prophylaxis. After contact with infected birds, within 48 hours after exposure and for minimum 7 days. Oseltamivir is not recommended for children <13 years of age. However, recent evidence shows that it is safe and efficacious also in children6. Just as for adults, the dose is the same as for treatment (by body weight), but given once daily instead of twice.
- If oseltamivir has not been given prophylactically, and workers then present with symptoms suggestive of avian influenza, treatment with oseltamivir 75mg twice daily for 5 days should be initiated.

It is recommended that oseltamivir be readily available

for the treatment of suspected H5N1 respiratory infections.

In order to avoid a false perception of full protection, workers under antiviral prophylaxis must be made aware of the need for general protective measures.

(There may be other antiviral drugs that could be used, but at present oseltamivir is the only centrally authorised agent in Europe; see EMEA website: www.emea.eu.int/htms/human/epar/a-zepar.htm).

7. Vaccination with normal seasonal influenza vaccine

Targeted vaccination with the current seasonal influenza vaccine is being recommended as one of several measures for reducing opportunities for the simultaneous infection of humans with avian and human influenza viruses. Minimising the opportunities for dual infections reduces the chance for viral reassortment and for the eventual emergence of a novel influenza virus with pandemic potential.

Note: This vaccination does not protect against infection with bird flu. This fact must be understood by those exposed so that they are still aware of the need for general protective measures.

In addition to usual target groups, the following should be considered for current seasonal flu vaccination:

- All persons who are expected to be in contact with poultry or poultry farms potentially being affected with highly pathogenic avian influenza, especially cullers involved in destruction of poultry, and people living and working on poultry farms where HPAI has been reported or is suspected or where culling takes place.
- Health care workers involved in the daily care of strongly suspected or confirmed human cases of influenza HPAI.
- Health care workers in emergency care facilities in areas where there is confirmed occurrence of influenza HPAI in birds.
- Close contacts of influenza HPAI human cases.

8. Close observation of people potentially exposed

All persons exposed to infected poultry, birds or their droppings should be under close monitoring by themselves, their employers and local health authorities. It should be clear that the responsibility for this happening lies with the employer though the follow-up will be by health authorities. Particular care will be needed when contract labour are involved. Persons involved in culling operations should check their temperature twice daily for up to 14 days following their last contact with poultry or their environment. Any illness (such as fever ”e38 oC, cough, sore throat, shortness of breath, but also gastroenteritis) in themselves or their families must be immediately reported to the health authorities. Symptomatic persons should seek medical attention, should not self-medicate, should limit their social interactions and they should remain at home until free of fever for at least 24 hours, unless a diagnosis of influenza has been excluded.

A register of those exposed should be maintained by employers or contractors. Adherence to this and the above protective measures should be written into contracts. At the end of the outbreak a report should be prepared by the health authorities.

Suggestions for additional activities

- A serological follow-up of all persons involved in an HPAI outbreak should be considered, in order to acquire further scientific knowledge about the risk of transmission of AI viruses to humans. Such serology should always be supported by a WHO reference laboratory.
- These activities should be overseen by a group with both animal and human health experts established in each Member State.
- Specific surveillance for adverse events to antiviral drugs should be encouraged.

References

1. Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5. Avian Influenza A (H5N1) Infection in Humans. NEJM 2005; 353:1374-1385.

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3. Koopmans M, Wilbrink B, Conyn M, et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. Lancet 2004; 363:587-593.

4. World Health Organization - Western Pacific Region Publications on Avian Influenza http://www.wpro.who.int/health_topics/avian_influenza/publications.htm

5. EFSA. Opinion of the AHAW Panel related to animal health and welfare aspects of Avian Influenza. Sept. 2005. http://www.efsa.eu.int/science/ahaw/ahaw_opinions/1145_en.html

6. Hayden FG, Belshe R, Villanueva C, et al. Management of Influenza in Households: A Prospective, Randomized Comparison of Oseltamivir Treatment With or Without Postexposure Prophylaxis. J Infect Dis 2004, 189: 440-9.

Background

A dead cat in northern Germany has been found to be infected with the A/H5N1 avian influenza virus.

- This is no surprise. Felines are known to be susceptible and sensitive to the virus. Less is known about the ability of an infected cat to pass on the virus.
- The fact that the cat was discovered and diagnosed shows good veterinary surveillance.
- This finding does not imply any change in the virus.
- It should be underlined that no human cases have been associated with exposure to felines, and no outbreaks of A/H5N1 in cats have been reported even though sporadic infections have been reported in Asia and Iraq.
- However, exposure to virus from an infected cat in the household could be substantially greater than, for example, the exposure from just picking up a dead bird infected with A/H5N1.

Note: The advice below is provisional and builds on current and incomplete knowledge. It may well have to be revised within a short time, as more data on the epidemiological situation and on the actual risk appear. The issue of risk of infection from cats (and other pets) is presently under consideration in the ECDC Scientific Panel on avian influenza.

Provisional ECDC Advice

The following advice should generally be applied within the surveillance area (10 km radius of a verified A/H5N1 infection in birds). The extent of this area may have to be modified after a local risk assessment.

- Keep domestic cats inside the house to avoid exposure to potentially infected birds
- Keep semi-domestic or stray cats outside the house and avoid contact with them
- If a cat brings a sick or dead bird into the house, put on ordinary gloves and dispose of the bird as recommended by your Department of Agriculture
- If your cat is sick and has potentially been in contact with birds, contact the local veterinary authorities
- Notify dead cats to the local veterinary department

There are also hygiene rules that apply in general, regardless of any risk of A/H5N1 infection:

- Wear gloves when cleaning cat litter and wash hands afterwards
- Do not touch dead animals. If you must, wash your hands afterwards
- Always wash hands before handling food

Also note that washing hands with soap and water and washing clothes at recommended temperature with an ordinary detergent is enough to destroy influenza virus.

The human cases of H5N1 avian influenza seen in Turkey and Iraq this winter have reminded us that this virus can pose a serious health risk to people who have close contact with infected birds. The presence of H5N1 now in birds within the Union makes this even more of an EU public health issue. The question of how to communicate about these risks was discussed by public health officials from across the EU at a meeting of the Health Security Committee in January 2006. ECDC was asked to formulate some science based messages for the "at risk" populations, in particular, people who keep birds around their house (e.g. backyard flocks of hens, ducks or geese).

This paper is based on the state of scientific knowledge in mid-February 2006 – it may need to be reviewed as our understanding of avian influenza develops. The aim is to finalise this guidance at a meeting of the EU's Health Security Committee in March.

As well as circulation to the Health Security Committee and the EU's EWRS Committee, this interim guidance has been sent to Ministers of Health and Chief Medical Officers in the EU and EEA Member States and the ECDC's Management Board. The Management Board brings together senior health officials from Member States and the European Commission and representatives of the European Parliament.

1. Suggested key messages for the general public

- The threat to human health from "bird flu" (influenza virus type A/H5N1) is currently very low but not zero.
- "Bird flu" is an influenza virus found in birds. It is only people who have close contact with infected birds or with their droppings and other body fluids (e.g. blood, guts) from infected birds that are at risk from bird flu. There is no evidence of any sustained human-to-human transmission.
- Though for most people the risk of catching "bird flu" from birds is close to zero, following a few simple precautions can minimise the risk to you and your family still further:
  - If you see dead or sick birds, do not touch them yourself, but inform the veterinary authorities
  - Warn your children against touching dead or sick birds and discourage them from playing with birds
  - Wash your hands thoroughly with soap many times per day, especially before eating
- Hunters should be aware that they run a risk of being exposed to avian influenza if they hunt wild birds. Hunters should also be aware that hunting is banned in the 10 km zone surrounding any place where H5N1 avian influenza has been found.

2. Suggested advice to vulnerable populations

2.1 People who work on poultry farms

See ECDC guidelines on occupational exposure (paper 4).

2.2 People who keep domestic birds (chickens, ducks or geese near where they live)

Protecting your birds against avian influenza

- Ask the local veterinary authorities for advice on the level of risk in your area, and on the measures they suggest to minimise the possibility of your birds being infected.

Protecting yourself and your family

- Do not allow your birds into the house.
- Discourage children from playing with the birds. Forbid children from touching sick or dead birds. Teach them to tell adults quickly if birds are sick.
- Make sure that children always wash their hands before eating.
- If you notice sick or dead birds in your flock **do not** touch the birds yourself. Inform the veterinary authorities as soon as you can.
- If it is not possible for the veterinary service to come quickly, and you have to take care of sick birds yourself put on protective clothing:
  - a gown or apron covering your body
  - a hat covering your hair
  - a mask or wet cloth over your mouth and nose
  - goggles or glasses
  - gloves
  - boots
- If you need to dispose of a dead bird use gloves and a mask, bury it in a place which does not pose a risk to drinking water wells and other water sources. After this, immediately contact the veterinary services.
- Once you have finished having contact with sick or dead birds take off the clothes you were wearing, hat, goggles and mask/cloth last, and clean them using a disinfectant. Wash your hands thoroughly before you touch anything else.
- Humans get infected from sick birds, their droppings, or other fluids and secretions (e.g. blood, guts, feathers). Cages, shed equipment or places where infected birds have been kept can be a source of infection for several days.
- Use disinfectant to disinfect cages, cloths or equipments that have been in contact with infected birds. The veterinary or public health authorities in your country can advise on which types of product to use.
- Do not eat sick wild, game and/or backyard birds or birds that have died from disease even if they are cooked and do not feed them to other animals or birds.
- If there have been sick birds in your backyard/hobby flock, and someone in the family becomes ill with fever, cough or a sore throat, contact a doctor immediately and let them know what has happened.

Background

This document was stimulated by requests from Member States seeking expert guidance over what to do in relation to exposure of humans to dead birds with proven or suspected highly pathogenic avian influenza type A/H5N1 infection. It was agreed within ECDC and by the Advisory Forum that it would be useful to list a wider number of the situations where we were aware that the issue has arisen, including exposure to other Avian Influenza (AIs) types . The document should be read with existing ECDC guidance on Highly Pathogenic Avian Influenza, notably the Occupational Guidance http://www.ecdc.eu.int/avian_influenza/occupational_exposure.php.

Using this Document

This guidance is not intented to replace national guidance already prepared by Member States (MS) and should always be used in the light of a local or national risk assessment of the particular circumstance. Rather the guidance has been developed recognizing that not all MS have specific guidance, that a document like this could save them time and that there are advantages to some standardisation across Europe. It is intended to be treated as guidance and not as a set of rules or regulations.

The evidence base underpinning this guidance has a number of gaps and the base itself is, at present, under review by the World Health Organization. Relevant publications are listed towards the end of the document. Hence this is an interim set of practical guidance designed for use in Europe. This draft has already benefited considerably from comments on earlier drafts from members of ECDC's Advisory Forum and their specialist colleagues.

Types of Prophylaxis

Two forms of prophylaxis against AIs with oseltamivir have been proposed:

Pre-exposure – when there is a foreseen or continuing risk of exposure to a highly pathogenic avian influenza, especially H5N1

Post-exposure – when there has been a possible or certain exposure (sometimes described as early treatment but here called post-exposure prophylaxis).

This advice will mostly deal with the second case – post-exposure prophylaxis. It will not deal with treatment and care of individual patients when there is proven or strongly suspected infection

General criteria

Post-exposure prophylaxis should be used only when confirmed or strongly suspected cases of highly pathogenic avian influenza (HPAI) including H5N1 occur in birds, animals and humans. There is little justification for using pre or post exposure prophylaxis where the avian influenza is known to be of low pathogenicity for birds (LPAI). When outbreaks of seeming LPAI occur a local risk assessment should be undertaken taking national specialist advice. Though there has been occasional cases of LPAI viruses infecting humans the of low pathogenicity to date these have been sporadic and always mild. People who are exposed need to be made aware of this possibility and what to do should they develop symptom. Such cases should then be treated with antivirals.

When dealing with known or suspected HPAI, post-exposure prophylaxis should be started as early as possible. For those occupationally exposed post-exposure or pre-exposure prophylaxis is not an alternative to good use of personal protective equipment. Post-exposure prophylaxis should be given as soon as possible. It is not required if the last exposure occurred more than 7 days previously.

People who are exposed need to be aware of the risks, what the symptoms of infection are in humans and what to do in the unlikely event that they develop such symptoms. Written materials are a huge advantage and have been developed by some countries.

Specific Circumstances

Thirteen situations are listed below, with a note on the global experience so far and the actions that would recommended by ECDC.

'Global Experience – no cases' means no confirmed cases of H5N1 infection have been reported in humans where this exposure situation is considered to be the most likely source of infection. However, human cases can be associated with multiple exposures and therefore it should not be concluded that there is absolutely no risk via this route.

There have also been instances where other Avian Influenza viruses that are seemingly sometimes more transmissible to humans have caused human infections. Different types of Avian Influenzas viruses do not behave identically and that is why ECDC emphasizes the importance of local risk assessments around each outbreak or incident.

At times decisions will have to be taken on the basis of partial information and the precautionary principle followed. For example if it is known that an Avian Influenza is involved, that people have been exposed but that its not yet clear if this is H5N1 or even a Highly Pathogenic Virus. In that case it can be wise to assume it's a HPAI, start people on prophylaxis and review the situation when more laboratory testing is undertaken.

Specialist ECDC staff are happy to advise on these public health decisions and can be contacted urgently via the ECDC Duty Officer (+46 841047878).

Comments on this interim guidance is welcomed and should be directed to influenza@ecdc.eu.int

Setting	Type of Contact	Global Experience	Required additional actions	ECDC Advice on prophylaxis
Exposure to wild birds	1. Physical contact with a healthy wild bird in an area where H5N1 in birds has been demonstrated or is strongly suspected	No human H5N1 case		No case for offering prophylaxis.
	2. Physical contact with a sick or dead wild bird in an area where H5N1 in birds has not yet been demonstrated	No H5N1 human case	Joint risk assessment by local veterinary and human authority. If appropriate, laboratory investigation of the bird.	No rationale for offering prophylaxis.
	3. Physical contact with a sick or dead* wild bird in an area where H5N1 in birds has been demonstrated or is strongly suspected	Some H5N1 human cases following significant exposure	Rapid laboratory investigation of the bird. Joint risk assessment by local veterinary and health authorities.	Usually no rationale for offering post-exposure prophylaxis unless there is high risk exposure (e.g. preparing bird for cooking, feather plucking etc.
	4. Physical contact with a sick or dead wild bird that is later verified to be infected with H5N1	Some H5N1 human cases following significant exposure	Undertake rapid joint risk assessment by local veterinary and health authorities.	Consider offering post-exposure prophylaxis depending on level of exposure.
Exposure to domestic poultry	5. Physical contact with healthy domestic poultry in an area were H5N1 is not yet suspected or verified in domestic poultry	No H5N1 human cases		No case for offering prophylaxis.
	6. Physical contact with healthy domestic poultry in an area were H5N1 is strongly suspected or verified in domestic poultry	Some H5N1 cases in affected countries where the exact risky contact with sick poultry can be unclear. However the exposure has to be significant e.g. slaughtering poultry	Undertake a rapid joint risk assessment by local veterinary and health authorities.	Only consider post-exposure prophylaxis if there is a significant exposure and the poultry are likely to have been infected themselves
	7. Physical contact with (or being within one meter of) sick or dead domestic poultry strongly suspected or verified as having H5N1 and no PPE has been used	Human H5N1 cases in a number of countries	Undertake a rapid joint risk assessment by local veterinary and health authorities.	Urgently give post-exposure prophylaxis to all household members who have had contact with or have been within 1 meter of the poultry in the past week.

Setting	Type of Contact	Global Experience	Required additional actions	ECDC Advice on prophylaxis
Household and Social Contacts	8. Close household member of a verified or strongly suspected case of human H5N1	Human H5N1 cases in a number of countries, probably because of shared exposure though there have also been some human to human transmissions.	Undertake a rapid joint risk assessment by local veterinary and health authorities.	Strongly recommend giving post-exposure prophylaxis and urgently – these people are most at risk.
	9. Non-household social contact of verified or strongly suspected case of human H5N1	No H5N1 human cases		No case for offering prophylaxis.
Occupational Exposure	10. Laboratory staff analysing samples for suspect or proven H5N1or another HPAI	No H5N1 human cases	Undertake a rapid joint risk assessment by local veterinary and health authorities if there has been a significant breach in procedures..	Only offer prophylaxis if there has been a clear break of good laboratory practice.
	11. Health care staff exposed to a patient verified or strongly suspected to have with H5N1 or another HPAI	One human H5N1 case in 1997 in Hong Kong	Undertake a rapid joint risk assessment by local veterinary and health authorities if there has been a significant breach in procedures	Offer prophylaxis, and always if there is failure of protective procedures and use of personal protective equipment (PPE)
	12. Culling or poultry working staff exposed to a bird verified or strongly suspected to be with H5N1 or another HPAI including those using PPE	No H5N1 cases world-wide but this happened with other HPAIs (notably H7N7 in the Netherlands)	Undertake a rapid joint risk assessment by local veterinary and health authorities.	Offer pre-exposure prophylaxis, and post-exposure if not given in advance
	13. Veterinary staff exposed to birds with confirmed or strongly suspected H5N1 or another HPAI	No H5N1 cases world wide but one happened with another HPAI (type H7N7 in the Netherlands – causing one fatality in a vet)	Undertake a rapid joint risk assessment by local veterinary and health authorities.	Offer pre-exposure prophylaxis, and post-exposure if not given in advance.

The Evidence Base - Relevant Published Information:

H5N1 transmission to Humans

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N Engl J Med 2005; 353:2636-2637, http://content.nejm.org/cgi/reprint/353/25/2636.pdf

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7. Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5. Avian Influenza A (H5N1) Infection in Humans. NEJM 2005; 353:1374-1385. http://content.nejm.org/cgi/reprint/353/13/1374.pdf

8. WER – Eurosurveillance article on Azerbaijan (in press)

9. WHO Time Line on Avian Influenza http://www.who.int/csr/disease/avian_influenza/timeline.pdf

Transmission of other Avian Influenza Viruses to Humans

10. Puzelli S, Di Trani L, Fabiani C, Campitelli L, De Marco MA, Capua I, Aguilera JF, Zambon M, Donatelli I. Serological analysis of serum samples from humans exposed to avian H7 influenza viruses in Italy between 1999 and 2003. J Infect Dis. 2005 Oct 15;192(8):1318-22. Epub 2005 Sep 12

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12. Kurtz J, Manvell J, Banks J. Avian influenza virus isolated from a woman with conjunctivitis. Lancet 1996; 348: 901-2.

13. Koopmans M, Wilbrink B, Conyn M, Natrop G, van der Nat H, Vennema H, Meijer A, van Steenbergen J, Fouchier R, Osterhaus A, Bosman A. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. Lancet. 2004 Feb Feb 21;363(9409):587-93

14. Du Ry van Beest Holle M, Meijer A, Koopmans M, de Jager C. Human-to-human transmission of avian influenza A/H7N7, The Netherlands, 2003. Euro Surveill. 2005 Dec 1;10(12) http://www.eurosurveillance.org/em/v10n12/1012-222.asp

15. Fouchier RA, Schneeberger PM, Rozendaal FW, Broekman JM, Kemink SA, Munster V, Kuiken T, Rimmelzwaan GF, Schutten M, Van Doornum GJ, Koch G, Bosman A, Koopmans M, Osterhaus AD. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. Proc Natl Acad Sci U S A. 2004 Feb 3;101(5):1356-61. Epub 2004 Jan 26.

Annex Treatment Doses

Recommended Oseltamivir Dosage and Treatment if it is decided to give post exposure prophylaxis

Adult prophylaxis: 75 mg per day for 10 days
Paediatric dosage (not licensed for use under one year):

Weight	Dosage (prophylaxis)
Under 15 kg	30 mg daily
15 to 23 kg	45 mg daily
24 to 39 kg	60 mg daily
40 kg and over	75mg daily

When there has been significant exposure serological testing is recommended to determine whether or not people have not been infected, but this is to build up the global experience. Serological testing for H5N1 is a specialist subject and should only be embarqued upon after consultation with one of the specialised laboratories is required. These can be approached through National Influenza Centre's.

If a person exposed develops symptoms suggestive of infection with H5N1 then they need to be handed over for urgent clinical assessment by specialists who are likely to offer treatment which is at a higher dose than for prophylaxis. A person starting on the prophylactic dose moves over to clinical care and treatment dose if they develop symptoms.

Purpose

The following definition is developed from the WHO guidelines for global surveillance of influenza A/H5 (http://www.who.int/csr/disease/avian_influenza/guidelines/globalsurveillance.pdf) and is intended for European countries. It should be used, in the current situation (WHO, Prepandemic Phase 3) for the purpose of undertaking surveillance for cases of influenza A/H5N1 infections in humans in EU. The definition is not intended to be used for diagnosis or management of cases.

Clinical description

Any individual with:

- Acute onset of fever (temperature ›38°C) with sign and symptoms of an acute respiratory infection

OR

- Death from an unexplained acute respiratory illness

Epidemiological link

At least one of the following exposures (a, b, c) within 7 days prior to onset of symptoms:

a. Human Contact Having been in close contact (within one metre) of a person reported as probable or confirmed case of influenza A/H5N1

b. Laboratory Contact Having worked in a laboratory where there is potential exposure to influenza A/H5N1

c. Contact with poultry or wild birds Reside in or have visited an area[1] where influenza A/H5N1 is currently suspected or confirmed as reported in the European Commission Joint Research Centre web-site: http://disasters.jrc.it/AvianFlu/

AND

- Having been in close contact with sick or dead[2] domestic poultry or wild birds[3] in the affected area

OR

- Having been in a home or farm where sick or dead domestic poultry have been reported in the previous six weeks in the affected area

Laboratory criteria for diagnosis

Influenza A/H5 or A/H5N1 will be demonstrated by at least one of the following lab tests:

- **a** Positive RT-PCR for Influenza A/H5 or A/H5N1
- **b** Positive viral culture for Influenza A/H5N1
- **c** Immunofluorescence antibody (IFA) test positive using Influenza A/H5 monoclonal antibodies
- **d** 4-fold rise in Influenza H5-specific antibody titre in paired serum samples

Case categories for Influenza A/H5N1

Possible case

Any individual meeting the clinical description and with an epidemiological link

Probable case

A possible case with one positive laboratory test for influenza A/H5 performed in a laboratory which is not a National Reference Laboratory participating in the EU Community Network of Reference Laboratories for Human Influenza (CNRL)

Nationally confirmed case

An individual, irrespective of the clinical and epidemiological picture with a positive test for influenza A/H5 or A/H5N1 performed by a National Reference Laboratory participating in the EU Community Network of Reference Laboratories for Human Influenza (CNRL)

All samples from nationally confirmed cases should be sent to a WHO Collaborating Centre for H5 (Institut Pasteur, Paris or National Institute for Medical Research, Mill Hill, London) for final confirmation (WHO confirmation).

1 Definition of affected area within the EU will be further developed and continuously updated

2 Dead domestic poultry does not include poultry meat commercially available in shops and supermarkets

3 This does not include seemingly well birds that have been killed, for example by hunting

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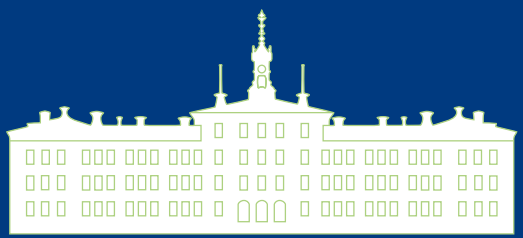

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