Avian Influenza vaccine development: practical application in developing countries

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Avian Influenza vaccines

**Inactivated:**
(Whole virus)

- Homologous
  (i.e. H7N7 for H7N7 virus)
- Heterologous
  (i.e. H5N2 for H5N1 virus)

**Recombinant:**

- Reverse genetics H5N1 (inactivated)
- Fowlpox H5 (vector)
- Newcastle Disease H5 (vector)

**Experimental:**

- *Universal vaccine, M protein*
# Avian Influenza Vaccine Characteristics

<table>
<thead>
<tr>
<th>Ideal Vaccine</th>
<th>Homologous Inactivated (e.g. H5N1)</th>
<th>Heterologous Inactivated (e.g. H5N2)</th>
<th>Recombinant Fowlpox (e.g. H5)</th>
<th>Recombinant RG H5N1</th>
<th>Recombinant AI/ND (e.g. H5/ND)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure/safe/potent</td>
<td>+/+/+</td>
<td>+/+/±</td>
<td>+/+/±</td>
<td>+/+/±</td>
<td>+/+/±</td>
</tr>
<tr>
<td>Thermo stable</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Single dose</td>
<td>No (2-3)</td>
<td>No (2-3)</td>
<td>Yes (yearly)</td>
<td>Yes/No (2-3)</td>
<td>No (every 4 months)</td>
</tr>
<tr>
<td>Easy administration (oral/mucosal)</td>
<td>No: injection</td>
<td></td>
<td></td>
<td>Yes: Eye drop</td>
<td></td>
</tr>
<tr>
<td>DIVA</td>
<td>No</td>
<td>Yes NA tests</td>
<td>Yes NP, M, NS1 or NA tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheap</td>
<td>Cheap</td>
<td>Cheap</td>
<td>Expensive</td>
<td>Cheap?</td>
<td>?</td>
</tr>
</tbody>
</table>
Vaccination versus Culling

- Until 2004: culling is the recommended control option for HPAI

- Number of birds culled because of HPAI worldwide:
  - 1959-1998 (40 years): 23 millions birds culled
  - 1999-2004 (5 years): >200 millions birds culled

- Since 2004:
  - Culling is no longer acceptable for **economical and ethical reasons**
  - Vaccination is recommended as an additional control tool from OIE/FAO/WHO

**Now:** Vaccination still illegal in many of the infected countries (e.g. Nigeria)

- Lack of knowledge on AI vaccinology (different species; farming systems; ecological and epidemiological context)

- Lack of field data
World map of AI vaccine use

Before 2003

Since 2003

H5N1 outbreaks in poultry since 2003

Vietnam: H5N1; H5N2 (2005)

Indonesia: H5N1; H5N2 (2006)

EU (2006): H5N2

Italy: H7 (2000)

Russia (2006):

Korea (2003): H5N1; H5N2

Hong Kong (2003): H5N2; H5N1

North America:
H1 (1980)
H7 (1995)

Fowlpox


Indonesia: H5N1; H5N2 (2006)

Egypte (2006):

Sudan (2006):

Ivory coast (2006):

Malaysia: H5N2 (2006)

Vietnam: H5N1; H5N2 (2005)
H5N9 (2007)
## AI Vaccination: Advantages and Issues

<table>
<thead>
<tr>
<th>Vaccine Efficacy</th>
<th>General Limits</th>
<th>Specific limits to developing countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increase host resistance to infection</td>
<td>• Laboratory validation ≠ field results</td>
<td>• Lack of vaccine quality control and</td>
</tr>
<tr>
<td></td>
<td>→ immune status of the host</td>
<td>• Lack of field trials</td>
</tr>
<tr>
<td></td>
<td>• Species specific</td>
<td></td>
</tr>
<tr>
<td>• Reduce viral shedding / transmission dynamics</td>
<td><strong>Do not prevent infection</strong></td>
<td>• Limited monitoring: Practical issues (sentinels) Economical issues Human resources</td>
</tr>
<tr>
<td></td>
<td>• Need to monitor virus circulation:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>→ undetected outbreaks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>→ risk for mechanical transmission</td>
<td></td>
</tr>
<tr>
<td></td>
<td>→ antigenic drift</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Differentiate vaccinated from infected animals (DIVA)</td>
<td>• Not a priority, economical and practical issues</td>
</tr>
</tbody>
</table>
# AI Vaccination strategies

<table>
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<tr>
<th>Vaccination Strategies</th>
<th>Context</th>
<th>Limits</th>
</tr>
</thead>
</table>
| Preventive (prevent disease introduction) | • Country or area free of disease  
• High introduction risk  
• High dissemination risk | • Export bans  
• Cost-benefit issue  
• **Associated with strong biosecurity measures** |
| Emergency (disease containment)      | • Ring vaccination around an outbreak                                    | • Time delay for immunity onset  
Efficacy depends on vaccine availability and rapid administration  
• **Associated with strong biosecurity measures** |
| Prophylactic (disease control)       | • Endemic situation  
• Mass or strategic vaccination  
• Long term plan               | • Post-vaccination monitoring for efficacy and virus circulation  
• Cost-benefit issues (mass vs targeted vaccination)  
• **Associated with strong biosecurity measures** |
AI Vaccination strategies

Efficient strategy

= Vaccination + strict biosecurity measures (including culling infected birds)
# UPDATE on VACCINATION CAMPAIGNS

<table>
<thead>
<tr>
<th>Country</th>
<th>Strategy</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| SAR Hong Kong | Mass vaccination since 2003  
Efficient monitoring  
High level of biosecurity | Control +  
Eradication (last poultry outbreak: 2003) |
| PR China | Mass vaccination since 2003  
Poultry systems with limited biosecurity  
Monitoring difficult | Control  
One reported outbreak in poultry in 2007  
(2 human cases) |

- ≠ scale of territory to control (SAR HK=1000km²; RP China=9 millions km²)
- heterogeneity in poverty and industrialisation levels between regions  
(SAR HK GDP= 7 x Shangai GDP)
- Natural reservoirs: wildbirds/environment
## UPDATE on VACCINATION CAMPAIGNS

<table>
<thead>
<tr>
<th>Country</th>
<th>Strategy</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| **Indonesia** | Emergency and preventive vaccination 2004  
Targeted 2006 (limited vaccine supply) | No control  
Numerous outbreaks and human cases 2006-2007 |
| **Vietnam** | Mass vaccination since 2005  
2 campaigns / year  
Some virus circulation monitoring  
Some vaccine efficacy monitoring | Control  
No outbreaks between Dec 2005- Dec 2006 (Last 08/07)  
No outbreak in vaccinated flocks  
No human cases in 2006 (Last: 07/07) |

- Extensive farming systems  
- No efficient vaccines for waterfowls  
- Insular situation of Indonesia, autonomy era of provinces, districts  
- Indonesia: limited budget and human resources
### AI vaccination constraints for developing countries, summary

<table>
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<tr>
<th>Choice of vaccine and strategy</th>
<th>Post-vaccination surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reinforcement of Biosecurity measures and Surveillance systems</td>
<td>Economic aspect</td>
</tr>
<tr>
<td>Awareness programs</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

• Research Needs

Virology/Vaccinology

• AI vaccines optimisation (administration, storage)
• AI vaccines field efficacy (species, immune status, breeding type)
• Non-invasive techniques for viral circulation (water; faeces)

Epidemiology/Economics

• Decision tools: models for evaluation of vaccination strategies (multiple farming systems and mixed species breeding)
  • Cost-benefit analysis (≠ levels; ≠ strategies)
  • Vaccination coverage (serological status, spatial analysis)
Acknowledgments

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• Guo Fusheng, FAO, China

Poster:
« Cost-benefit evaluation of AI vaccination in Vietnam ». T.Phan Dang et al.
Thank you for your attention
Conclusion 2

• Illegal vaccine markets
  • National vaccination plans
  • Awareness programs

• Local vaccine production
  • Independent supply
  • Safety issues
  • Quality control
  • Potency assessment
World map of AI vaccine use

Before 2003

North America:
- H1 (1980)
- H7 (1995)

Italy:
- H7 (2000)

Mexico:
- H5N2 (1995)
- Fowlpox

Pakistan:
Since 2003

- H5N1 outbreaks in poultry since 2003

- World map of AI vaccine use

- EU (2006): H5N2

- Russia (2006):
  - H5N1; H5N2

- Russia
  - H5N1; H5N2
  - Fowlpox

- RP China (2003):
  - H5N1; H5N2

- Hong Kong (2003):
  - H5N2
  - H5N1

- Korea (2003):
  - H5N1; H5N2

- Egypte (2006):

- Ivory coast (2006):

- Sudan (2006):

- Indonesia:
  - H5N1; H5N2 (2006)

- Malaysia:
  - H5N2 (2006)

- Vietnam:
  - H5N1; H5N2 (2005)
  - H5N9 (2007)