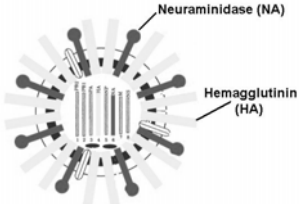


S l i d e  1	<div data-bbox="292 231 568 304" data-label="Section-Header"> <h2>Avian Influenza (Highly Pathogenic)</h2> </div> <div data-bbox="292 315 503 378" data-label="Text"> <p><i>Fowl plague, Fowl pest, Brunswick bird plague, Fowl disease, Fowl or bird grippe</i></p> </div> <div data-bbox="470 399 592 451" data-label="Image"> </div>	<p>Disease from highly pathogenic avian influenza is also known as fowl plague, fowl pest, <b>peste aviaire</b>, <b>geflugelpest</b>, <b>typhus exudatious gallinarium</b>, Brunswick bird plague, <b>Brunswick disease</b>, fowl disease, fowl or bird grippe. <b>BOLD=DELETE</b></p>
S l i d e  2	<div data-bbox="324 504 454 535" data-label="Section-Header"> <h2>Overview</h2> </div> <div data-bbox="194 546 462 766" data-label="List-Group"> <ul style="list-style-type: none"> <li>• Organism</li> <li>• Economic Impact</li> <li>• Epidemiology</li> <li>• Transmission</li> <li>• Clinical Signs</li> <li>• Diagnosis and Treatment</li> <li>• Prevention and Control</li> <li>• Actions to take</li> </ul> </div> <div data-bbox="397 525 592 766" data-label="Image"> </div> <div data-bbox="470 777 592 798" data-label="Text"> <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p> </div>	<p>In today's presentation we will cover information regarding the organism that causes highly pathogenic avian influenza virus and its epidemiology. We will also talk about the economic impact the disease has had in the past and could have in the future. Additionally, we will talk about how it is transmitted, the species it affects, clinical and necropsy signs seen, as well as diagnosis and treatment of the disease. Finally, we will address prevention and control measures for the disease and actions to take if highly pathogenic avian influenza virus is suspected.</p>
S l i d e  3	<div data-bbox="292 934 495 976" data-label="Section-Header"> <h2>The Organism</h2> </div> <div data-bbox="470 1081 592 1144" data-label="Image"> </div>	
S l i d e  4	<div data-bbox="292 1186 495 1228" data-label="Section-Header"> <h2>Influenza Virus</h2> </div> <div data-bbox="194 1239 462 1438" data-label="List-Group"> <ul style="list-style-type: none"> <li>• Family Orthomyxoviridae</li> <li>• Three main types <ul style="list-style-type: none"> <li>– Type A <ul style="list-style-type: none"> <li>• Multiple species</li> </ul> </li> <li>– Type B <ul style="list-style-type: none"> <li>• Humans</li> </ul> </li> <li>– Type C <ul style="list-style-type: none"> <li>• Humans and swine</li> </ul> </li> </ul> </li> </ul> </div> <div data-bbox="454 1281 576 1396" data-label="Image"> </div> <div data-bbox="470 1459 592 1491" data-label="Text"> <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p> </div>	<p>Influenza viruses belong to the family <i>Orthomyxoviridae</i>. They are classified into three main types. Influenza type A viruses affect multiple species. Influenza types B and C both infect humans, but type C is also known to infect swine. We will discuss each of these further in the next few slides. (Photo: ISU-FAD course section by Dr. Corrie Brown)</p>
S l i d e  5	<div data-bbox="308 1533 470 1575" data-label="Section-Header"> <h2>Influenza A</h2> </div> <div data-bbox="194 1585 544 1795" data-label="List-Group"> <ul style="list-style-type: none"> <li>• Multiple species <ul style="list-style-type: none"> <li>– Humans</li> <li>– Avian Influenza</li> </ul> </li> <li>• Most virulent group</li> <li>• Classification by surface antigens into subtypes <ul style="list-style-type: none"> <li>– Hemagglutinin (H or HA)</li> <li>– Neuraminidase (N or NA)</li> </ul> </li> </ul> </div> <div data-bbox="470 1806 592 1837" data-label="Text"> <p><small>Center for Food Security and Public Health Iowa State University - 2004</small></p> </div>	<p>Influenza type A infects multiple species. Several human influenza strains are type A while all avian strains are type A. They are considered the most virulent group, although not all strains cause clinical disease. Type A influenza viruses are classified into subtypes based on two surface antigens known as hemagglutinin (H) and neuraminidase (N), sometimes also referred to as HA and NA respectively.</p>

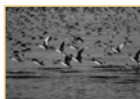
S l i d e  6	<p style="text-align: center;"><b>Surface Antigens and Subtypes</b></p> <ul style="list-style-type: none"> <li>• 15 HA and 9 NA for influenza A <ul style="list-style-type: none"> <li>– All in aquatic birds</li> </ul> </li> <li>• Hemagglutinin (HA) <ul style="list-style-type: none"> <li>– Function: Sites for attachment to infect host cells</li> </ul> </li> <li>• Neuraminidase (NA) <ul style="list-style-type: none"> <li>– Function: Remove neuraminic acid from mucin and release from cell</li> </ul> </li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>There are 15 different HA and 9 different NA antigens in influenza A. All of these different antigens can be found in aquatic birds. The HA is the hemagglutinin antigen and it functions as the site for attachment to host cells. The NA or neuraminidase antigen serves to remove neuraminic acid from mucin allowing the virus to be released from the cell.</p>
S l i d e  7	<p style="text-align: center;"><b>Influenza A</b></p>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>This picture depicts the major antigenic components of the influenza A virus. The virus is composed of eight segments of RNA. Having segments makes it easier for reassortment to occur. The yellow bars represent the hemagglutinin (HA) part of the virus. The pink protrusions represent neuraminidase (NA).</p>
S l i d e  8	<p style="text-align: center;"><b>Influenza B</b></p> <ul style="list-style-type: none"> <li>• Mostly humans</li> <li>• Common</li> <li>• Less severe than A</li> <li>• Epidemics occur less often than A</li> <li>• Human seasonal vaccine <ul style="list-style-type: none"> <li>– Two strains of type A</li> <li>– One strain of type B</li> </ul> </li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Influenza type B viruses infect mostly humans. They are not categorized into subtypes. They are quite common, but clinical disease is usually less severe than influenza A. Epidemics do occur, but are seen less often than type A. Human seasonal vaccines usually contain two strains of influenza A and one strain of B.</p>
S l i d e  9	<p style="text-align: center;"><b>Influenza C</b></p> <ul style="list-style-type: none"> <li>• Humans and swine</li> <li>• Different pattern of surface proteins</li> <li>• Rare <ul style="list-style-type: none"> <li>– Mild to no symptoms</li> </ul> </li> <li>• By age 15, most have antibodies</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Influenza type C has been identified in both humans and swine. Their pattern of surface proteins are different than the other influenza's and are not categorized into subtypes. They are rare and usually produce mild or no clinical symptoms. It has been found that most individuals have antibodies to influenza C by the age of 15.</p>
S l i d e  10	<p style="text-align: center;"><b>Avian Influenza</b></p> <ul style="list-style-type: none"> <li>• Pathogenicity based on genetic features and/or severity of disease in poultry <ul style="list-style-type: none"> <li>– Low pathogenic AI (LPAI) <ul style="list-style-type: none"> <li>• H1 to H15 subtypes</li> </ul> </li> <li>– Highly pathogenic AI (HPAI) <ul style="list-style-type: none"> <li>• Some H5 or H7 subtypes</li> <li>• LPAI H5 or H7 subtypes can mutate into HPAI</li> </ul> </li> </ul> </li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Avian influenza only includes type A viruses and described based on their pathogenicity. Genetic features and/or severity of disease in poultry determines whether the virus is classified as low pathogenic (LPAI) or high pathogenic (HPAI) avian influenza. Low pathogenic avian influenza (LPAI) includes viruses in all H1 to H15 subtypes. On the other hand, highly pathogenic avian influenza (HPAI) have traditionally been either H5 or H7 subtypes. H5 and H7 LPAI viruses do exist and are of concern because they can mutate into a HPAI.</p>

## Importance



## History

- 1878: First identified case in Italy
- 1924-25: First U.S. cases
- Low pathogenic avian influenza first identified mid-twentieth century
- 1970's: Migratory waterfowl carriers
- Outbreaks in mink, seals and whales



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Avian influenza was first identified in Italy in 1878. The first US cases of highly pathogenic avian influenza (HPAI) were reported in the U.S. in 1924-25 and 1929. Quarantine, depopulation, cleaning and disinfection were used to eradicate HPAI from the United States. Milder disease of influenza were recognized in the middle of the twentieth century. Today these avian influenza (AI) viruses are termed low pathogenic avian influenza (LPAI). In the 1970's surveillance for Newcastle disease virus showed that migratory waterfowl were asymptomatic carriers of AI. Since then it has been shown that wild waterfowl (especially ducks and geese) and other aquatic birds are the primordial reservoir of all influenza viral genes. Avian influenza viruses have caused epizootics of respiratory disease in mink, seals and whales. (Photo: US FWS)

## Economic Impact

- Direct losses:
  - Depopulation and disposal
  - High morbidity and mortality
  - Quarantine and surveillance
  - Indemnities
- 1978-1996: Seasonal outbreaks of LPAI in Minnesota cost taxpayers \$22 million



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Economic losses from avian influenza vary depending on the strain of virus, species of bird infected, number of farms involved, control methods used and the speed of implementation of control or eradication strategies. Direct losses include depopulation and disposal costs, high morbidity and mortality losses, quarantine and surveillance costs and indemnities paid for elimination of birds. In most developed countries, HPAI and LPAI have not been endemic diseases in the commercial poultry industries. LPAI outbreaks have caused significant economic losses. Losses from seasonal outbreaks of LPAI in Minnesota between 1978 and 1996 cost a total of \$22 million US. (Photo: ISU-FAD course section by Dr. Corrie Brown)

## Economic Impact

- 1983: U.S. outbreak (H5N2)
  - \$65 million in losses
  - Destruction of 17 million birds
  - 30% increase in egg prices
- 1999-2000: Italy outbreak (H7N1)
  - \$100 million in compensation to farmers
  - 18 million birds destroyed
  - Indirect losses of \$500 million

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The 1983 outbreak of HPAI (H5N2) in the northeastern United States resulted in losses of nearly \$65 million, the destruction of more than 17 million birds, and a 30% increase in egg prices. In the 1999-2000 outbreak of HPAI (H7N1) in Italy the government paid farmers \$100 million (U.S.) in compensation for 18 million birds with total indirect losses at \$500 million.

## Economic Impact

- 1997: Hong Kong outbreak (H5N1)
  - \$13 million for depopulation and indemnities
  - 1.4 million birds
- 2001: Hong Kong outbreak (H5N1)
  - 1.2 million birds
  - \$3.8 million



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The 1997 outbreak of HPAI (H5N1) in Hong Kong live poultry market cost \$13 million (U.S.) for depopulation and indemnities for 1.4 million birds. The 2001 outbreak, also in Hong Kong cost \$3.8 million dollars and 1.2 million birds were destroyed. (Photo: USDA)

### Economic Impact

- 2003: European outbreak (H7N7)
  - Over 33 million birds destroyed
  - ¼ of Netherlands' poultry stock
  - Cost?
- 2004-2005: SE Asia (H5N1)
  - 8 countries
  - >100 million birds destroyed
  - Cost?

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The 2003 European outbreak of (H7N7) strain resulted in the destruction of 30 million birds in the Netherlands (one quarter of the country's poultry stock), with 2.7 million destroyed in Belgium and some 400,000 in Germany for a total of over 33 million birds. The total costs of this outbreak as of April 2005, is unknown. The 2004-2005 outbreak in Southeast Asia includes 8 countries, and has resulted in the destruction of more than 100 million birds (as of April 2005). The cost of this outbreak, also, is yet to be determined.

### Epidemiology

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### Geographic Distribution

- Worldwide distribution
- Reservoir
  - Free flying aquatic birds: Ducks, geese, shorebirds, gulls, terns, auks
- Recent outbreaks
  - The Netherlands, Australia, Mexico, U.S., SE Asia
- Similarity to Newcastle Disease makes actual distribution difficult to define
- Altered avian ecosystems have created new niche for AI viruses




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Highly pathogenic AI viruses can be found worldwide. Recent outbreaks have occurred in Australia, England, Ireland, Scotland, Pakistan, South Africa, Mexico, United States and the Netherlands. There is serological evidence of infection in penguins from the Antarctic. The most frequent source of AI viruses has been free flying aquatic birds, ducks, geese, and shorebirds, gulls, terns and auks, which are considered the genetic reservoirs of all AI viruses. Because laboratory facilities are not readily available in some parts of the world to differentiate Newcastle disease from HPAI, the actual incidence of HPAI in the world's poultry is difficult to define. Humans have altered the natural ecosystems of birds through captivity, domestication, industrial agriculture, and nontraditional raising practices. This has created new niches for AI viruses and caused a change in the incidence and distribution of AI infections.

### Morbidity/Mortality

- Approaches 100% in commercial poultry flocks
- Deaths within 2 to 12 days after first signs of illness
- Survivors in poor condition







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Morbidity and mortality in commercial poultry flocks often approach 100% within 2 to 12 days after the first signs of illness. Any survivors are usually in poor condition and do not begin laying again for several weeks.

### Transmission


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S l i d e  2 1	<p style="text-align: center;"><b>Animal Transmission</b></p> <ul style="list-style-type: none"> <li>Initial source of infection <ul style="list-style-type: none"> <li>Other poultry, migratory waterfowl, pet birds</li> </ul> </li> <li>Spread by aerosol, shared drinking water, fomites</li> <li>Virus in respiratory secretions and feces</li> <li>Virus present in eggs but eggs unlikely to survive and hatch</li> </ul>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Migratory waterfowl are widely considered to be the reservoirs of avian influenza virus. Feces and respiratory secretions contain large amounts of virus, which can infect a new host through the conjunctiva or respiratory tract. Avian influenza virus can spread by aerosols when birds are in close proximity, and might also be transmitted through shared drinking water. The virus appears to be present in eggs laid by infected hens, but they are unlikely to survive and hatch. Fomites and infected birds can transmit the disease between flocks. In one outbreak in Pennsylvania, the virus may have been spread by garbage flies. Airborne dissemination may be possible as well as movement of infected poultry. In experimental studies AI viruses can be excreted in the feces and maintained in the environment and can re-emerge after a significantly stressful event. Once a flock is infected, it should be considered a potential source of virus for life.</p>
S l i d e  2 2	<p style="text-align: center;"><b>Human Transmission</b></p> <ul style="list-style-type: none"> <li>Previously considered non-pathogenic for humans</li> <li>1997, Hong Kong <ul style="list-style-type: none"> <li>18 humans infected, 6 died</li> <li>H5N1 virus linked to outbreak in live bird market and area farms</li> </ul> </li> <li>2003, the Netherlands <ul style="list-style-type: none"> <li>83 confirmed cases in humans, 1 death</li> <li>H7N7 strain</li> </ul> </li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>AI viruses were once thought to be nonpathogenic for humans because humans lack receptors for avian influenza viruses (locations that the virus utilizes to attach for infection to occur) 1997 when 18 people were infected and six people died from a highly pathogenic H5N1 strain of avian influenza virus in Hong Kong. The virus was linked to birds in a live bird market and on farms that were experiencing an outbreak of HPAI. An outbreak in the Netherlands in early 2003 resulted in 83 confirmed cases of Avian Influenza in humans. A 57 year old veterinarian who visited a poultry farm affected by the H7N7 strain died of acute respiratory distress syndrome and H7N7 was isolated from the patient; he was the only death known from that outbreak.</p>
S l i d e  2 3	<p style="text-align: center;"><b>Human Transmission</b></p> <ul style="list-style-type: none"> <li>2004-2005, SE Asia <ul style="list-style-type: none"> <li>79 cases, 49 deaths <ul style="list-style-type: none"> <li>Viet Nam, Thailand, Cambodia</li> </ul> </li> <li>H5N1 strain</li> <li>Within the vicinity of poultry outbreaks</li> <li>Evidence for human-to-human transmission</li> </ul> </li> <li>Swine are proposed "mixing vessel"</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>The 2004-2005 outbreak of the H5N1 strain in Southeastern Asia has resulted in 79 cases and 49 deaths from the countries of Viet Nam, Thailand, and Cambodia combined. Investigations are currently underway to determine how individuals have come into contact with the virus; however, reported cases have mostly come from locations near the poultry avian influenza outbreak. In Viet Nam, human cases have been reported in clusters of family members. There is some evidence to indicate human to human transmission occurred, but it is rare. Contact with sick poultry still remains the major risk factor for human transmission. Swine have been proposed as a "mixing" vessel for co-infection by influenza viruses from birds and mammals because they have receptors for both mammalian and avian influenza viruses. This co-infection with avian and mammalian influenza viruses can lead to the development of new strains (reassortants) that could have the ability to infect people and other mammals.</p>
S l i d e  2 4	<p style="text-align: center;"><b>Animals and Highly Pathogenic Avian Influenza</b></p>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University</p>	



S l i d e  2 5	<p style="text-align: center;"><b>Clinical Signs</b></p> <ul style="list-style-type: none"> <li>• Incubation period: 3-14 days</li> <li>• Birds found dead</li> <li>• Drop in egg production</li> <li>• Neurological signs</li> <li>• Depression, anorexia, ruffled feathers</li> <li>• Combs swollen, cyanotic</li> <li>• Conjunctivitis and respiratory signs</li> </ul>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Incubation period is from 3-14 days and is dependent on the dose of virus, the route of exposure, the species exposed. Some birds are found dead prior to observance of any clinical signs. There may be neurological signs and reduction in normal vocalizations. Depression is common as is a precipitous drop in egg production. Respiratory signs are less prominent but can include rales, sneezing and coughing. In mature chickens, the combs and wattles are often swollen and may be cyanotic. Conjunctivitis, edema of the head and neck, coughing, sneezing and nasal discharge may also be seen. Egg production in hens stops; the last eggs laid often have no shells. Death is common, but severely affected hens occasionally recover. (Photos: ISU-FAD course by Dr. Corrie Brown, showing a dead bird [top] and cyanotic comb and wattles [bottom].)</p>
S l i d e  2 6	<p style="text-align: center;"><b>Post Mortem Lesions</b></p> <ul style="list-style-type: none"> <li>• Lesions may be absent with sudden death</li> <li>• Severe congestion of the musculature</li> <li>• Dehydration</li> <li>• Subcutaneous edema of head and neck area</li> </ul>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Lesions may be absent in the case of sudden death. There may be severe congestion of the musculature and dehydration. Subcutaneous edema may be present on the head and neck area. (Photo ISU-FAD course section by Dr. Corrie Brown, showing facial edema)</p>
S l i d e  2 7	<p style="text-align: center;"><b>Post Mortem Lesions</b></p> <ul style="list-style-type: none"> <li>• Nasal and oral cavity discharge</li> <li>• Petechiae on serosal surfaces</li> <li>• Kidneys severely congested</li> <li>• Severe congestion of the conjunctivae</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>During necropsy, excessive fluid can flow from the nares and oral cavity. Petechial hemorrhages may be found on serosa and in the body cavity. The kidneys are often severely congested and occasionally plugged with white urate deposits. In young birds and birds with peracute disease, the only significant lesions may be dehydration and severe congestion of the muscles.</p>
S l i d e  2 8	<p style="text-align: center;"><b>Sampling</b></p> <ul style="list-style-type: none"> <li>• Before collecting or sending any samples, the proper authorities should be contacted</li> <li>• Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease</li> <li>• HPAI samples may be zoonotic</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Some isolates of the avian influenza virus may be zoonotic; samples should be collected and handled with all appropriate precautions.</p>
S l i d e  2 9	<p style="text-align: center;"><b>Diagnosis</b></p> <ul style="list-style-type: none"> <li>• Clinically indistinguishable from virulent Newcastle Disease</li> <li>• Suspect with: <ul style="list-style-type: none"> <li>– Sudden death</li> <li>– Drop in egg production</li> <li>– Facial edema, cyanotic combs and wattles</li> <li>– Petechial hemorrhages</li> </ul> </li> <li>• Virology and serology necessary for definitive diagnoses</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Highly pathogenic Avian Influenza (HPAI) is clinically indistinguishable from virulent Newcastle Disease. HP AI should be suspected when severe depression, inappetence, and a drastic drop in egg production are followed by sudden deaths in the flock. Facial edema, swollen and cyanotic combs and wattles, and petechial hemorrhages on the internal organs support this diagnosis. Because of the broad spectrum of signs and lesions a definitive diagnosis must be made by virology and serology.</p>

S l i d e  3 0	<h3>Differential Diagnosis</h3> <ul style="list-style-type: none"> <li>• Virulent Newcastle disease</li> <li>• Avian pneumovirus</li> <li>• Infectious laryngotracheitis</li> <li>• Infectious bronchitis</li> <li>• Chlamydia</li> <li>• Mycoplasma</li> <li>• Acute bacterial diseases <ul style="list-style-type: none"> <li>– Fowl cholera, <i>E. coli</i> infection</li> </ul> </li> </ul> <small>Center for Food Security and Public Health Iowa State University - 2006</small>	<p>Differentials for highly pathogenic avian influenza include Newcastle disease virus, which is clinically indistinguishable from HP AI; avian pneumovirus and other paramyxoviruses, infectious laryngotracheitis, infectious bronchitis, chlamydia, mycoplasma and other acute bacterial diseases including fowl cholera and <i>E. coli</i> infections.</p>
S l i d e  3 1	<h3>Diagnosis</h3> <ul style="list-style-type: none"> <li>• Laboratory Tests <ul style="list-style-type: none"> <li>– HP AI is usually diagnosed by virus isolation</li> </ul> </li> <li>• Presence of virus confirmed by <ul style="list-style-type: none"> <li>– AGID</li> <li>– ELISA</li> <li>– RT-PCR</li> </ul> </li> <li>• Serology may be helpful</li> </ul> <small>Center for Food Security and Public Health Iowa State University - 2006</small>	<p>Avian influenza is usually diagnosed by virus isolation. The presence of virus can be confirmed by agar gel immunodiffusion (AGID) tests, ELISA or reverse-transcription polymerase chain reaction (RT-PCR) tests. Highly pathogenic strains are identified by their lethality in susceptible chickens and by molecular considerations. Serology can also be helpful in diagnosis and ELISA and AGID tests are available. However, not all species of birds make precipitating antibodies. Hemagglutination inhibition tests are also used, but are subtype specific and may miss some infections.</p>
S l i d e  3 2	<h3>Treatment</h3> <ul style="list-style-type: none"> <li>• No specific treatment</li> <li>• Supportive care and antibiotics for secondary infections</li> <li>• Antivirals (Amantadine) effective in reducing mortality <ul style="list-style-type: none"> <li>– Not approved in food animals</li> <li>– Results in resistant viruses</li> </ul> </li> </ul>  <small>Center for Food Security and Public Health Iowa State University - 2006</small>	<p>No practical, specific treatment exists for avian influenza virus infections in commercial poultry. Supportive care and antibiotic treatment have been used to reduce the effects of concurrent bacterial infections. Amantadine has been shown experimentally to be effective in reducing mortality but the drug is not approved for food animals and quickly results in amantadine resistant viruses. Amantadine hydrochloride, and other antivirals have been licensed for use in humans to treat influenza since 1966. The medication is effective in reducing the severity of influenza Type A in humans. (Photo: ISU-FAD course section by Dr. Corrie Brown)</p>
S l i d e  3 3	<h3>Avian Influenza in Humans</h3> 	
S l i d e  3 4	<h3>Clinical Signs in Humans</h3> <ul style="list-style-type: none"> <li>• 1997: Hong Kong (H5N1) <ul style="list-style-type: none"> <li>– Fever, respiratory, vomiting, diarrhea, pain</li> <li>– Fatal cases: severe bilateral pneumonia, liver dysfunction, renal failure, septic shock</li> </ul> </li> <li>• 1979: MP AI in harbor seals (H7N7) <ul style="list-style-type: none"> <li>– Conjunctivitis in humans in contact</li> </ul> </li> </ul> <small>Center for Food Security and Public Health Iowa State University - 2006</small>	<p>The 1997 Hong Kong outbreak resulted in hospitalization of 18 people and 6 deaths in Hong Kong. The patients had fever, upper respiratory and gastrointestinal disease including vomiting, diarrhea and pain. The patients that died had severe bilateral pneumonia with other complications of liver dysfunction, renal failure, septic shock and pancytopenia. In 1979, a MP AI virus caused an outbreak of respiratory illness and death in harbor seals in northeastern U.S. Self-limiting conjunctivitis was reported in workers handling the seals during the outbreak.</p>



S l i d e  3 5	<h3>Clinical Signs in Humans</h3> <ul style="list-style-type: none"> <li>• 2003: Netherlands (H7N7) <ul style="list-style-type: none"> <li>– Conjunctivitis</li> <li>– Mild influenza or respiratory symptoms</li> <li>– Fatal case: Acute respiratory distress syndrome</li> </ul> </li> </ul> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>The H7N7 outbreak in the Netherlands in 2003 resulted in 83 confirmed cases of avian influenza in humans. The most common clinical signs included conjunctivitis and/or mild influenza or respiratory signs. The veterinarian who died after visiting a poultry farm died of acute respiratory distress syndrome.</p>
S l i d e  3 6	<h3>Public Health Significance</h3> <ul style="list-style-type: none"> <li>• Risk is low</li> <li>• Strains vary in ability to infect humans</li> <li>• High occupational exposure may increase risk</li> <li>• 2003: 83 cases <ul style="list-style-type: none"> <li>– Human infections from non-compliance with personal biosafety measures</li> <li>– Evidence of human-to-human transmission</li> </ul> </li> </ul> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>Generally the risk for infection with AI is low. Strains vary in their ability to transmit and infect humans. In the 1983-4 US outbreak and the 1999-2000 outbreak in Italy, individuals with high occupational exposure showed lack of virus infection and lack of serum antibody against it. But the 1997 outbreak in Hong Kong indicated that infection was much more widespread in people with high occupational risk, such as poultry workers. Most of the human infections in the 2003 outbreak resulted from non-compliance with personal bio-safety measures such as wearing gloves, gowns and masks. There was also evidence of transmission from poultry workers to family members. This outbreak emphasizes the need for continuing cooperation between the public health and veterinary medical communities in controlling diseases with a zoonotic potential.</p>
S l i d e  3 7	<h3>Prevention and Control</h3> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University</small></p>	
S l i d e  3 8	<h3>Recommended Actions</h3> <ul style="list-style-type: none"> <li>• Notification of Authorities <ul style="list-style-type: none"> <li>– Federal: <ul style="list-style-type: none"> <li>Area Veterinarian in Charge (AVIC)</li> <li><a href="http://www.aphis.usda.gov/vs/area_offices.htm">www.aphis.usda.gov/vs/area_offices.htm</a></li> </ul> </li> <li>– State veterinarian</li> <li><a href="http://www.aphis.usda.gov/vs/sregs/official.htm">www.aphis.usda.gov/vs/sregs/official.htm</a></li> </ul> </li> <li>• Quarantine</li> </ul> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>Due to the economically devastating nature of this disease, authorities should be notified immediately of any suspicious cases of highly pathogenic avian influenza. While waiting for the authorities or a confirmed diagnosis, all suspect animals should be quarantined.</p>
S l i d e  3 9	<h3>Recommended Actions</h3> <ul style="list-style-type: none"> <li>• Confirmatory diagnosis</li> <li>• Depopulation may occur <ul style="list-style-type: none"> <li>– Infected premises</li> <li>– Contact-exposed premises</li> <li>– Contiguous premises</li> </ul> </li> </ul> <div style="display: flex; align-items: center;">  </div> <p style="text-align: right;"><small>Center for Food Security and Public Health Iowa State University - 2004</small></p>	<p>Should highly pathogenic avian influenza be confirmed by diagnosis, depopulation may need to occur. Depopulation protocols include plans for the infected premises, contact-exposed premises, and contiguous premises. Proper destruction of all exposed cadavers, litter and animal products are required. (Photos: USDA-APHIS 2002-2003 California END outbreak. Top: backyard chicken flock; bottom: depopulating using CO<sub>2</sub> gas chambers-garbage cans.)</p>



S l i d e  4 0	<p style="text-align: center;"><b>Control and Eradication</b></p> <ul style="list-style-type: none"> <li>• Eliminate insects and mice</li> <li>• Depopulate flock and destroy carcasses</li> <li>• Remove manure down to bare concrete</li> <li>• High pressure spray to clean equipment and surfaces</li> <li>• Spray with residual disinfectant</li> </ul>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>To control an outbreak of HPAI the premises must be thoroughly cleaned and disinfected. Insects and mice on the premises should be eliminated, then the flock depopulated and the carcasses destroyed by burying, composting, or rendering. Once the virus have been killed, the manure and feed should be removed down to a bare concrete floor. If the floor is earthen, one inch or more of soil should also be removed. The manure can be buried at least 5 feet deep. It may also be composted for 90 days or longer, depending on the environmental conditions. The compost should be tightly covered with black polyethylene sheets to prevent entry of birds, insects, and rodents. Feathers can be burned; alternatively, they may be removed and the area wet down with disinfectant. High pressure spray equipment should be used to clean all equipment and building surfaces. Once all surfaces are clean and free of all organic material, the entire premises should be sprayed with an approved residual disinfectant. Cresylic or phenolic disinfectants are usually effective. (Photos: USDA-APHIS 2002-2003 California END outbreak-photo illustrates some of the difficulty in cleaning and disinfecting backyard operations)</p>
S l i d e  4 1	<p style="text-align: center;"><b>Prevention</b></p> <ul style="list-style-type: none"> <li>• Appropriate biosecurity <ul style="list-style-type: none"> <li>– Control human traffic</li> <li>– Introduction of new birds into flock</li> <li>– Avoid open range rearing in waterfowl prevalent areas</li> </ul> </li> <li>• Education of the poultry industry</li> <li>• Prompt response to MP AI outbreaks</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>The practice of accepted sanitation and biosecurity procedures in poultry operations is of the greatest importance in the prevention, control and eradication of HPAI. In areas where waterfowl, shorebirds or sea birds are prevalent, the rearing of poultry on open range is incompatible with a sound AI prevention program. Appropriate biosecurity practices should be applied, including the control of human traffic and introduction of birds of unknown disease status into the flock. One critical goal of prevention and control is the education of the poultry industry regarding how the virus is introduced, spread and how it can be prevented. HPAI can emerge from MP AI outbreaks so prompt response to MP AI outbreaks is important.</p>
S l i d e  4 2	<p style="text-align: center;"><b>Influenza Vaccine Development</b></p>  <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	
S l i d e  4 3	<p style="text-align: center;"><b>Avian Influenza Vaccine</b></p> <ul style="list-style-type: none"> <li>• Traditional killed vaccines are effective</li> <li>• Vaccines will protect only against other avian influenza viruses with the same hemagglutinin (H) type.</li> </ul> <p style="text-align: right; font-size: small;">Center for Food Security and Public Health Iowa State University - 2004</p>	<p>Killed vaccines against avian influenza are effective against other strains of the virus that have the same Hemagglutinin (H) type. For example, vaccines made using an H5 type Avian influenza virus will protect against all other H5 avian influenza viruses, but will not protect against other H types such as H7.</p>

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## Influenza A Viruses

- Mutate frequently
  - Antigenic drift
    - Point mutations accumulated during virus replication
  - Antigenic shift
    - Hybrid virus emerges when cell infected with two different influenza viruses
      - Human, avian, swine, equine
  - Transfer of influenza virus to a different species

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Influenza A viruses are known to mutate frequently. There are two main ways for mutations to occur. In antigenic drift, small point mutations (that is, mutations at one location only) occur during the normal virus replication process. This type of mutation usually results in no major changes in the pathogenicity of the virus. On the other hand, antigenic shift occurs when major changes in genetic material have occurred. This usually occurs when cells are infected with two different strains of influenza virus at the same time. This co-infection is of concern when it involves viruses from different species (human, avian, swine, or equine). Because of the segmented RNA in the virus (8 genes) movement of genes from one virus to another are possible. This antigenic shift can then create a new hybrid virus which can become pathogenic to a different species.

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## Influenza A Viruses

### Human influenza vaccines

- Antigenic drift
  - Requires new strains to be used in vaccines each year
- Antigenic shift
  - Caused pandemics in 1918, 1957, 1968, and ?
- Current human influenza vaccines have no efficacy against avian influenza

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Human influenza vaccines are formulated differently each year due to antigenic drift. Changes need to be made in order to try and match the most prevalent strain in circulation. It is believed that the last three pandemics (1918, 1957, and 1968) have all involved antigenic shifts. When the next antigenic shift will occur that will lead to the next influenza pandemic is not known. Current human influenza vaccines are not effective in protecting against avian influenza.

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## Vaccination

- Drawbacks to vaccination
  - Expensive
  - No cross protection between 15 H subtypes
  - Possible creation of reassortant virus
- Inactivated H5 and recombinant vaccine licensed in the U.S. for emergency in HPAI outbreaks

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Inactivated influenza virus vaccines, although fairly expensive, have been used and their effectiveness in reducing mortality and preventing disease is well documented. The basic drawback to vaccination is that there is no cross protection between the 15 known H subtypes. It is not practical to vaccinate against all subtypes. After an outbreak occurs and the subtype of the virus is known, vaccination may be a useful tool. More economically viable vaccines prepared using naturally avirulent or attenuated strains have the disadvantage of the possible creation of reassortant influenza viruses with unpredictable characteristics. These could result when a single host bird is simultaneously infected with both the vaccine and another AI virus. This could result in the creation of a new virulent influenza virus. An inactivated H5 vaccine and a recombinant vaccine are licensed in the United States for emergency use in future HPAI eradication efforts. A recombinant fowl pox virus vaccine containing the gene that codes for the production of the H5 antigen has recently been licensed.

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## Additional Resources



## Internet Resources

- World Organization for Animal Health (OIE)  
– [www.oie.int](http://www.oie.int)
- USAHA Foreign Animal Diseases – “The Gray Book”  
– [www.vet.uga.edu/vpp/gray\\_book/index](http://www.vet.uga.edu/vpp/gray_book/index)
- World Health Organization  
– [www.who.int](http://www.who.int)

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