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HIGHLY PATHOGENIC AVIAN INFLUENZA:

CHALLENGES ENCOUNTERED AND MEASURES FOR PREVENTING ITS SPREAD

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***Summary**: In December 2014, highly pathogenic avian influenza (HPAI) was detected in the United States for the first time in over 10 years. From 11 December 2014 to 16 January 2015, the US Department of Agriculture (USDA) received a total of seven reports of HPAI H5N2 or H5N8 in captive wild birds and backyard flocks from the northwestern United States. Additional detections occurred in wild birds. The first infected commercial flock was identified on 23 January 2015, in California. From January to March 2015, the disease spread slowly to multiple states, including Minnesota, Missouri, Arkansas, and Kansas. A significant increase in HPAI H5N2 in turkey flocks occurred through early April in Minnesota, followed by a rapid increase in Iowa during late April and throughout May where large numbers of table-egg layer flocks were affected. The last case of HPAI was confirmed on 16 June 2015.*

In total there were 211 detections in commercial operations and 21 detections in backyard premises. HPAI was detected in commercial premises, backyard flocks, wild captive birds, and/or wild birds in 21 States (Arkansas, California, Iowa, Idaho, Indiana, Kansas, Kentucky, Michigan, Minnesota, Missouri, Montana, North Dakota, Nebraska, New Mexico, Nevada, Oregon, South Dakota, Utah, Washington, Wisconsin, and Wyoming). Approximately 7.4 million turkeys and 43 million egg-layers/pullet chickens were affected and died from the disease or were depopulated as part of the response activities. On 18 November 2015, the United States sent a final report to the World Organisation for Animal Health (OIE) and declared the event closed. Over USD 850 million was paid out for response activities and indemnity payments. Another USD 100 million was expended for further preparedness efforts. This outbreak was the most expensive animal health incident recorded in the United States.

Depopulation, disposal, and virus elimination activities posed significant challenges due to the number of affected premises and the number of affected birds. Foaming was the most common method of depopulation, composting the most common method of disposal, and wet disinfectant the most common mode of virus elimination.

***Keywords:** Americas – highly pathogenic avian influenza.*

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1. Nature of the disease

Avian influenza (AI) is a viral respiratory disease that infects all avian species. AI is a common disease, but the virus frequently changes or mutates. Based on the severity of illness, the AI is classified as either highly pathogenic avian influenza (HPAI) or low pathogenicity avian influenza (LPAI). AI viruses are named by two groups of proteins, hemagglutinin ([HA] ranging from H1–H17) and neuraminidase (ranging from N1–N9), e.g. H5N2 or H5N8.

In natural environments, HPAI viruses have always contained an H5 or H7. HPAI tends to cause high mortality in domestic gallinaceous species (e.g. turkeys and chickens). Depending on the species and subtype of the virus, it may or may not cause severe illness in wild birds. Some HPAI viruses also cause illness in humans and other mammals. Common AI signs in birds include decreased food and water consumption, coughing, sneezing, and decreased egg production. HPAI infections may also cause sudden death, lack of energy, production of soft or deformed eggs, swelling (of head, eyelids, comb, wattles, and/or hocks), purple discoloration (of wattles and/or comb), nasal discharge, loss of coordination, and/or diarrhoea. Transmission of HPAI typically occurs through direct contact with infectious respiratory secretions and faeces. Viral spread via indirect contact with contaminated equipment and supplies (also known as fomites) is also common.

2. Prior outbreaks in the United States

LPAI is commonly found in wild birds with occasional introductions into domestic poultry flocks. However, in countries considered to have developed veterinary infrastructure and advanced animal agriculture industries, HPAI is not frequently detected in commercial poultry.

Historical summary of HPAI outbreaks in the United States is provided in Table I.

Table I – HPAI outbreaks in the United States

Year(s)	Subtype
1924	H7
1927	Unknown
1983–1984	H5N2
2004	H5N2
2014–2015	H5N8, H5N1 (wild birds only), H5N2
2016	H7N8

3. Scope of the 2014–2015 outbreak

HPAI viruses were detected in commercial poultry, backyard flocks, captive wild birds, and wild birds in 21 States during the outbreak. There were 211 commercial premises affected in 9 States (Fig. 1); 11 States had infections in backyard flocks, with 21 affected premises (these numbers include Dangerous Contact Premises[2] that were also depopulated).

In total, for both commercial and backyard premises, approximately 43 million chickens (primarily layers or pullets), and 7.4 million turkeys died from the disease or were depopulated as part of the response and eradication effort. The outbreak primarily impacted turkeys, layer chickens (and pullets), and a limited number of game fowl. Most of these birds were affected by the HPAI H5N2 virus.

2 Dangerous contact premises are those directly epidemiologically linked to an infected premises and with a high probability of also becoming infected.

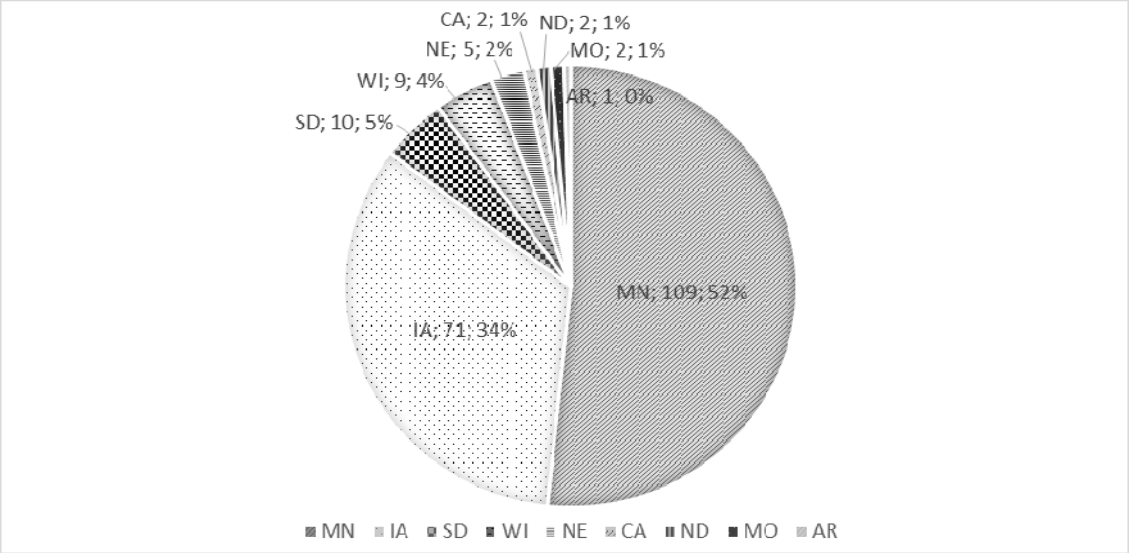

Fig. 1 – Number of affected commercial premises by State

The impact of the outbreak in terms of commercial inventories is shown in Table II.

Table II – Approximate percentage of US poultry affected in outbreak

Flock type	Percent losses
Layer chickens[a]	10.01% average US inventory
Pullet chickens	6.33% average US inventory
Turkeys	3.16% annual production; 7.46% average US inventory

[a] This includes flocks that were identified as 'commercial layers' and/or 'layer breeders.'

4. Disease incidence and epidemiology

In December 2014, HPAI H5N2 was identified in commercial poultry in the Fraser Valley region of southern British Columbia, Canada. Soon after, samples were collected from wild birds in the United States. Combined with mortality events associated with captive wild raptors, the test results from these samples showed that there were at least two HPAI virus strains in circulation: H5N2 and H5N8. For these first detections, migratory birds from the Pacific Flyway were the most likely source of introduction. The H5N2 virus was a reassortment of the Eurasian H5N8 HPAI virus (that was also detected) and a North American LPAI strain.

On 11 December 2014, HPAI H5N8 was detected in a captive wild bird, and from December to the end of March 2015, 82 wild bird samples tested positive for H5 HPAI. Additionally during this same time period, 14 backyard flocks or captive wild birds tested positive for H5 HPAI in six States (Idaho, Kansas, Missouri, Montana, Oregon and Washington). Evidence suggested that these detections were point-source introductions.

In commercial birds, the first occurrence of HPAI was of the H5N8 virus in a California turkey operation on 23 January 2015. From January to the end of March, 9 (8 infected and 1 dangerous contact) commercial turkey premises were found positive for H5 HPAI in four States (Arkansas, California, Missouri and Minnesota). Again, these introductions were believed to be point-source. However, by mid-April, 36 additional HPAI-Infected Premises (and some Dangerous Contact Premises) were detected; 26 of these were in Minnesota and hypothesized to be infected due to lateral spread of the virus. Other States affected by mid-April were Iowa, North Dakota, South Dakota, and Wisconsin. Fig. 2 illustrates the first detection, by flock type, in each State (e.g. first commercial detection in the State and first backyard detection in the State; captive wild bird detections are also illustrated). This is shown by the date of National Veterinary Services Laboratories (NVSL) confirmation.

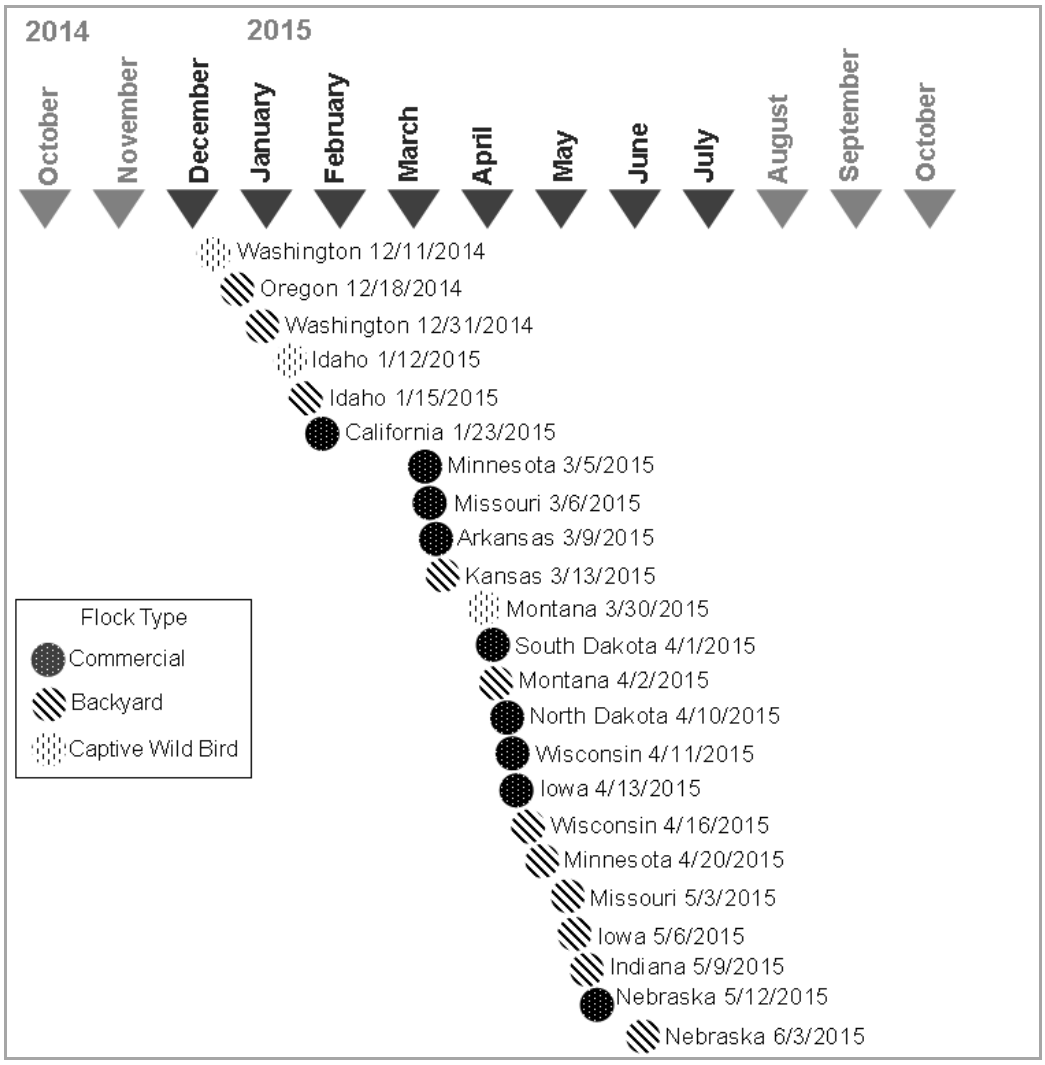

Fig. 2 – First detection by flock type in each State by NVSL confirmation date

On 11 April 2015, HPAI was detected on a layer premises in Wisconsin. Then, on 18 April 2015, the first chicken layer premises in Iowa was identified as H5N2 HPAI positive; this premises housed over 4 million birds. At this point, detections increased dramatically: 188 of the 211 total commercial detections occurred in the upper Midwest in April and May. These detections are illustrated, by bird type, in Fig. 3.

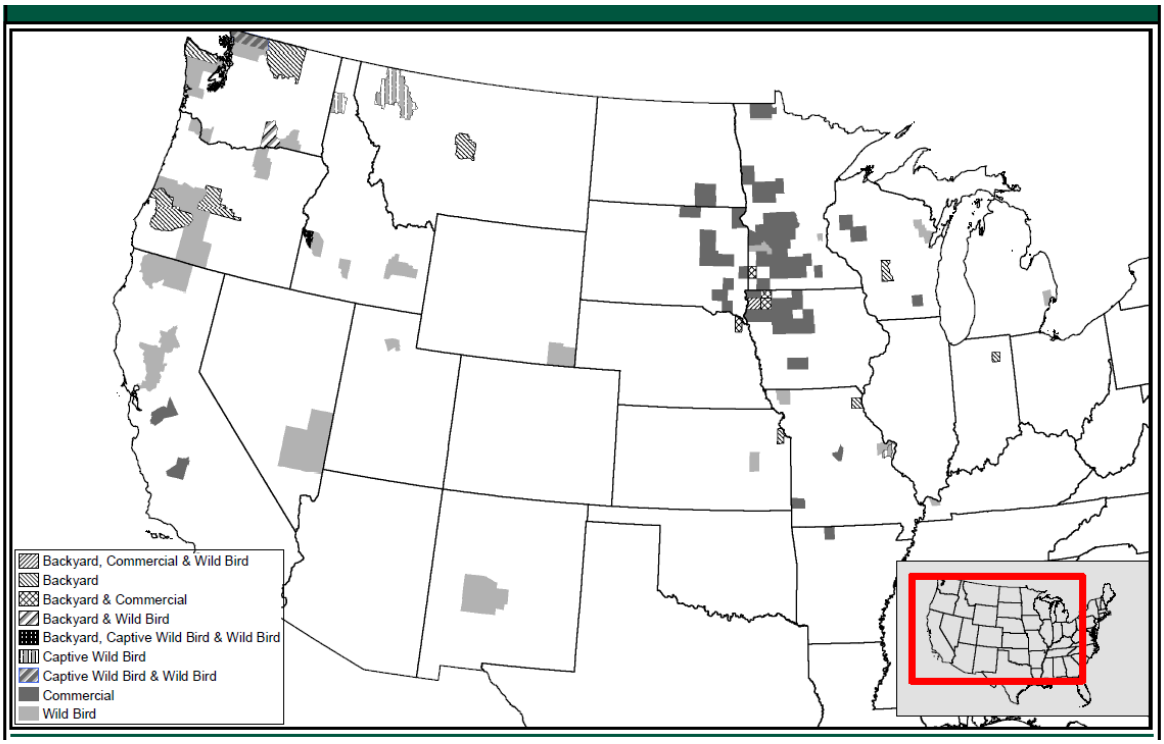

Fig. 3 – Map illustrating HPAI detections in the United States

For wild birds, between December 2014 and June 2015, there were 98 detections of H5 influenza (65 of these were sequenced; 33 were based on molecular detection though no virus was isolated). Over 7,000 wild birds were sampled, predominately in the Mississippi and Pacific flyways (29% and 48% of total samples, respectively). However, samples were also collected from the other flyways. No positive sample was detected along the Atlantic Flyway, and only two positive samples were detected in the Central Flyway.

Figure 4 shows the epidemiological curve, which was typical for a highly contagious disease outbreak, with few detections each week until an increase in cases was seen beginning in early April. The last case was detected on 15 June 2015, confirmed as H5 by NVSL on 16 June, and sequenced as H5N2 on 17 June 2015. The reduction in cases was likely due to both control measures and the onset of summer heat, which helps to inactivate AI viruses.

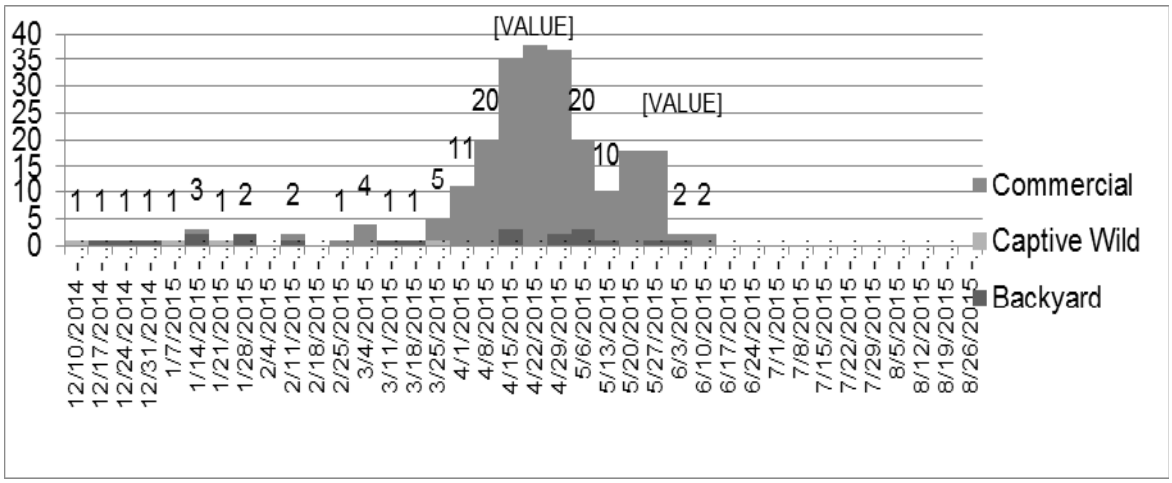

Fig. 4 – Total incidence of HPAI in the United States by week. Date pictured is earliest available date indicating clinical signs. This is a clinical sign date if known, a suspect status, or a presumptive positive status. Some premises may only have a confirmed positive status date.

5. Surveillance and epidemiology

Routine surveillance and investigations led to the initial detection of HPAI in December 2014 and January 2015. When a positive HPAI flock was detected, a 10 kilometer Control Area was established around the premises. As part of the epidemiological investigation, all movements on and off Infected Premises (known as trace-backs and trace-forwards) were identified and evaluated for the possibility of HPAI transmission. Additionally, after a Control Area was established, both backyard and commercial flocks were placed under active surveillance.

Within the first six months of the outbreak, field-based observational studies of farm biosecurity, management practices, and exposure risks were conducted. There were also geospatial analyses examining correlations between wind patterns and disease spread as well as phylogenetic analyses. Epidemiologists led the survey and interview process in the field to gather information from the premises. In addition, they conducted diagnostic sampling for disease detection on both commercial and backyard operations.

Table III provides summary information on the number of samples tested for both commercial and backyard flocks as well as additional surveillance conducted during the outbreak in wild birds.

Table III – HPAI outbreak response testing summary (number of samples)

Domestic bird testing (commercial and backyard)	Matrix PCR tested	H5 PCR tested	H7 PCR tested	Virus isolation tested	Total Tests
14 NAHLN Laboratories	72,314	2,772	2,675	1,366	79,127
NVSL	2,825	4,688	1,149	1,105	9,767
Total	75,139	7,460	3,824	2,471	88,894

Wild bird testing	Matrix PCR tested	H5 PCR tested	H7 PCR tested	Virus isolation tested	Total Tests
9 NAHLN Laboratories	42,259	6,234	6,138	0	54,631
NVSL	252	1,407	650	797	3,106
Total	42,511	7,641	6,788	797	57,737

Abbreviations:
NAHLN: National Animal Health Laboratory Network
NVSL: National Veterinary Services Laboratories
PCR: polymerase chain reaction

6. Quarantine, movement control, and continuity of business

State quarantines were placed on all Infected Premises and Dangerous Contact Premises. State quarantines were also frequently placed on premises inside an Infected Zone as a preventive measure to halt the spread of the virus, even if that premises was not infected. The majority of the premises had quarantines lasting between 100 and 175 days.

In a regulatory Control Area, permits were required for movement into, within, and out of a Control Area. Items permitted during the outbreak included those for both continuity of business (e.g. poultry products) and for movement control (e.g. the movement of feed or manure) to prevent the spread of HPAI to non-infected premises. Movements (for either continuity of business or movement control) were to processors, landfills, slaughter establishments, hatcheries, renderers, and other destinations.

These movement controls successfully kept animals and products moving during the outbreak, demonstrating successful collaboration between States (both sending and receiving product) and the federal authorities. Typically, depending on the movement, two negative rRT-PCR tests (real-time reverse transcription PCR tests) were required, with one test within 24 hours of movement.

7. Depopulation

Depopulation (also referred to as stamping-out) was implemented throughout the 2014–2015 HPAI outbreak to prevent or mitigate the spread of disease. Depopulation was implemented immediately after the first infected premises was detected and continued throughout the outbreak. Of the 232 Infected Premises detections (211 commercial and 21 backyard), and 7 Dangerous Contact premises, more than 50 million birds were depopulated.

There were significant challenges in rapidly depopulating flocks in a timely manner as the outbreak progressed. At the height of the backlog from late-April to mid-May, there was a depopulation delay of at least 7 days for newly detected premises. USDA addressed this shortage by deploying additional personnel and resources, with personnel and equipment.

The primary methods used for depopulation during the response included the application of foam or carbon dioxide (CO_2) gas. Foam was the preferred method to depopulate turkeys. In many chicken layer houses, the use of foam was problematic and other measures had to be employed. Techniques for CO_2 'whole house' gassing had not yet been developed, requiring smaller CO_2 gas carts to be used for chicken layer depopulation, which is an extremely slow process on premises with hundreds of thousands or millions of birds. Seventy two percent of commercial premises used foam; 27% used CO_2. For backyard premises specifically, CO_2 was the method of depopulations that was most commonly used.

The average time from NVSL confirmation to depopulation complete for all premises was 6.2 days. Due to flock size and difficult conditions, on average, it took 15.4 days to depopulate commercial chicken layer flocks and 3.6 days to depopulate commercial turkey premises.

8. Disposal

There are many options for disposing of animal carcasses and materials. Effective disposal is a key component of a successful response to a foreign animal disease outbreak. During the 2014–2015 outbreak, the use of composting as a disposal method was critical. Composting was the most effective and efficient way to dispose of carcasses.

As with depopulation, disposal requirements outpaced available resources at the height of the outbreak. Other options were considered and used to a lesser extent in the outbreak, including landfill, incineration, and burial (Fig. 5). As an additional option, USDA acquired four incinerators to augment disposal operations; however, incinerators could not keep pace with the capacity required.

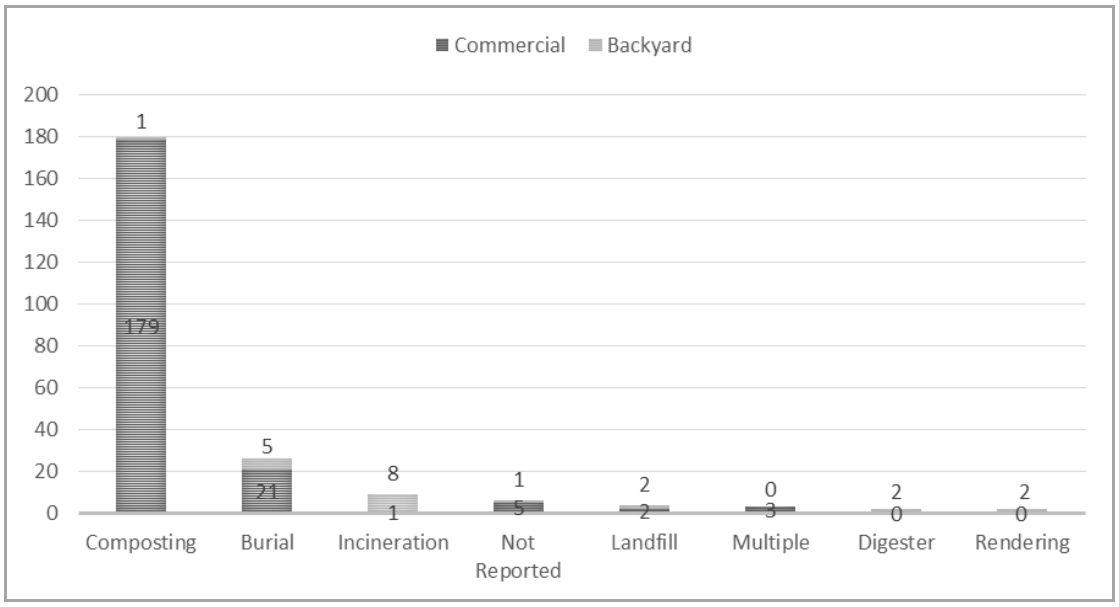

Fig. 5 – Primary disposal method for carcasses (commercial and backyard), excludes dangerous contacts

9. Virus elimination (cleaning and disinfection)

The HPAI virus survives for extended periods in organic material and under certain environmental conditions. As such, virus elimination activities – to get rid of the virus on Infected Premises – were critical for an effective response effort. While traditionally wet cleaning and disinfection has been performed in most disease incidents, this incident showed that dry cleaning and subsequent heat treatment of the affected facility was a cost effective method to ensure the elimination of the virus.

As with depopulation and disposal, virus elimination activities required rapid contracting to obtain additional personnel for the response efforts. As seen in Fig. 6, application of wet disinfectant was by far the most common method of virus elimination, used by 87% of commercial premises, followed by heat treatment which was used by 10% of premises. Of the backyard flocks, 9 of 21 flocks (43%) elected to complete an extended fallow period instead of other virus elimination procedures.

To be able to restock a farm with poultry again, owners had to have completed cleaning and disinfection (C&D) and virus elimination procedures 21 days prior to requesting permission to restock, completed environmental sampling with no evidence of HPAI (using PCR and/or virus isolation testing), met the requirements of the official plans, and have written approval from State and Federal authorities.

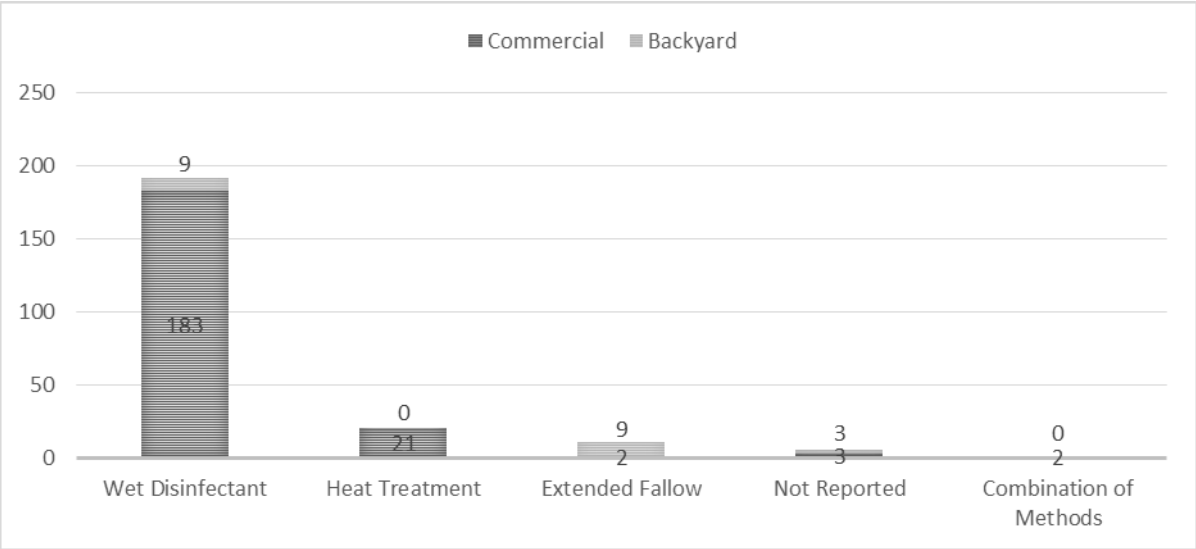

Fig. 6 – Disinfection method used (commercial and backyard)

10. Viral traits

The traits of this HPAI H5N2 virus that spread throughout the Midwest was in many ways consistent with the typical profile of HPAI. This virus was highly pathogenic in poultry and caused signs consistent with the genetic profile of an HPAI virus. However, additional research identified a few unique characteristics of the virus. For instance, based on the epidemiological investigation, incubation periods were estimated at between 3 to 11 days for this outbreak (3 to 5 days is typical with HPAI viruses). Additionally, the H5N2 virus circulating in the 2014–2015 outbreak appeared to be more virulent and better adapted to infect turkeys than chickens [1].

Phylogenic studies indicated that this H5N2 virus was genetically very similar to other HPAI strains circulating in the United States, however it also had an HA protein derived from the HPAI Eurasian H5N8 virus [2]. This specific H5N2 virus represented a reassortant combination of that H5N8 virus and an LPAI virus of North American origin. According to this research, the virus did not contain molecular markers commonly associated with antiviral resistance or increased transmission and virulence in mammals, which indicated that this virus likely posed a low risk to humans. Tests to monitor genetic changes continued during the outbreak [3].

11. Transmission

Epidemiological investigations and other analyses indicated that there were multiple pathways of introduction and HPAI transmission. Sharing equipment between farms, entry of wild birds into barns, and unmonitored movement of farm workers/visitors all were likely to have contributed to virus spread. Other possible pathways included short-distance aerosol spread, carcass disposal techniques, and other biosecurity breaches. Both common source exposures and independent introductions contributed to the spread of the H5N2 in the United States.

While specific risk factors for infection were identified, there was no sufficient evidence to point to a single pathway for the spread of the virus [6]. Anecdotally, there was much discussion over whether airborne spread was responsible for virus transmission. While it is possible that aerosol transmission was responsible for disease spread, the epidemiological analysis was 'not able to determine with certainty whether aerosol transmission was responsible for a farm becoming infected.' [7].

12. Biosecurity

One of the greatest concerns and a probable contributing factor to the spread of HPAI was the lack of effective farm biosecurity measures. Stringent biosecurity, especially during a large-scale response, remained one of the most challenging aspects of the response effort. Written guidance and materials were provided to affected owners and producers on proper biosecurity practices. Emphasis was placed on ensuring farm-specific and flock-specific biosecurity plans, with adequate compliance checks.

USDA helped by carefully monitoring and auditing biosecurity practices on premises where response operations were underway. In addition, all States that were affected by the 2014–2015 HPAI outbreak implemented one or more changes at the State-level to increase biosecurity. As a result of the 2014–2015 outbreak, many new biosecurity materials were developed for the poultry industry to support implementation of revised biosecurity recommendations. These materials are available from www.poultrybiosecurity.org.

13. Vaccination

While vaccination was not used during this outbreak, USDA/APHIS does allow for H5 and H7 vaccines to be used as a tool for combating any potential outbreak of HPAI. The policy supports that vaccination be available as part of a science-based influenza control strategy. Such a vaccination strategy would include enhanced biosecurity, controlled vaccination of flocks deemed to be a risk, monitoring of all flocks at risk, and of all vaccinated flocks, and a repopulation plan. Factors to be considered for any decision to vaccinate include:

- the probability that the disease cannot be rapidly contained;
- the proximity of high value genetic birds;
- the poultry density in the area;
- the prevalence of the disease in other environments (live bird markets, wild birds, backyard flocks);
- the availability of physical and economic resources.

Use of the vaccine would be strictly controlled and applied over a limited area for a limited time period. Valuable zoological collections in a geographic area where emergency vaccine is used would also be considered for a protective vaccination strategy.

14. Economic and trade impact

In addition to response and indemnity payments, the HPAI outbreak had a very significant economic impact. To provide perspective to the overall magnitude of this outbreak, estimates show that the 2014–2015 HPAI incident resulted in about USD 1.6 billion in direct losses from turkeys and chicken layers that had to be euthanized. When accounting for factors like restocking and lost future production, the impact to the US economy is closer to USD 3.3 billion (4).

As a result of HPAI, consumers experienced wholesale egg prices reaching nearly USD 2.80 per dozen, more than doubling the previous three-year average cost of large eggs. Although prices continually decreased throughout the remainder of 2015, costs were sustained above the three-year average [5]. The economic impact was also related to trade bans imposed by trading partners. While the United States lost 18 trading partners – particularly several countries in Asia – valued at USD 898 million in 2014 (or 13.9% of the year's total trade revenue), the United States worked with many of its trading partners to maintain trade or limit the restrictions. Thirty-eight countries regionalized the United States during the outbreak, which allowed trade to continue from areas of the United States that were not affected. This helped preserve 86% of the value of traded US poultry and poultry products (including eggs), based on 2014 values.

15. Conclusion

With 232 affected premises and over 50 million affected birds, the scale of the 2015 HPAI outbreak was unprecedented in US history. The response effort involved over 3,000 Federal, State, and contracted personnel at an expense of USD 850 million (for indemnity payments and response activities). Control measures, coupled with an increase in warm weather, ultimately interrupted HPAI transmission leading to a halt of new cases in June 2015.

USDA had prepared the organization and its employees for HPAI through training and exercises. However, the scale of this outbreak grew rapidly and response activities – in particular depopulation and disposal – could not keep pace with new HPAI detections during the height of the incident. An Incident Coordination Group was rapidly established at the start of the outbreak to coordinate resources and provide policy guidance, and was significantly expanded to handle the demands of the outbreak.

Many lessons were learned during the outbreak, in particular that depopulation needed to occur more rapidly to stop the amplification of virus and ongoing transmission. Financial processes were cumbersome and time consuming. Additionally, biosecurity measures needed strengthening on premises to not only stop HPAI transmission during the outbreak, but prevent HPAI introductions into commercial poultry flocks in the future. Policy guidance documents on alternate depopulation methods, heat treatment for virus elimination, and financial processes were developed to address the challenges encountered during the response activities. New biosecurity guidance was developed collaboratively by the industry, State, and Federal officials for implementation by producers.

The last HPAI positive premises of the 2015 HPAI outbreak was confirmed by NVSL on 16 June 2015. However, given the migratory patterns in the United States, and although it did not occur, there was significant concern that HPAI would reemerge during the fall of 2015. The United States continues to engage all stakeholders to prepare for another event, using the lessons learned during the 2014–2015 outbreak to improve operations and coordination in the field.

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