Avian Influenza: HPAI Outbreaks and Control Methods

David E. Swayne

Southeast Poultry Research Laboratory
Agricultural Research Service
U.S. Department of Agriculture
Athens, Georgia

26 HPAI Epizootics

1. 1959-Scotland, H5N1
2. 1961-S. Africa, H5N3
3. 1963-England, H7N3
4. 1966-Canada, H5N9
5. 1975-Australia, H7N7
6. 1979 –Germany, H7N7
7. 1979-England, H7N7
*8. 1983-84 - USA, H5N2
9. 1983-Ireland, H5N8
10. 1985-Australia, H7N7
11. 1991-England, H5N1
12. 1992-Australia, H7N3
13. 1994-Australia, H7N3
*§14. 1994-95-Mexico, H5N2
§15. 1995 & 2004 – Pakistan, H7N3
16. 1997-Australia, H7N4
17. 1997-Italy, H5N2
**§18. 1996-2008 – Asia/Europe/ Africa, H5N1
*19. 1999-2000 - Italy, H7N1
*20. 2002 - Chile, H7N3
*21. 2003 – Netherlands, H7N7
*22. 2004 – USA, H5N2
*23. 2004 – Canada, H7N3
24. 2004, 2006 – S. Africa, H5N2
§25. 2005? – N. Korea, H7N7 #
26. 2007 – Canada, H7N3

*LPAIV ⇒HPAIV

**Largest epizootic in 50 yrs

§Vaccine used in the control strategy

Asian H5N1 HPAI Epizootic

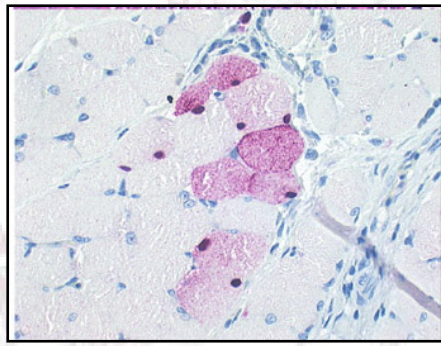
The Beginning, 1996

- Guangdong, China
- Geese with some mortality
- H5N1 AI virus – HP for chickens

- 1997, Hong Kong:
  - 18 human cases, 6 deaths
  - Depopulation of 1.4m poultry LPM and farms

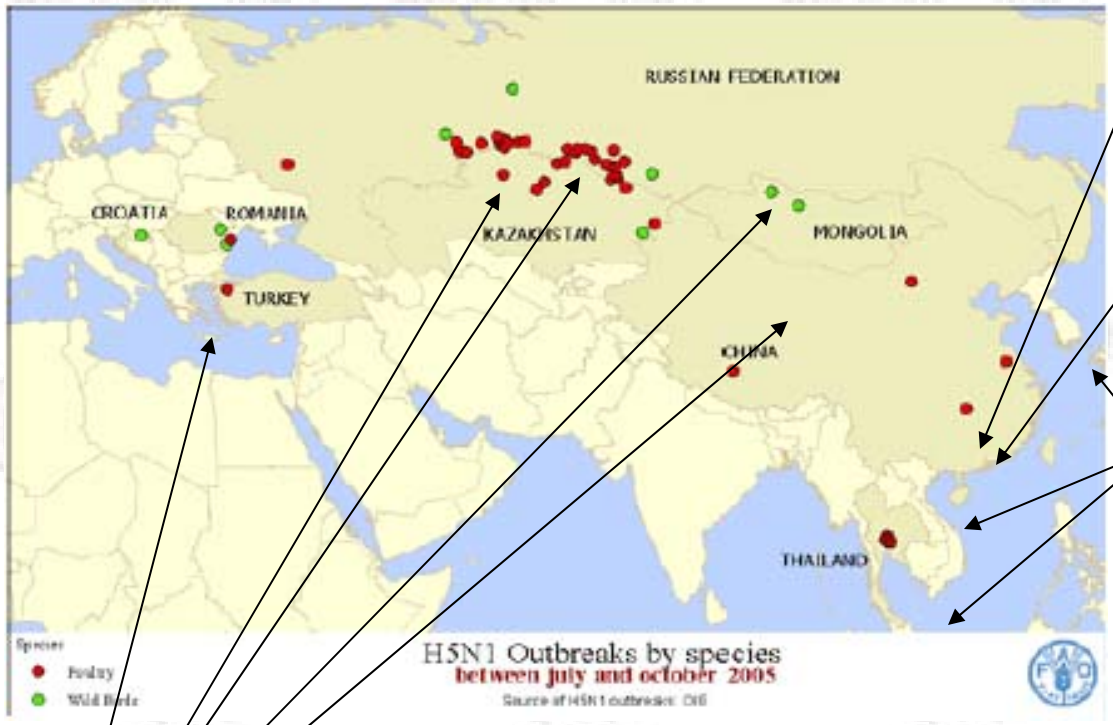
Asian H5N1 HPAI Epizootic

- **2001 H5N1 isolated from duck meat exported to S. Korea**
  - **Isolated from meat juice - thawed and refrozen meat**
  - **Meat from south China**
- **AI virus:**
  - **HP, chickens**
  - **NP, ducks**



- **2003: H5N1 isolated in Japan from imported duck meat from China**

Asian HPAI Epizootics

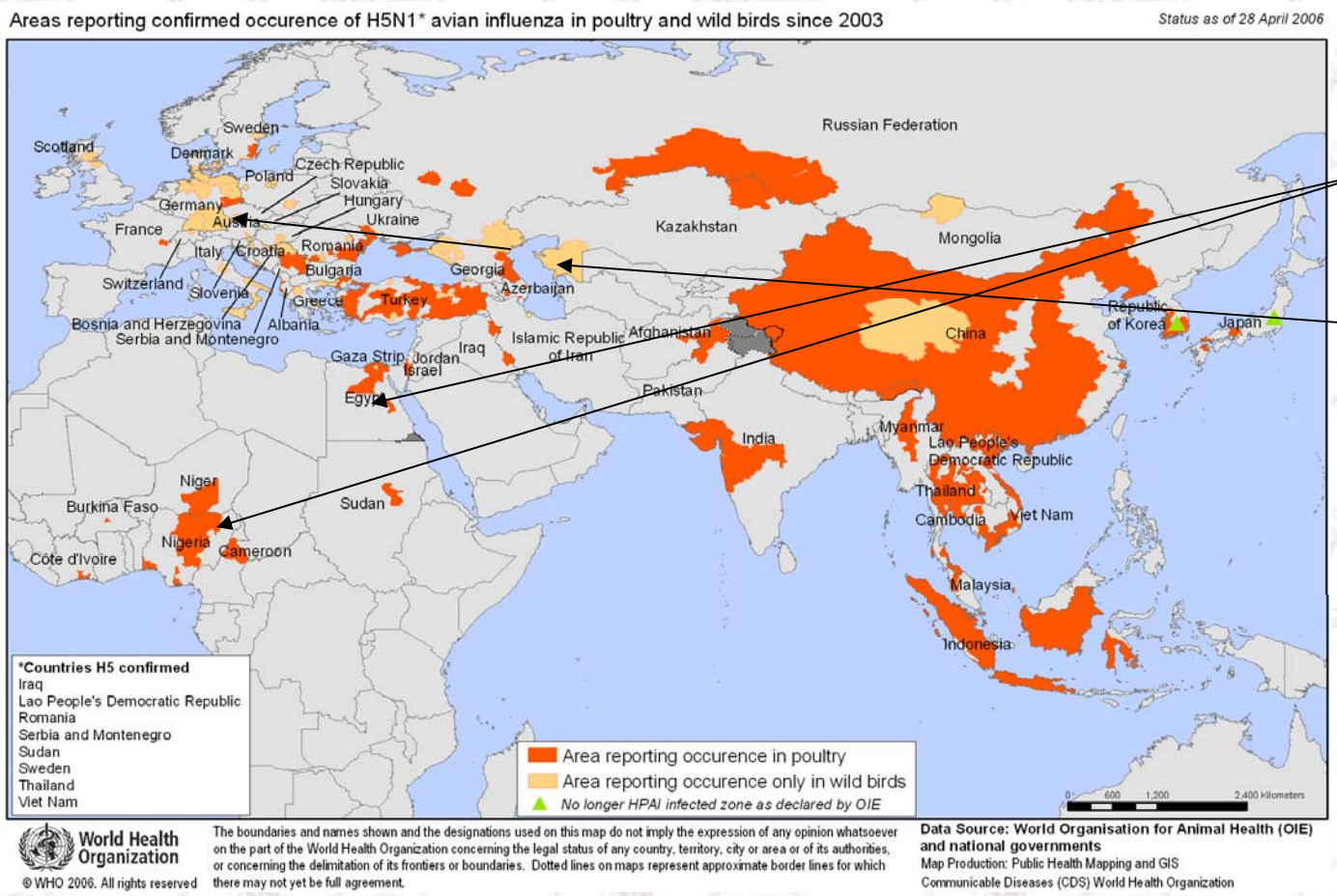


H5N1 HPAI

4. Central Asia & E. Europe, wild bird –
   - Mid-2005: China (Qinghai Lake), Russia, Mongolia, Kazakhstan
   - Late-2005: Turkey, Romania, Kuwait, Croatia, Ukraine, Cyprus: (H5N1)

1. Beginning - China: 1996-2006 (H5N1)
2. Local extension - Hong Kong: 1997, 2001-3 (H5N1)
3. SE Asian Regional Extension - Agriculture
   - S. Korea: 2003-4 (H5N1)
   - Vietnam: 2004-6 (H5N1)
   - Japan: 2004 (H5N1)
   - Thailand: 2004-6 (H5N1)
   - Cambodia: 2004-6 (H5N1)
   - Laos: 2004-6 (H5N1)
   - Taiwan (smuggled ducks): 2003 & 5 (H5N1)
   - Indonesia: 2003-6 (H5N1)
   - Malaysia: 2004 (H5N1)

Extension of H5N1 HPAIV: 2006



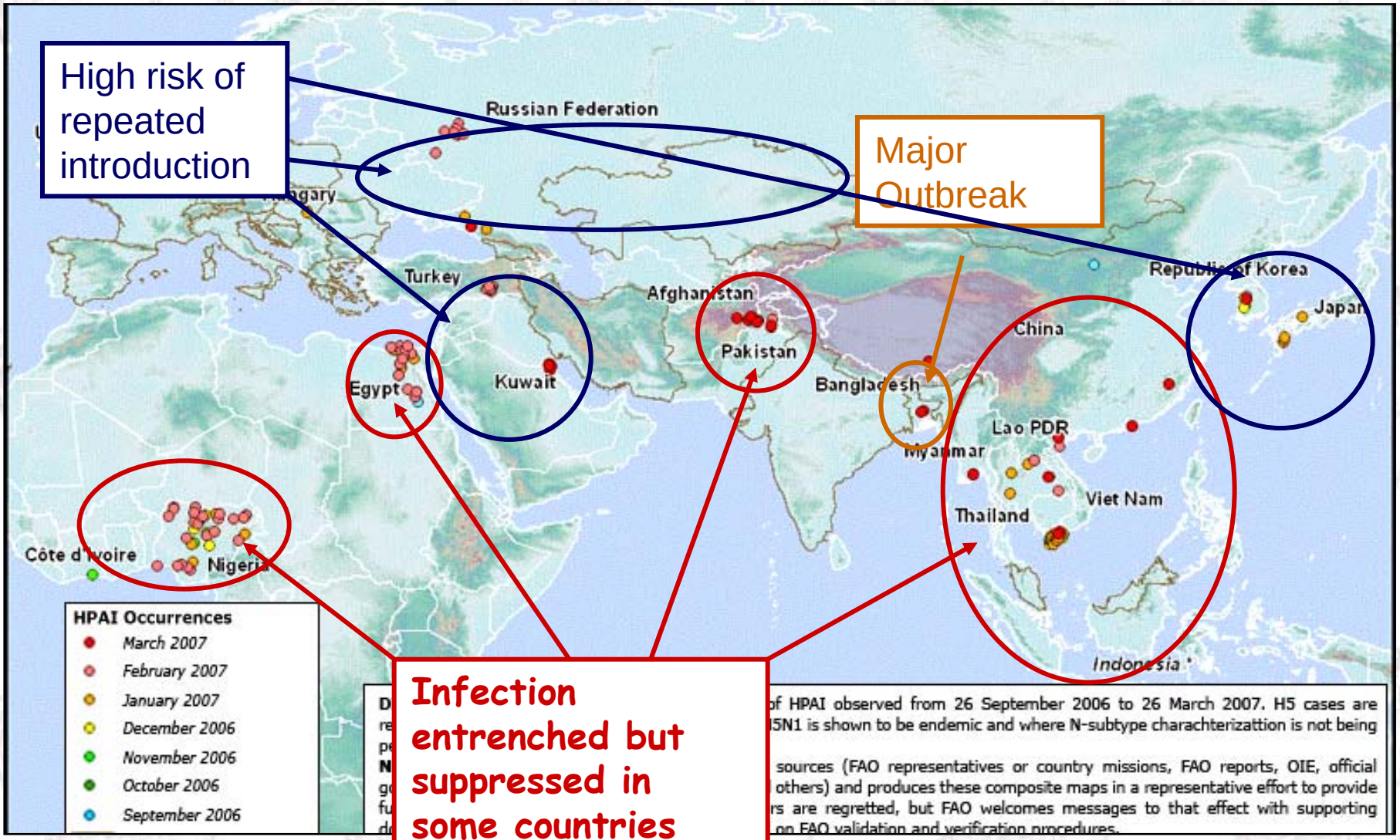
6. Africa – Feb 2006

7. Europe – Winter 2006

8. 28 countries 2007

- **60 countries with cases in wild birds and/or poultry**
- **Over 250 million birds dead or culled since Jan. 2004 (FAO)**
- **Eradicated of HPAI have occurred, but reintroductions have occurred in Japan, S. Korea, Malaysia and Thailand**

Summary of Status in 2008



Status in 2008

1. Sector 1 – Industrial Sector
   a. Concentrated production – high populations
   b. Vaccination and biosecurity practices vary
   c. Best control and even eradication from compartment

Poultry Production Features

2. Sectors 2 and 3 – commercial but not integrated industrial
   a. Biosecurity is limited
   b. Movement controls and veterinary care variable to minimal
   c. Re-infections are common place

Poultry Production Features

3. Sector 4:Native Chickens

- Lack of movement controls
- “Syndromic surveillance”
- Adequate vaccination coverage is a challenge
- Illegal production

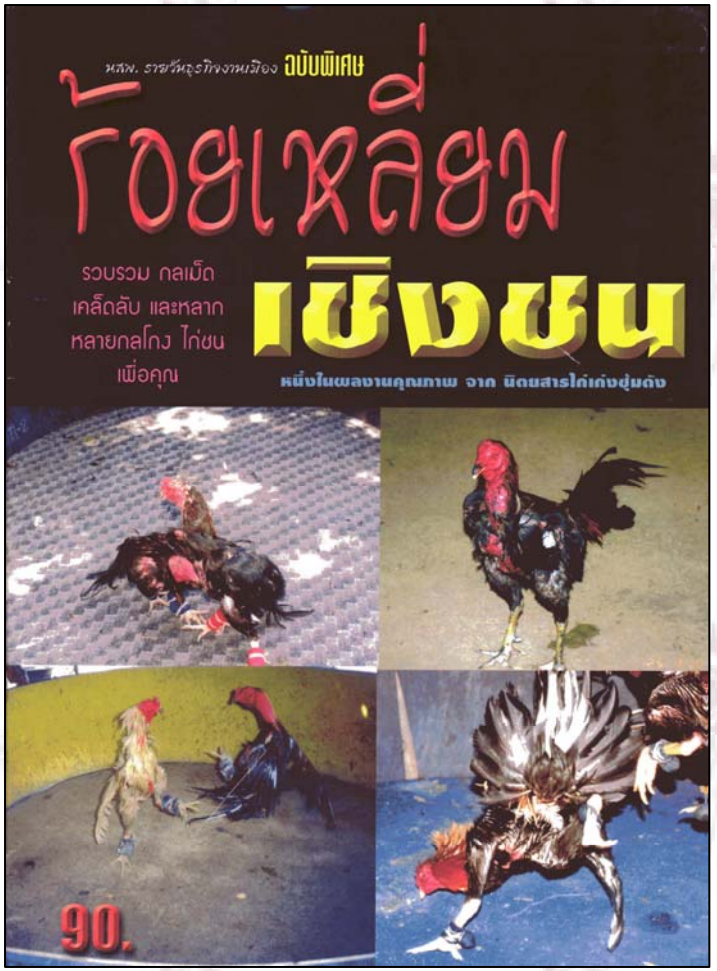
Poultry Production Features

4. Sector 4 - Fighting cocks

a. Movement over great distances

b. Variable biosecurity

c. Minimal movement controls

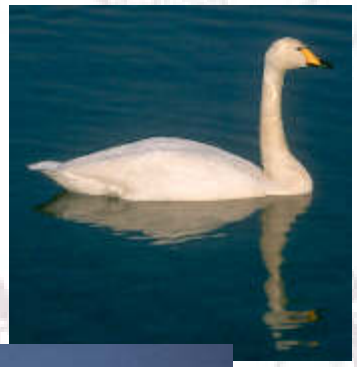


Poultry Production Features

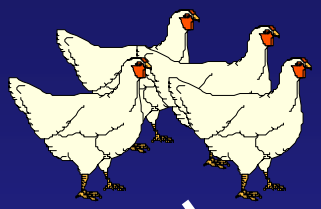
5. **Sector 4 – Domestic Ducks and Geese**
   - **1° Outdoor reared**
   - **Asymptomatic infection**
   - **Major reservoir and biomass issue**

Role of Free-Living Aquatic Birds

6. **Infected free-living aquatic birds**
   - **Major outbreaks in 2005 and 2006**
   - **Fewer infections and disease in 2007**
     - **Swans, geese and ducks**
   - **Reservoir verses re-infection from infected domestic poultry?**



Sources for Poultry

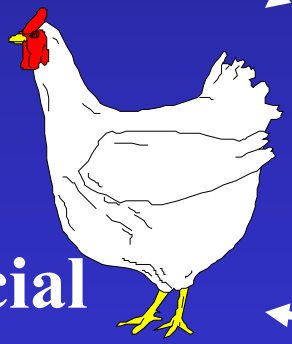


Infected Commercial Poultry

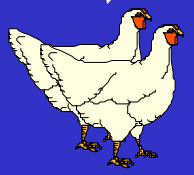
Wild waterfowl

Domestic Ducks

Clothing, shoes & equipment (Mechanical)



Naïve Commercial Poultry



Village Poultry

Disease Control Basics

- **Strategies for dealing with poultry disease are developed to achieve one of 3 goals or outcomes:**
  - *Prevention*: preventing introduction
  - *Management (Control)*: reducing losses by minimizing negative economic impact through management practices
  - *Eradication*: total elimination
- **These goals are achieved through various strategies developed using universal components:**
  - Biosecurity (exclusion and inclusion) including quarantine
  - Diagnostics and surveillance
  - Elimination of AI virus infected poultry
  - Decreasing host susceptibility to the virus (vaccines and host genetics)
  - Education

Swayne, Dev. Biol. Basel 119:219-228, 2004

Avian Influenza Vaccines: Poultry

- **Protection: Humoral Immunity**
  - **Anti-hemagglutinin antibodies are protective**
  - **Anti-neuraminidase also protective, less effective**
- **No single universal vaccine for AI viruses**
- **The practice of vaccination varies**
  - **Not routine in developed countries – targeted vaccination**
  - **Maybe routine in parts of developing countries; e.g. H5N1 HPAI and H9N2 LPAI**
- **Issue: Reports of inconsistent field protection by AI vaccines usually related to vaccine quality and appication**

Avian Influenza Vaccines: Poultry

Categories of Vaccine Technologies

1. **Inactivated whole AI virus (C,E)**
2. ***In vitro* expressed HA protein: (E)**
   - **Eukaryotic tissue cultures (plant and animal), plants, yeast, bacteria and viruses (e.g. baculovirus (E), vaccinia (E), adenovirus (E))**
3. ***In vivo* expressed HA protein:**
   - **Viruses and bacterial vectors**
   - **Fowl Poxvirus (C), Adenovirus (E), VEE (E), ALV (E), ILT (E), NDV (C,E), AI-NDV chimera (E), ΔaroA Salmonella (E)**
4. **Naked Nucleic acids – cDNA HA gene (E)**

Avian Influenza Vaccines: Past

- **LPAI -**
  - **Waterfowl - origin viruses:**
    - **Meat turkeys, MN USA: 22 million doses over 20 years, 1978-1997**
    - **Turkeys & chickens, Italy (2002-2006) - 202 million doses (Marangon, 2007)**
  - **H1N1, H1N2 and H3N2 swine influenza: turkey breeders, ex. 2.6 million doses USA 2001**
  - **H9N2 Middle East and Asia (late 1990s-present): billions? doses**
- **HPAI -**
  - **Mexico, Guatemala & El Salvador (1995-2006) - H5N2: 1.8b doses inactivated & 2b doses Fowlpox recombinant**
  - **Pakistan (1995-07) – Trivalent H7, H5 and H9 inactivated**
  - **North Korea (2005) – H7N7 inactivated - layers**
  - **H5 inactivated (2002-7); usage in Hong Kong, Vietnam, Russia, Egypt & Indonesia; limited Holland and France**
  - **China (2004-2006) – 22.7 billion doses**

Example: AI Vaccines in Asia

1. **Inactivated vaccine strains:**
   - **A/turkey/England/N28/73 (H5N2) LPAIV**
   - **A/chicken/Mexico/232/94 (H5N2) LPAIV**
   - **A/chicken/Legok-Indonesia/03 (H5N1) HPAIV**
   - **A/turkey/Wisconsin/68 (H5N9) LPAIV**
   - **A/chicken/Italy/22A/1998 (H5N9) LPAIV**
   - **Two reverse genetic strains: H5 & N1 genes of A/goose/Guangdong/96 or Shanxi strain, 6 I. genes from PR8**
   - **Reverse genetic strains: H5 gene from A/chicken/Vietnam/C58/04 (H5N1), N3 gene from A/Duck/Germany/1215/73 (H2N3), & 6 internal genes of PR8**
2. **Recombinant fowlpox with cDNA inserts of AI viral genes: 1) H5 gene - A/turkey/Ireland/83, 2) H5 & N1 genes - A/goose/Guangdong/96**
3. **Recombinant Newcastle disease virus with H5 AI gene insert from A/BHG/Qinghai/3/2005 (H5N1)**

Laboratory Protection

- **Increased Resistance to AIV Infection**
  - **Requires 10^2 EID_{50} higher dose to infect vaccinated compared to non-vaccinated turkeys**
  - **Requires $>10^5$ EID_{50} higher dose to infect recombinant fowlpox vaccinated compared to non-vaccinated chickens**

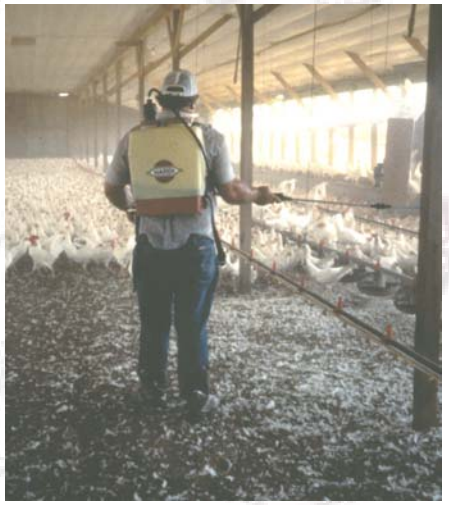
Laboratory Protection

- Prevent illness and death in birds
- Reduced replication of challenge virus in respiratory and intestinal tracts
  - Minimum – 10^2 EID_{50} reduction
  - Typical – 10^{3-5} EID_{50} reduction
- Prevents infection of meat, blood and bone
- Best vaccines protect from high challenge doses (10^{6-8} EID_{50})
- Translation:
  - Reduced environmental contamination
  - Reduced transmission

Swayne et al., Avian Pathology 35(2):141-146, 2006

Needs in the Next Generation of AI Vaccines

- **Mass immunization methods: water, feed, spray and *in ovo* administration**
- **Increase use of biotechnology to address genetic drift and antigen content of vaccines**
- **Vaccine combinations and protocols – e.g. AI and vector maternal antibody impact on immunization**
- **Improved adjuvants for inactivated AI vaccines in waterfowl**
- **Longer, enhanced immunity with few vaccinations**
- **Consistent quality for inactivated vaccines – including purity, safety, efficacy and potency**



Conclusions

1. 26 HPAI epizootics in last 50 years
2. Current H5N1 HPAI epizootic is the largest and larger than the other 25 combined
3. H5N1 epizootic began in China, spread to Hong Kong and other SE Asian countries by agricultural and trade practices
4. Less clear as to how it spread to eastern Asia, Middle East and Africa
5. Wild bird involvement with spread to Europe
6. Domestics ducks have emerged as the primary reservoir in developing countries

Conclusions

7. **Humoral immunity to HA is the primary protective response**
8. **Three vaccine technologies used in the field: inactivated AIV, rFPV-AIV-H5 and rNDV-AIV-H5**
9. **Protection related to:**
    1. **Prevention of disease and death**
    2. **Reduced virus replication and shedding**
    3. **Prevention or reduction in transmission**

Thank You For Your Attention!