ACM/663

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

AVIAN INFLUENZA RISK ASSESSMENT

1. Following an outbreak of Avian Influenza among poultry in the Netherlands, the Food Standards Agency (FSA) sought ACMSF advice on the potential human health risk through food chain exposure pathways.[1] The Agency's preliminary conclusion was that the risk to human health through the food chain from avian influenza viruses, whether of high or low pathogenicity, appeared to be extremely small, a view supported by the Committee. However, the FSA sought the ACMSF's more formal assessment of the risk, in order to determine appropriate risk management strategies.

2. The Committee agreed to this request and asked Dr Brown (its virologist member) to perform the risk assessment, in consultation with experts in the field. This is now attached.

3. Members' views are sought on the conclusions reached. Members are also asked to indicate whether they are content for these conclusions to be conveyed to the FSA as the ACMSF's advice on this question.

Secretariat
November 2003

[1] ACM/MIN/47 paragraph 6 and ACM/631

Avian influenza: review of risks to human health

Background

Two developments have led the FSA to seek expert advice from the ACMSF regarding the risk to human health through the food chain from strains of Avian Influenza (AI). The first is a study of the incidence of low pathogenicity H5 and H7 strains of AI in chickens, turkeys, geese and ducks; and the second is the recent series of outbreaks of highly pathogenic AI in laying flocks in the Netherlands leading to significant numbers of human infections.

Summary

1. The risk of acquiring AI through the food chain is low, and there is no direct evidence to support this route of infection.

2. AI outbreaks in humans in recent years have shown that there is no absolute species barrier between humans and birds.

3. Evidence from these outbreaks indicates that direct contact with infected birds is the main risk factor for human infections, and that consumption of infected chickens has not been identified as a risk factor.

4. Limited studies of AI infections in occupationally exposed groups, and general population studies, have failed to identify unrecognised human AI infection.

5. Several factors will contribute to preventing or limiting infection following ingestion of viruses, including lack of appropriate receptors, and non-specific defences such as saliva or gastric acid. Proper cooking will destroy any virus present in meat or eggs.

Viruses

The influenza viruses are single stranded RNA viruses with segmented genomes, which belong to the Orthomyxoviridae family. Influenza virus can be classified into A, B and C types. All these infect humans, but only influenza A viruses are found in bird and other animals. A wide range of influenza A viruses has been described. They are subtyped based on sequencing or antigenic characterisation of the two biologically important surface proteins; the haemagglutinin (H) and the neuraminidase (N). Fifteen H types and 9 N types have been described, and they are found in different combinations. All H and N type subtypes have been found in birds, indicating their role as the main reservoir, but only a limited range of subtypes have been shown to circulate in humans (currently H3N2, H1N1). Avian influenza strains are commonly described as either ‘low pathogenicity’ or ‘high pathogenicity’ strains based on differences in the haemagglutinin gene and disease caused in chickens.

One important biological feature of influenza viruses influencing their infectivity is the ability to bind to cells to initiate infection. This receptor binding specificity varies amongst influenza strains; avian influenza strains preferentially bind to sialic acid α 2.3 – galactose linkage, human strains to α 2.6 galactose. Both receptors are found in the upper respiratory tract epithelia of pigs, but only the α 2.3 receptors are found in birds and the majority of receptors on human tracheal epithelial cells are of α 2.6 specificity.

Avian influenza viruses are enveloped RNA viruses. AI strains appear to be more resistant to lower pH (<4.0) than human and animal strains, but no infectivity is detectable after exposure below pH 3.0. AI viruses have been shown to survive in the environment for >3 months at 4°C, but much higher rates of inactivation occur at higher temperatures ($>6 \times 10^6$ loss of infectivity within 2 weeks at 20°C).

Epidemiology

Influenza A viruses infect a large variety of animal species including humans, pigs, horses, sea mammals and birds. A wide variety of birds, including wild birds, caged birds, ducks, chickens and turkeys are naturally infected. Birds are the most important reservoir of influenza infection. Wild ducks are an important reservoir of avian influenza for many strains, and shorebirds and gulls are also significant host species.

Influenza A viruses cause a large burden of human illness every year and there have been 3 pandemics of influenza A during the last 50 years caused by viruses new to the human population:

- 1957 H2N2Asian flu
- 1968 H3N7 Hong Kong influenza
- 1977 H1N1 Russian influenza

Avian influenza strains rarely infect humans directly. However, in recent years there have been several AI infections described in humans:

- In 1996, an H7N7 influenza virus of avian origin was isolated from a woman in England with a self-limiting conjunctivitis. She kept ducks with which wild ducks mingled.
- During 1997 in Hong Kong, an H5N1 avian influenza virus was recognised as the cause of death of 6 of 18 people from which this virus was isolated. Genetic analysis revealed these human isolates of H5N1 subtype to be indistinguishable from a highly pathogenic avian influenza virus that was endemic in the local poultry population. Subsequent serological studies in occupationally exposed poultry workers indicate that limited clinically unrecognised infection occurred.

- In March 1999, two independent isolations of influenza subtype H9N2 were made from girls aged 1 and 4 who recovered from flu-like illnesses in Hong Kong. Subsequently, 5 isolations of H9N2 virus from humans on mainland China in August 1998 were reported. H9N2 viruses have been widespread in poultry in China and other Asian countries since that time.
- In 2003, an H5N1 virus was isolated from a father and son in Hong Kong who presented with respiratory illness after returning from the Chinese mainland; the father died. A daughter became ill and died while visiting the Chinese mainland – it is not known if she was infected with the H5N1 virus. There were some genetic differences between the 1997 and 2003 H5N1 viruses.
  See WHO website: http://www.who.int/mediacentre/releases/2003/pr17/en/
- Recently there has been an outbreak of an H7N7 virus in various poultry farms in the Netherlands which started in late February. Over 80 cases were confirmed in humans. The majority of cases exhibited conjunctivitis, but 13 exhibited minor respiratory disease, and one vet died. Three family members of poultry workers have also fallen ill with minor respiratory disease, suggesting a possible small scale human-to-human transmission.
- These reports indicate that both high and low pathogenicity strains of AI can cause human infection. In the outbreaks recognised, the number of human infections was small, consistent with a significant species barrier for transmission between birds and humans. Human to human transmission was very limited.
- The risk factors associated with human AI infections in these outbreaks were direct contact with infected birds and infected family members, and not with consumption.
- There have been limited serological studies of people occupationally exposed to chicken populations, with a significant prevalence of low pathogenicity strains of AI. Studies in Italy and Taiwan have failed to show any evidence of human AI infection. However, it should be pointed out that these studies are of limited scope, and the serology tests used are insensitive for detecting antibodies to AI virus in humans and so are not conclusive.

Clinical features

In birds:
In wild ducks, influenza A virus replicates mainly in the intestinal tract and is excreted in high concentration in faecal samples (up to 10^7 $TCID_{50}$ per gramme).

AI viruses can be divided into two groups dependant on their pathogenicity. Highly virulent strains can cause up to 100% mortality; the virus causes a viraemia, and can be found in many tissues. A second group, which is more frequent, comprises low pathogenicity strains, and cause little or no mortality in poultry. Infection is confined to the intestine, and no viraemia has been described.

In human infection:
Avian influenza rarely infects humans, and a wide range of illness has been associated with infection - from mild-flu like illness to severe pneumonia, organ failure and high mortality. Conjunctivitis has been reported following infection with several strains.

Avian influenza and the food chain: discussion points

- There is a theoretical risk that AI strains could enter the human food chain, but this risk is low, and no risk has been defined in studies of human AI outbreaks.
- The risk of high pathogenicity strains entering the food chain is likely to be contained, because clinically affected poultry will be excluded from slaughter as a result of pre-slaughter veterinary checks. Thus, the only exposure in poultry meat should be to low pathogenicity AI viruses.
- Low pathogenicity AI viruses are confined to the intestinal tract in poultry, and will not replicate after slaughter. Consequently, there is a low risk of contamination of chicken carcasses with AI, which could lead to exposure of individuals involved in food handling and preparation.
- In May 2003, highly pathogenic H5N1 was isolated from duck meat imported from China to Japan. Highly pathogenic AI strains usually cause no symptoms in water birds, so an AI infection may not be diagnosed. There is consequently a low risk of contamination of duck carcasses.
- Proper cooking will destroy any virus present in meat or eggs. Moreover, non-specific defences, such as saliva or gastric acid, provide a primary barrier against infection following ingestion of viruses.

Conclusions

- AI outbreaks in humans in recent years have shown that there is no absolute species barrier between humans and birds.
- Evidence from these outbreaks indicates that direct contact with infected birds is the main risk factor for human infections, and that consumption of infected chickens has not been identified as a risk factor.
- Limited studies of AI infections in occupationally exposed groups, and general population studies, have failed to identify significant unrecognised human AI infection.
- Several factors will contribute to preventing or limiting infection following ingestion of viruses, including lack of appropriate receptors, and non-specific defences such as saliva or gastric acid. Proper cooking will destroy any virus present in meat or eggs.
- The risk of acquiring AI through the food chain is low, and there is no direct evidence to support this route of infection. However, more studies of the factors affecting human infection, and studies of occupationally exposed groups, should be encouraged.