Current Status and Future Needs in Diagnostics and Vaccines for High Pathogenicity Avian Influenza

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# 31 HPAI Epizootics Since 1955

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
19. 1999-2000: Italy, H7N1
20. 2002: Chile, H7N3
21. 2003: Netherlands/Belgium/Germany, H7N7
22. 2004: USA, H5N2
23. 2004: Canada, H7N3
25. 2005: N. Korea, H7N7
26. 2007: Canada, H7N3
27. 2008: England, H7N7
28. 2009: Spain, H7N7
29. 2011: S. Africa, H5N2 (Ostriches)
30. 2012: Chinese Taipei, H5N2
31. 2012: Mexico, H7N3

*Larger than the other 30 combined
*§Vaccine used in the control strategy
Eradication Strategies

Components:

• Education (including behavioral change communications)
• Biosecurity (including modifications to the way poultry are reared and sold, movement management, and cleaning and disinfection)
• Diagnostics and surveillance
• Elimination of infected poultry
• Decreasing host susceptibility (vaccines/vaccination & genetics resistance in host)
Avian Influenza Virus Diagnostic Overview

**Active infection**
- Virus detection
  - Type A influenza
    - Real-time RT-PCR
    - Virus isolation
    - Antigen immunoassays

**Suspected infection or surveillance target**
- **Antibody detection**
  - Type A specific ELISA
  - AGID
  - HA subtype specific HI assay

**Prior exposure**
- Antibody detection
  - Type A specific ELISA
  - AGID

**Subtype Identification**
- Real-time RT-PCR
- Serological tests (HI and NI)
- Gene sequencing

**Pathotype classification**
- In vivo assay
- Gene sequencing

**H5 or H7**

**Highly pathogenic**
- Low pathogenic
AIV Testing in Poultry

• Flock based, not individual
• Often for trade
  – Programs defined by regulatory bodies
    • National Poultry Improvement Plan (USA), OIE (International)
  – Impact of inaccurate test results can be especially devastating
    • False positives can prompt trade restrictions (which can be levied against the entire country, not just affected regions)
    • False negatives can result in delays in implementing control measures
AIV testing in poultry

• Poultry is a low profit-margin industry, cost will be a major factor in whether a test can be implemented
  – Many current tests are public domain
  – Market for commercialization limited (unless it saves time and money versus current methods)

• Many innovations in influenza tests reported for public health applications are not appropriate for poultry use

• Many innovations in influenza testing reported for experimental poultry or veterinary use are not appropriate for regulatory poultry use
  – Not practical for a diagnostic lab (research labs ≠ diagnostic lab)
  – Not validated
The “perfect” diagnostic test

- Fast
- Cheap
- Simple
- Robust
- Sensitive
- Specific
- Scalable
- Practical for workflow
- Validated

Fulfills “fit for purpose”
Influenza Type A Specific Tests

• Current type specific tests
  – rRT-PCR
  – Virus isolation
    • Will not be replaced: isolates needed for confirmation and characterization
  – Antigen detection immunoassays
• Adequately sensitive and specific for defined use
• Needs (beneficial, but not critical) :
  – Method (e.g. media) of stabilizing the virus when the cold chain can not be maintained
  – Rapid, low complexity penside test (e.g. antigen immunoassay, nucleic acid assay) with sensitivity similar to virus isolation and rRT-PCR
Subtype identification

- Current tests
  - Serology: hemagglutination inhibition and neuraminidase inhibition
    - Cumbersome, expensive reagents, difficult to interpret (specificity inconsistent), but relatively fast
  - Gene sequencing
    - Highly accurate, but slow; More difficult with variants

- Needs (critical): Rapid, highly accurate method of subtyping
  - Sequencing platform
    - Must be able to: amplify and sequence unknown HA and NA templates but not host and adventitious RNA
    - The problem is with producing template, not the sequencing process
  - Antibody based platform
    - Improve specificity of reagents and reduce cost of producing the reagent sets
Pathotype Identification for H5 and H7 Subtype

• The pathotype classification of “high” or “low” pathogenicity notifiable AIV in gallinaceous poultry is a regulatory definition

• Two pathotyping tests are used:
  – *In vivo* testing (in chickens)
    • Accurate and biologically relevant, resource intensive, slow
  – Gene sequencing to determine if molecular markers for pathogenicity in the HA gene are present
    • Relatively rapid, not accurate from a biological perspective
    • The molecular markers in the regulatory definition are not definitive biologically (high PPV)

• Needs (important, but not critical)
  – Rapid, inexpensive method of pathotyping, which fulfills the regulatory needs of the OIE
  – Any change would require regulatory changes
Serology: Tests for Antibody to AIV

• Serology for AIV is primarily used in trade; demonstrate freedom from infection or have never been exposed to the virus

• Type A influenza specific tests (chickens and turkeys)
  – ELISA - commercial kits available
  – Agar gel immunodiffusion (AGID)

• Needs (important, not critical)
  – Validated indirect ELISA assay for chickens so that AGID is not longer needed as a confirmation test
  – Validated blocking ELISA with sera from additional domestic poultry species (e.g. ducks, geese, ostriches, etc.)
Serology: Subtype Specificity of Antibody

• Subtype specific
  – Hemagglutination inhibition assay
  – Neuraminidase inhibition assay

• Needs (critical, highest priority)
  – A test to accurately identify the subtype specificity of type A positive sera from poultry.
    • Difficult to accurately determine which HA subtype a type A positive sera sample is directed against
    • Identifying sera to H5 and H7 AIV critical
    • Possible solutions could involve developing better reagents for HI assay
Epizootic Metrics

Timeline HPAI:

Traditional stamping-out (26)

Vaccination included (5)

- 24 epizootics, < 1 year
- 26 epizootics used comprehensive control programs with stamping-out; mostly leading to eradication
- Vaccination added as a component with 5 epizootics
  - There is no “one control strategy”
- Vaccination used as a tool to reduce infection pressure, allow food security (poverty prevention), control of the disease, and development of infrastructure to eradicate
H5N1 HPAI

• H5N1 HPAI panzootic is unique:
  – 16 yrs of outbreaks, 9 yrs of multi-country control experience, multiple introductions into some countries and wild bird involvement
  – Affected 63 countries, > 250 million poultry dead or culled: 1) 13 countries w/vaccine, and 2) 50 countries w/o vaccine

• Successes:
  – Eradication in 57 countries. What did they do “right”? 
  – Reduction in number of outbreaks in poultry, reduced time to eradication & reduction in projected rate of human cases
  – Progressive re-definition of the role of vaccines and vaccination as tools in a comprehensive control program

• Issues:
  – Vaccines – quality, potency and seed strain matching
  – Vaccination – application, logistics and field program goals
# Vaccine Technologies

<table>
<thead>
<tr>
<th>Vaccine Category</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated AIV</td>
<td>Adjuvanted whole avian influenza virus*</td>
</tr>
<tr>
<td>Live AIV</td>
<td>Live wild-type LPAI virus</td>
</tr>
<tr>
<td></td>
<td>Attenuated LPAI virus</td>
</tr>
<tr>
<td>Live Vector</td>
<td>rd-Adenovirus</td>
</tr>
<tr>
<td></td>
<td>Avian leukosis virus</td>
</tr>
<tr>
<td></td>
<td>Avian paramyxovirus type 1 (rNDV)*</td>
</tr>
<tr>
<td></td>
<td>Duck enteritis virus (rDVE)</td>
</tr>
<tr>
<td></td>
<td>Fowlpox virus (rFPV)*</td>
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<tr>
<td></td>
<td>Herpesvirus Turkey (rHVT)*</td>
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<tr>
<td></td>
<td>Infectious laryngotracheitis virus vector</td>
</tr>
<tr>
<td></td>
<td>att-Salmonella typhimurium</td>
</tr>
<tr>
<td></td>
<td>Vaccinia</td>
</tr>
<tr>
<td></td>
<td>rd-Venezuelan Equine Encephalitis virus</td>
</tr>
<tr>
<td>In vitro Produced</td>
<td>Baculovirus in insect cell culture</td>
</tr>
<tr>
<td>Hemagglutinin</td>
<td>Eukaryotic systems (plants or cells cultures)</td>
</tr>
<tr>
<td>DNA</td>
<td>Naked DNA</td>
</tr>
</tbody>
</table>
What can Vaccines/Vaccination do?

- Increase resistance to AIV infection
- Reduce replication of AIV in respiratory & GI tract
- Prevent illness and death in poultry
  - Reduced environmental contamination
  - Reduced transmission to birds
  - Reduced human exposure and infections
- Maintained livelihood and food security of rural poor

What can Vaccines/Vaccination not do?

- Eradicate
## Ideal AI Vaccine Properties

<table>
<thead>
<tr>
<th>Desired Property</th>
<th>Current Situation</th>
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<tbody>
<tr>
<td>Inexpensive</td>
<td>$0.05-0.10/dose + $0.05-0.07/dose administration</td>
</tr>
<tr>
<td>Multiple avian species</td>
<td>Chickens &gt;&gt; ducks &gt;&gt; turkeys, geese, quail, etc.</td>
</tr>
<tr>
<td>Single dose</td>
<td>Minimum 2 doses; boost 6-12 months</td>
</tr>
<tr>
<td>Mass application</td>
<td>96% parenteral, 4% spray</td>
</tr>
<tr>
<td>DIVA compatible</td>
<td>Most vaccine applied without DIVA</td>
</tr>
<tr>
<td>Overcome maternal antibody block</td>
<td>Need timing of vaccination with decline AIV antibody titers; anti-vector antibody impact</td>
</tr>
<tr>
<td>Given at 1d or <em>in ovo</em></td>
<td>Inactivated, poor protection given at 1d. Vectored vaccines given at 1d, but require a field boost</td>
</tr>
<tr>
<td>Antigenically relevant</td>
<td>Majority reverse genetic vaccine seed strains</td>
</tr>
</tbody>
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Vaccines/Vaccination in National Control

Why some countries have not used H5/H7 vaccines – top five responses*:

• Absence of AI in the country
• No immediate risk for outbreaks
• Stamping-out proved successful
• Lack of adequate resources for vaccination
• High cost of vaccines

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE

Assessment of national strategies for control of high-pathogenicity avian influenza and low-pathogenicity notifiable avian influenza in poultry, with emphasis on vaccines and vaccination

D.E. Swaen1,2,3, G. Pavade4, K. Hamilton5, B. Vallet5 & K. Miyagishima6
Why are some countries using, have used or may use H5/H7 vaccines – top five responses:

• Stamping-out measures were not enough in large outbreaks
• Control of localized infection “persistent” in some population of poultry species (i.e. domestic ducks)
• To protect expensive breeds and birds
• Enzootic disease was present
• Resources for vaccination were adequate

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE
**Vaccines/Vaccination in National Control**

• 58% had vaccination option for HPAI control strategies
  • Emergency – vaccine bank, field trials, exercised;
  • Preventive – high risk for introduction; and/or
  • Routine – enzootic infection
• 58% written plans w/specific vaccination use criteria
• 14% had completed AI vaccination simulation exercises or worked-out the logistics of implementing a vaccination program
  • Delayed implementation in 2006 in Egypt – no vaccine bank, no *in country* manufacturing and no logistics developed ahead

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE*
Vaccine Banks (13 of 69 countries)

- H5 (n=10) and both H5 & H7 (n=3) vaccine
- Quantity of vaccines ranged from 0.5-55m doses/subtype, but most countries ≤3.5m doses/subtype
- Vaccine acquired in 2006 (4), 2007 (1), 2008(1), 2009(1) & 2010 (3); Expiration dates 1-4 yrs
- Two future options as vaccines expire:
  - Rotating stocks from commercial vaccine manufacturers
  - Most countries did not indicated desire to purchase more vaccines for a bank (perceived decrease in risk)

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE*
Vaccines/Vaccination in National Control

• Field trials in poultry: 25% of countries for H5 & 7% for H7 vaccines
• Field use:
  • 30% for HPAI control:
    • Poultry (16%),
    • Zoo/other collections of birds (10%)
    • Both (4%)
  • 12% for control of H5/H7 LPNAI
  • 17% for control of non-H5/H7 LPAI
    • H9N2 was the most common
    • H1 & H3 swine influenza viruses in breeder turkeys
    • Sporadic H2, H4 & H6

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE
How Has Vaccination Been Used

• H5/H7 Vaccination used in different ways:
  • Zoo birds and captive held non-poultry (i.e. 14 EU and 2 other countries)
  • Single poultry farm (ex. Israel ostriches)
  • Ring vaccination zone after outbreak (Pakistan, Mexico)
  • Targeted for high risk poultry – ex. outdoor ducks (France), free-range layers (the Netherlands)
  • Focused sector-specific vaccination – (ex. Italy in turkeys and capons 2003-2005 in Northern Italy H5/H7 LPNAI)
  • Routine vaccination of poultry: ex. China (including Hong Kong), Egypt, Vietnam, Indonesia

*From 2002-2010 survey to OIE Delegate for countries with HPAI outbreaks (69 of 80; 86%) as part of 16 month sabbatical to OIE
Doses of H5 AI Vaccine Used 2002-2010*

* Data is preliminary; does not include all 2006 & 2010

>113b doses for at risk national poultry population of 131b (41.9% coverage); global production of 520b (10.9%)
Vaccination

• 95.5% inactivated whole virus vaccine while 4.5% recombinant virus (rNDV and rFPV)
• 14 countries vaccinated poultry against HPAI (2002-2010)
  • Preventive (<0.2%): Mongolia, Kazakhstan, France and The Netherlands
  • Emergency (<0.8%): Cote d’Ivoire, Sudan, North Korea, Israel, Russia, Pakistan
  • Routine (99%): China (including Hong Kong), Egypt, Indonesia and Vietnam
• 2012 – Mexico, H7N3 vaccination of layers in Jalisco & Bangladesh, H5N1 in commercial poultry
### Vaccine Used

#### Doses of Vaccine (millions): 2002-2010

<table>
<thead>
<tr>
<th>Country</th>
<th>Doses of Vaccine (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>103715 (90.99%)</td>
</tr>
<tr>
<td>Cote D'Ivoire</td>
<td>8</td>
</tr>
<tr>
<td>Egypt</td>
<td>5081 (4.65%)</td>
</tr>
<tr>
<td>France</td>
<td>816 (0.816)</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>86 (0.86)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2643 (2.32%)</td>
</tr>
<tr>
<td>Israel</td>
<td>0.006</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>35 (2.8)</td>
</tr>
<tr>
<td>Mongolia</td>
<td>2.068</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>2.2</td>
</tr>
<tr>
<td>PDR of Korea</td>
<td>108</td>
</tr>
<tr>
<td>Pakistan</td>
<td>425</td>
</tr>
<tr>
<td>Russia</td>
<td>6.3</td>
</tr>
<tr>
<td>Sudan</td>
<td>1626 (1.43%)</td>
</tr>
</tbody>
</table>

**Enzootic countries:** >99% of vaccine
National Vaccination Coverage

Average National Coverage Rate (%) for All Years of AI Vaccine Usage

Difficult for National Vaccination Campaigns to achieve population immunity
Vaccination Coverage

% Coverage for Selected Poultry Types

Each country had a different usage pattern
Vaccine Issues

• Proper seed strain: Can and should these change based on field viruses?
  • Antigenic drift in field viruses may require continual development of vaccine seed strains for optimal protection
  • Virological surveillance for variant strains
  • Banks of vaccine seed strains?

• Proper adjuvants for inactivated vaccine
  • Inactivated vaccines optimized for chickens and turkeys
  • Need adjuvants specific for waterfowl?

• Platforms for mass administration – e.g. rNDV
Vaccine Issues

• Sufficient and consistent potency (e.g. antigenic mass) of vaccine batches:
  – Only release batches that meet the minimum serological standard or antigen content
  – Should there only be one minimum standard? Emergency vs preventive vs enzootic plans

• Licensing of vaccines:
  – Which national challenge strain(s)?
  – Which host species?
  – Licensed for how long?
  – Was a challenge test completed for licensing?
Vaccine Issue: Antigenic Drift

Vaccine Seed Strains: Indonesia

- **Historical H5 Vaccines** – Similar antigenicity
- **Drifting of HA away from root**
  - Good protection: Ck/HK/220/97, Ck/Legok/03, VN/1203/04, Ck/WJ/HAMD/06
  - Intermediate protection: Ck/Papua/06
  - Poor protection: PWT/06

Swayne, Smith and Fouchier, 2008
Vaccine Issue: Antigenic Drift

• Egypt (2006-): Some field strains from commercial farms are resistant to immunity from Mexico/94 and Re-1 vaccines

• China (2004-):
  – Re-1 (rg A/gs/Guangdong/1/1996 [H5N1], clade 0): 2004-8
  – Re-5 (rgA/dk/Anhui/1/2006 [H5N1], clade 2.3.4): 2008-2012
  – Re-6 (rgA/dk/Guangdong/S1322/2010 [H5N1], 2.3.2): 2012-

• Vietnam: 2011 clade 2.3.2.1 resistant to immunity from Re-1 & Re-5 (Begun use of Re-6)

• Hong Kong (2008): clade 2.3.4

Solution: Most vaccine uses rg seed strains to match field virus
Laboratory & Field

• Best protection is in experimental studies with SPF layer chickens; 1 dose is protective, 7-21 post-vax
• Field protection less than in laboratory
  – Layer-breeds have best immunity, but immunity drops at peak of lay (i.e. pregnancy)
  – Broilers are more difficult to get good antibody titers; turkeys are difficult to get consistent titers
  – Management issues and immunocompetency
• Multiple doses are required
• Issue: HA protective so delivery (platform) is key to overcoming field delivery problems, but must be better and cheaper than inactivated whole AIV vax produced in eggs
Vaccination Issues

Why did vaccines/vaccination ‘work’ in some countries but not in others?

• Highly functional, coordinated, adequately funded national/provincial/local veterinary services to implement & monitor
• Pre-develop logistics for vaccination and exercise vaccination plan
• Vaccine availability - commercially or vaccine bank within the country
  – Completed vaccine licensing/registration process, or have emergency authority
  – Stockpiles available in country through manufacturing capacity or importation
Vaccination Issues

Why did vaccines/vaccination ‘work” in some countries & not in others?

• Timing of initial application – how quickly the index case is diagnosed and vaccination is implemented impacts success as an eradication tool

• Must have ‘effective’ population immunity in the control zone; >60% of susceptible population is minimum but >80% is optimal
  • Easier to achieve in commercial production, but difficult in semi-commercial and village production systems
  • There must be economic incentives for farmers to vaccinate; e.g. difficult to achieve if vaccinating for the good of public health or to prevent a ‘pandemic’ as in domestic ducks (H5N1)
  • Vaccination is linked to food security and rural livelihoods especially in semi-commercial and village production
Vaccination Issues

Why did vaccines/vaccination ‘work” in some countries & not in others?

• Relevant vaccine seed strain
  – Antigenically matched to circulating field viruses
  – Conduct *ongoing* surveillance of field strains
  – Should be challenge tested on biannual basis
  – May need more than one seed strain or bivalent vaccines in countries with long-term vaccine use

• Vaccination protocol development and tailoring to fit the species and type of bird, production sector and immune status of the population

• Movement controls on poultry populations; ex. sector 1&2 poultry being moved to local markets when infection is first detected
Vaccine/Vaccination Research Needs

• New vaccine vector platforms for cost-effective vaccination of short-lived meat poultry; i.e. no catching & handling of individual birds, mass application (spray, *per os* or *in ovo*), protection after a single vaccination & not inhibited by maternal immunity

• A vaccination system for village poultry such as thermostable vaccine that can be used within existing NDV village vaccination programs to boost participation and coverage rates

• More prime-boost vaccination protocols to maximize protection at least cost and provide better population immunity
Vaccine/Vaccination Research Needs

- Newer adjuvants for inactivated vaccines that will provide shorter withdrawal periods and elicit stronger, longer-lived mucosal immunity, especially for domestic waterfowl

- A more time-responsive vaccine licensing and registration process by national veterinary biological authorities; for example, the development of a process of updating replaceable “vaccine cassettes” without requirement of resubmitting a full licensing dossier; e.g. human influenza vaccine seed replacement
Conclusions

- Current diagnostic methods for AIV in poultry are tied to regulatory needs. Virus detection, subtype identification and pathotyping tests are prescribed by the USDA & OIE and any changes will need to fulfill regulatory needs.

- Although regulatory considerations harmonize AIV diagnostics, specifics of testing varies among countries and industry compartments to satisfy different needs and to accommodate the availability of resources.

- In order to be implemented new test formats and modifications of tests must:
  - Undergo thorough validation
  - Be practical for the field and veterinary diagnostic laboratory workflow
  - Be cost effective
Conclusions

• Current AI vaccines are potent & of consistent quality
• “Vaccine Failures” have occurred; primarily from failure to adequately administer the vaccine to at risk population, but also some examples of vaccine failure from antigenic drift
• Routine national AI vaccination programs are logistically difficult to implement & expensive to sustain with low potential for effective HPAI eradication
• AI vaccination programs should be updated to become risk-based utilizing inputs from science-based epidemiological surveillance, with the limited vaccine resources focusing on highest risk populations and reservoirs
• DIVA strategies should be incorporated to improve epidemiological surveillance
• Exit strategies should be developed based on field conditions and risk assessment
Future for next 5-10 years?

- China and other developing/transition countries will be the primary users and will drive commercialization of new technologies for AI vaccines, with China being the major user, driving innovation and commercialization of vaccine technologies for domestic demand and a modest export market to other developing/transition countries.

- Inactivated whole AIV vaccines will dominate the market, mostly using antigenically-relevant, reverse genetic generated AIV seed strains to address antigenic drift, and usage of specific seed strains will become more focused to specific national/regional geographic needs as H5N1 HPAI became more geographically-isolated and continue to evolve into different genetic sub-clades or antigenic subgroups.
Future for next 5-10 years?

• The current routine nationwide HPAI vaccination programs will be converted to risk-based programs based upon real-time field surveillance with vaccine use being focused to the poultry species, region, and production sectors that are at highest risk of HPAI outbreaks as well as the reservoirs; and these vaccination programs will be continuous and age-specific, and not based on seasonal campaign system, in order to achieve 60-80% coverage in at risk poultry

• Developed countries will focus more on preventative measures such as enhanced biosecurity and early detection, with stamping-out of infected and epidemiologically-linked premises, while vaccines and vaccination will only have minor usage as preventative tools used in focused, risk-based strategies
Merci Beaucoup!
Did vaccination create HPAI enzootic infection?

- Bangladesh and eastern India enzootic without vaccination
- Egypt – 383 outbreaks before vaccination began and 573 outbreaks with 1% poultry vaccinated
- Indonesia – first cases July 2003 with 312 outbreaks and 10.9 million deaths by June 2004
- Vietnam – by end of 2004, 24% of communes & 60% of towns had cases & 17% of the poultry population affected. Started vaccination Oct 2005

Data suggests H5N1 HPAI was enzootic before vaccination
Research and Control Program Needs

- Current test are adequate for most AIV testing, however improvements and modifications would be beneficial
- AIV diagnostic improvements:
  - A transport method or media to stabilize viable virus in absence of cold chain
  - A rapid and high throughput RNA extraction method for tissues & cloacal swabs which removes substances that are inhibitory for rRT-PCR and which preserves the RNA
  - An AgIA for NDV as differential test for AIV, & improved sensitivity of AgIA’s for type A influenza near to that of virus isolation or rRT-PCR
  - A sensitive, specific, and well validated AgIA for identification of the H5 & H7 HA subtypes, & detects variants within each subtype
  - A rapid & inexpensive test to determine pathotype in a biologically relevant manner
  - A method to accurately identify the HA specificity of antibody to AIV (type A influenza)