

2015年家禽流行性感冒預防與控制國際研討會議程
2015 International Symposium on Avian Influenza Prevention and Control
Morning Agenda

目 錄

- 主題一、台灣面對家禽流行性感冒之控制和準備
- Topic 1 : Control and preparedness for avian influenza pandemic in Taiwan.
主講人：張淑賢 局長 行政院農業委員會動植物防疫檢疫局
Speaker : Dr. Su-san Chang, Director General, Bureau of Animal and Plant Health Inspection and Quarantine, Taiwan
- 主題二、如何做好高病原性家禽流行性感冒之控制和準備
- Topic 2 : How to control and prepare for highly pathogenic avian influenza and pandemic Influenza.
主講人：喜田宏 主任 日本北海道大學人畜共通傳染病控制中心
Speaker : Dr. Hiroshi Kida, Head, Research Center for Zoonosis Control, Hokkaido University, Japan
- 主題三、韓國高病原性禽流感(H5N8)流行病學及防治策略
- Topic 3 : Epidemiology and prevention strategies of highly pathogenic avian influenza (H5N8) in Korea.
主講人 Speaker : Dr. Jida Choi, Veterinary researcher, Veterinary Epidemiology Division, Animal and Plant Quarantine Agency (QIA), Korea
- 主題四、台灣高病原性家禽流感新病毒株之特徵
- Topic 4 : Characteristics of new avian influenza virus strains isolated from avian in Taiwan.
主講人：蔡向榮 所長 行政院農業委員會家畜衛生試驗所
Speaker : Dr. Hsiang-Jung Tsai, Director General, Animal Health Research Institute, Taiwan

主題五、亞洲高病原性家禽流行性感冒病毒之診斷和鑑定現況.....

Topic5 : Diagnosis and identification of highly pathogenic avian influenza viruses recently isolated in Asia.

主講人：迫田義博 教授 日本北海道大學獸醫學院獸醫學研究所

Speaker : Dr. Yoshihiro Sakoda, Professor, Graduate School of Veterinary Medicine Hokkaido University, Japan

主題六、荷蘭 H5N8 高病原性家禽流行性感冒之疫情防治與生物安全措施.....

Topic 6 : Highly pathogenic Avian Influenza H5N8 in The Netherlands; outbreaks, control and biosecurity measures.

主講人 Speaker : Dr. Jan Arend Stegeman, Professor, Utrecht University, Faculty of Veterinary Medicine, The Netherlands

主題七、提升家禽飼養設施及生物安全措施以面對家禽流行性感冒威脅.....

Topic 7 : Poultry raising facilities and biosecurity to face threat from avian influenza.

主講人：黃振芳 分所長 行政院農業委員會畜產試驗所宜蘭分所

主題八、改善動物福利的禽流感防疫撲殺措施新發展.....

Topic 8 : New developments to improve animal welfare during stunning and killing of poultry for disease control.

主講人 Speaker : Dr. David Pritchard, Consultant, Animal Welfare Science and Practice, Argyll House, United Kingdom

主題九、降低大規模爆發期間的傳播風險.....

Topic 9 : The reduction of the risks of spreading of infections during mass outbreak.

主講人 Speaker : Mr. Harm Kiezebrink, Principal consultant at AVT Applied veterinary technologies Europe AB, The Netherland

Curriculum Vitae

Su-San, Chang
Director General, Bureau of
Animal and Plant Health
Inspection and Quarantine,
Council of Agriculture, Executive
Yuan, Taiwan, ROC



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Education:

Doctor of Soil Science, University of California at Davis, the United States (1992); Master of Agricultural Chemistry, National Taiwan University, Taiwan, ROC(1978); Bachelor of Agricultural Chemistry, National Taiwan University, Taiwan, ROC (1976).

Experience:

Research Assistant, Taiwan Agricultural Research Institute (1978~1980), Assistant Researcher, Taiwan Agricultural Research Institute (1980~1986); Associate Researcher, Taiwan Agricultural Research Institute (1986~1994); Specialist, Department of Food and Agriculture, Council of Agriculture, Executive Yuan (1994~1998); Division Chief, Department of International Affairs, Council of Agriculture, Executive Yuan (1998~1999); Senior Specialist and Division Chief, Department of International Affairs, Council of Agriculture, Executive Yuan (1999~2003); Counsellor, Permanent Mission of Taiwan, Penghu, Kinmen and Matsu to the WTO (2003~2008); Director General, Department of International Affairs, Council of Agriculture, Executive Yuan, Taiwan, ROC (2008~2013).

Curriculum Vitae

HIROSHI KIDA

OFFICE ADDRESS

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Hokkaido University
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ACADEMIC DEGREES:

BVM	1967	Hokkaido University (Veterinary Medicine)
DVM	1967	Ministry of Agriculture and Fisheries
MVM	1969	Hokkaido University (Veterinary Medicine)
PhD	1977	Hokkaido University (Veterinary Medicine)

PROFESSIONAL APPOINTMENTS:

1969-76	Research Officer for Vaccine Development, Takeda Chemical Industries, Ltd
1976-78	Lecturer, Dept Veterinary Hygiene & Microbiology, Hokkaido University
1978-94	Associate Professor, Dept Vet Hygiene & Microbiology, Hokkaido Univ
1980-81	Visiting Scientist, WHO Collaboration Centre/ St. Jude C R H, Memphis, TN
1986-87	Visiting Professor, WHO Collaboration Centre/ St. Jude C R H
1989	Professor, University of Zambia School of Vet Med, Lusaka, Zambia
1994-95	Professor and Chairman, Dept Vet Hygiene and Microbiology, Hokkaido Univ
1995-date	Professor, Dept of Disease Control, Hokkaido Univ Graduate School Vet Med
1995-01	Hokkaido University Senator
1999-date	Expert, Member of Working Group for WHO Global Influenza Programme
2001-05	Dean, Hokkaido Univ School and Graduate School of Veterinary Medicine

2004-date	Head, OIE Reference Laboratory for Highly Pathogenic Avian Influenza,
2005-2012	Director, Hokkaido University Research Center for Zoonosis Control
2007-date	Member of the Japan Academy
2011-date	Head, WHO Collaborating Centre for Zoonoses Control
2012-date	Specially Appointed Professor, Graduate School of Veterinary Medicine
2012-date	Head, Hokkaido University Research Center for Zoonosis Control
2014-date	Distinguished Professor, Hokkaido University -

PUBLICATIONS:

294 original articles and 145 book chapters and reviews

RESEARCH INTERESTS:

Ecology and pathogenesis of influenza viruses, Zoonoses, Vaccinology

AWARDS:

- 1.The Japanese Society of Veterinary Science Award for “Studies on the Classification of Avian Paramyoviruses” (1982)
- 2.Hokkaido Science and Technology Award for “Studies on the Mechanisms of Emergence of Pandemic Influenza A Viruses and their Control Measures” (2002)
- 3.The 58th Hokkaido Shimbun Cultural Prize for “Ecology of Influenza Viruses in Birds, Animals and Humans” (2004)
4. The Japan Prize of Agricultural Science and the Yomiuri Agriculture Prize for “Ecology of Influenza Viruses” (2005)
5. The 95th Japan Academy Prize for “Studies for the Control of Influenza - Mechanism of Emergence of Pandemic Influenza Virus Strains in Poultry, Domestic Animals and humans, and Molecular Basis of the Neutralization of Viral Infectivity with Antibodies-” (2005)
6. Animal Science Prize for “Clarification of Ecology of Influenza Viruses and Establishment of Influenza Virus Library and its Application to the Diagnosis and Prevention of Highly Pathogenic Avian Influenza” (2009)
- 7.All Japan Agriculture Decoration for “the Achievement of Control of Avian Influenza” (2011)

Curriculum Vitae

Jida Choi

Animal and Plant Quarantine Agency (QIA)
Veterinary Researcher
175 Anyangro, Manangu, Anyang, Gyeonggi, Korea

E-mail: apjida@korea.kr



Education

2006. 03. ~
2011.08. Konkuk University, Department of Biomedical Science and
Technology (in Korea) Ph.D
1999. 03. ~
2005 .02. Konkuk University, College of Veterinary Medicine (in Korea)
D.V.M.

Professional Experience

2013.08 -
Present Veterinary researcher, Veterinary Epidemiology Division, Animal
and Plant Quarantine Agency, Korea
2011.09.
~2013.04. Post-doctorial researcher, Department of Biomedical Science and
Technology, Konkuk University, Korea
2011.11.
~2012.06. Visiting post-doctorial researcher, Department of Immunology,
Weizmann Institute of Science, Israel
2012.11.
~2013.04.
2009. 08. ~
2009. 11. Visiting scientist, Laboratory of Infectious Disease, Medical school,
University of Colorado, Denver, USA

Membership

2005~ The Korean Society of Veterinary Science
2006~ The Korean Association of Immunologists

Research interests

Epidemiology, Immunology

Curriculum Vitae

Hsiang-Jung, Tsai

Director General, Animal Health Research
Institute, Council of Agriculture.

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EDUCATION:

1991 Ph.D.in Veterinary Preventive Medicine, The Ohio State. University
(USA),

1980 Master in Veterinary Medicine, National Taiwan University.

1978 Bachelor in Veterinary Medicine, National Taiwan University.

Professional Experience

July 2012- present	Director General, Animal Health Research Institute, Council of Agriculture.
June 2012	Counselor, Council of Agriculture.
2006- May 2012	Professor, School of Veterinary Medicine, National Taiwan University.
2005-2011	Director, Center for Zoonoses Research, College of Bioresource and Agricultural, NTU
1995-2006	Associate Professor, School of Veterinary Medicine, NTU.
1982-1986, 1991-1995	Assistant Researcher, Department of Epidemiology Research, Animal Health Research Institute, Taiwan Provincial Government.

Curriculum Vitae

Yoshihiro Sakoda, DVM, PhD

Professor
Laboratory of Microbiology,
Graduate School of Veterinary Medicine,
Hokkaido University

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FAX: +81-11-706-5273
e-mail: sakoda@vetmed.hokudai.ac.jp



EDUCATION:

1988-1994: Faculty of Veterinary Medicine, Hokkaido University

ACADEMIC DEGREES:

Bachelor 1994 Hokkaido University (Veterinary Medicine)

Ph.D. 1999 Hokkaido University (Veterinary Medicine)

PROFESSIONAL APPOINTMENTS:

1994-2001: Researcher, Exotic Disease Division, National Institute of Animal Health, Japan

2001-2007: Assistant Professor, Graduate School of Veterinary Medicine, Hokkaido Univ.

2007-2014: Associate Professor, Graduate School of Veterinary Medicine, Hokkaido Univ.

2014-Present: Professor, Graduate School of Veterinary Medicine, Hokkaido Univ.

AWARDS

2006 Asian Veterinary Science Prize (The Asian Association of Veterinary Schools)

2008 Young Agricultural Researchers Prize (Ministry of Agriculture, Forestry and Fisheries, Japan)

2013 Prize of Japanese Society of Veterinary Science (Japanese Society of Veterinary Science)

RESEARCH INTERESTS:

1. Pathogenesis of classical swine fever virus, bovine viral diarrhoea virus, and border disease virus
2. Development of vaccine and diagnosis methods for pestivirus and influenza virus infections
3. Pathogenesis of influenza viruses
4. Interspecies transmission of influenza viruses

- ・豚コレラ抗体検出 ELISA の開発
- ・国産 鳥インフルエンザワクチンの開発
- ・BVD 診断キット「テストント」の開発

Curriculum Vitae

Jan Arend (Arjan) Stegeman

Professor
Farm Animal Health at Faculty of Veterinary Medicine,
Utrecht University, Utrecht, The Netherlands.
Yalelaan 7, 3584,
CL Utrecht, The Netherlands

E-mail: j.a.stegeman@uu.nl



Degrees and Qualifications

2002	Diplomate of the European Colleges of Veterinary Public Health (population medicine)
1995	Utrecht University, PhD
1989	Utrecht University, Doctor Veterinary Medicine

Professional Experience

2000 - Present	Farm Animal Health at Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands
1995-2000.	Central Veterinary Institute, Lelystad, The Netherlands
1989-1995.	Animal Health Service, Deventer, The Netherlands

Additional Tasks

1. Chair of Expertgroup on animal diseases of Dutch ministry of Economic Affairs.
2. Member of Dutch Health Council.
3. President of the Dutch Branch of the World Poultry Science association.
4. Member of the panel on Animal Health and Welfare (AHAW) of the European Food Safety Authority (EFSA), Parma, Italy.
5. Member of Dutch Animal Council

Research interests

1. Farm Animal Health.
2. Epidemiology.
3. Infectious Diseases and Health

Curriculum Vitae

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Ilan Branch, Livestock Research Institute,
Council of Agriculture

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EDUCATION:

- 2004 Received Ph.D. degree in the Department of Animal Science and Technology, National Taiwan University, Taipei, Taiwan
- 1995 Received Master's degree in the Department of Animal Science, Michigan State University, East Lansing, U. S. A.
- 1987 Received Bachelor degree in the Department of Animal Husbandry, National Taiwan University, Taipei, Taiwan

Professional Experience

- 2010-Present Researcher and Director at the Ilan Branch, Livestock Research Institute, Council of Agriculture, Executive Yuan
- 2002-2010 Associate Researcher and Chairperson at the Ilan Branch, Livestock Research Institute, Council of Agriculture, Executive Yuan
- 1999-2002 Assistant Researcher at the Ilan Branch, Livestock Research Institute, Council of Agriculture, Executive Yuan
- 1995-1999 Assistant Researcher at the Ilan Branch, Taiwan Livestock Research Institute
- 1989-1992 Research Assistant at the Ilan Branch, Taiwan Livestock Research Institute

Curriculum Vitae

David Pritchard

Animal Welfare Science and Practice
Argyll House,
All Saints Passage,
London
SW18 1E, United Kingdom

TEL: +44 20 3156 1157

E-mail: davidgeorgepritchard@gmail.com



Education and training

- 1975-1976 Meat and Livestock Commission Traveling Scholarship in Epidemiology for a Masters in Public Health Program at University of Minnesota.
- 1974-1975 Immunology course at Middlesex Hospital Medical School.
- 1967-1973 Veterinary Science course at The Royal Veterinary College of London University.
- 1969-1970 B. Sc. Special Honours intercalated course in Animal Physiology and Anatomy – London University (Neuroanatomy, Reproductive Biology and Animal Behaviour).
- 1960-1967 The Newport St. Julian's High School for Boys, Newport, Gwent, Wales.

Professional Experience

- 2014 - Present Consultant to an American company producing novel equipment for improving welfare during poultry processing and killing—policy and technical advice.
- Consultant (Organisation for respect and care of animals(ORCA) on EU approach to economics of farm animal welfare and development of Animal welfare in Serbia.
- 2014 Panel member - Conference on Animal Welfare: The Pleasure of Respecting Rights – Is animal welfare economically sustainable. Jointly organised with the European Commission and the Food and Agriculture Organization of the United Nations (FAO).
- Consultancy on policy development for Animal Welfare Councils to Western Balkan Veterinary Network and RSPCA.
- 2013 Contractor to European Agency for Health and Consumers to provide technical editing of BTSF booklet on. EU Animal Welfare

Acquis.

Consultancy on policy and technical advice on stray dog control to European Parliament mission to Romania 2013.

2012 - Present	Director Veterinary Consultancy Services Limited.
2010-2011	Deputy Director Senior veterinary consultant seconded to the Welsh assembly Government.
2010 - Present	Director/ Trustee of Universities Federation for Animal Welfare and Humane Slaughter Association.
1999-2006	Deputy Director- Head Animal Welfare Veterinary Team/Division, Veterinary Directorate MAFF/Defra.
1985-1989	Senior Research Officer (SRO) and Acting Head of Bacteriology Department, CVL.
1980-1985	SRO -Tuberculosis, Anthrax, Glanders, Leptospirosis, Q-Fever, Johnes Section CVL.
1978-1980	SRO – Head Mycology Unit.
1974-1978	Research Officer- Bacteriology Department CVL.
1972	Scientific Coordinator Royal Veterinary College Research Team to Uganda.

Research interests

1. High knowledge of disease control.
2. Trade and animal welfare legislation and enforcement in EU context.
3. Development, implementation and impact assessment of policies on animal health and welfare.

Curriculum Vitae

Harm Kizezbrink

Principal consultant at AVT Applied Veterinary
Technologies Europe AB
Storgatan 36^b, 26977 Torekov, Sweden

TEL :+46-761-731779
E-mail:harm.kie@gmail.com



Education

- 1983 ~1986 MBA Marketing and Communications. University of Twente/ (Post Academic Education)StichtingWetenschappelijkOnderwijsTwente, Holland.
- 1974 ~ 1978 Mechanical (Ship) Engineering, University of Applied Technical Sciences, Groningen/ Delfzijl.

Professional Experience

- 2009 ~ Present Principal consultant at AVT Applied Veterinary Technologies Europe AB
- 2014 ~Present Associate Research Fellow, Friedrich Loeffler Institute FLI, Institute of Animal Welfare and Animal Husbandry Celle, Germany.
- 2014 ~ Present Research Fellow, Queensland University, Centre for Animal Welfare and Ethics, School of Veterinary Science, University of Queensland, Australia.

Publications

- 2009 Co-author of the simulation exercise Poultopia, published by the America Association of Avian Pathologists AAAP.
- 2006 Co-author of the book Avian Influenza, Blackwell Publishing.
- 2013 Co-author of the multi media e-learning module “ Animal Welfare, at Slaughter and Killing of Animals for Disease Control”– BTSF⁴ program on the implementation of regulation EU 1099/2009.

**2015 International Symposium on
Avian Influenza Prevention and Control**

11 March 2015, Taipei, Taiwan

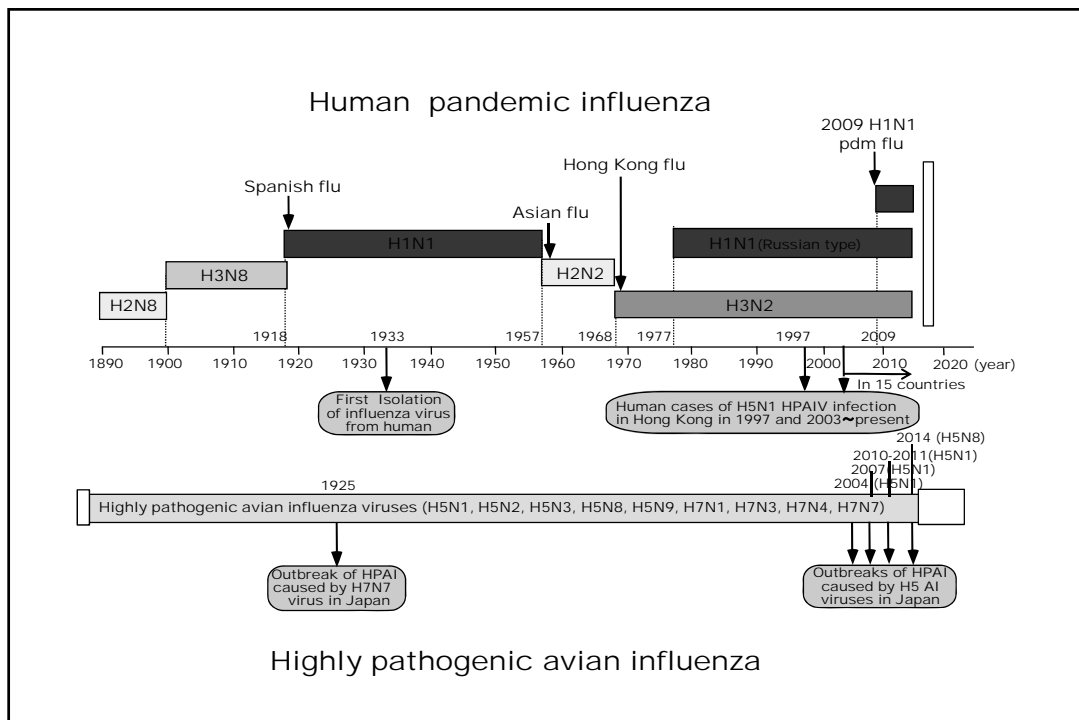
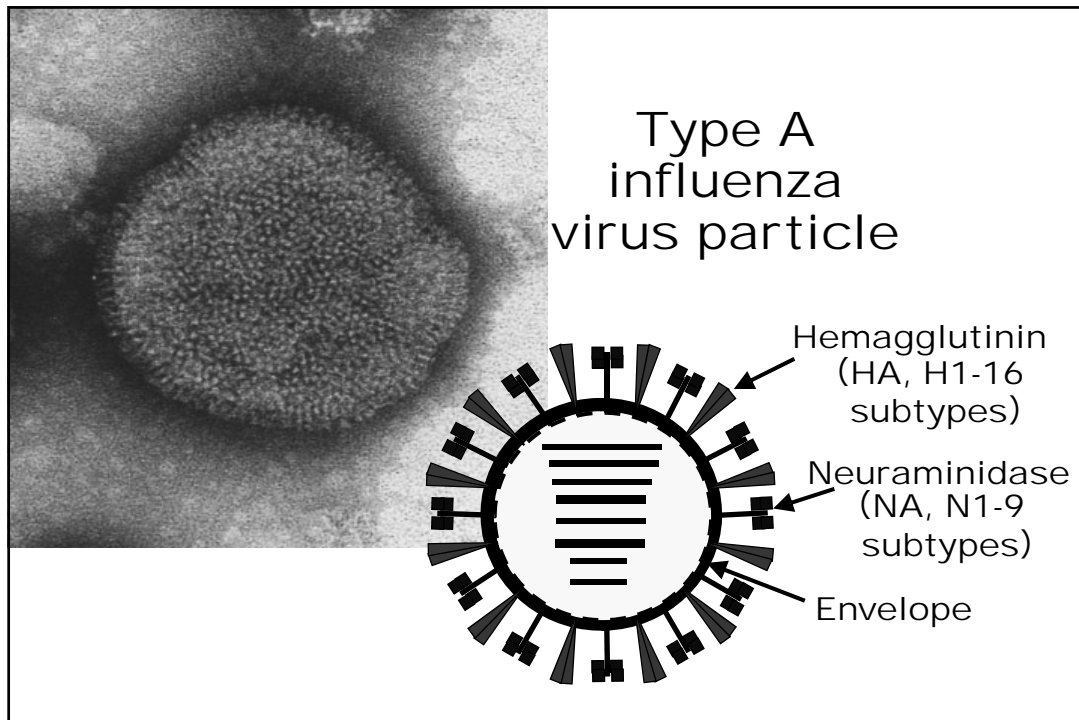
How to control avian influenza and how to prepare for pandemic influenza

Hiroshi Kida, DVM, PhD

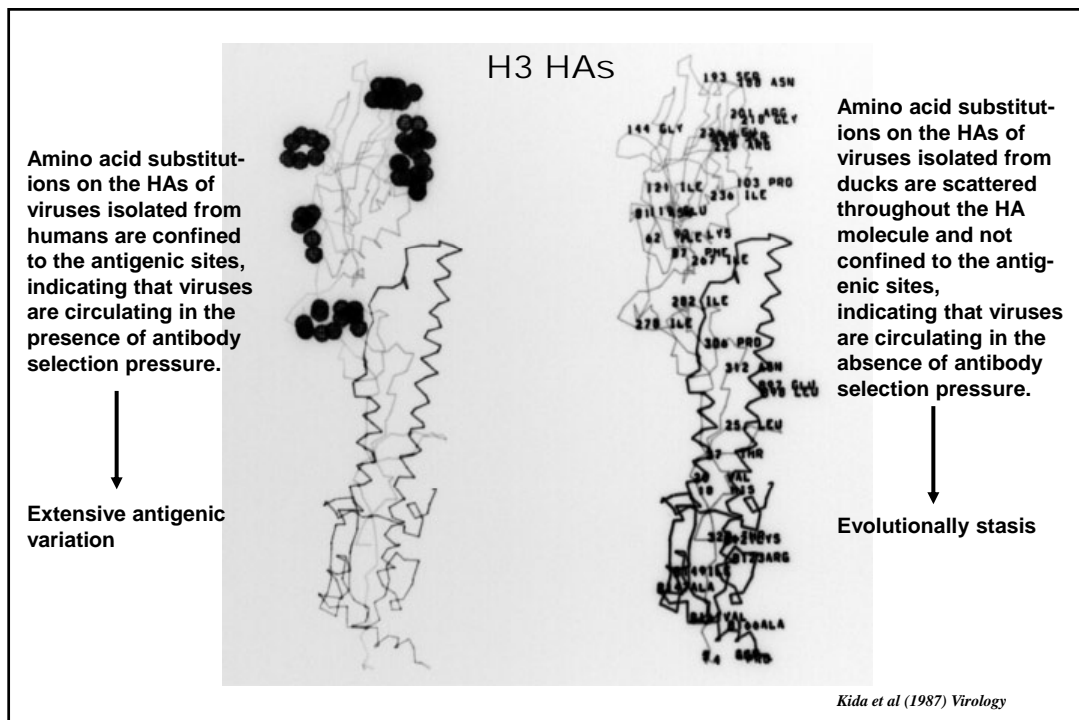
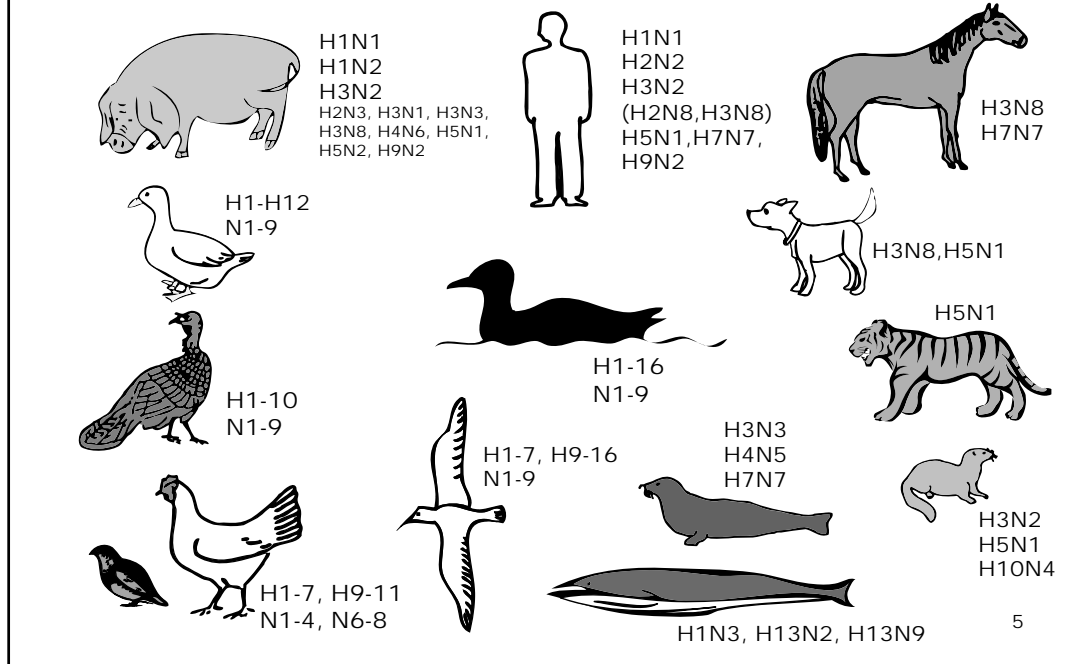
**Member of the Japan Academy
Specially Appointed Professor, Hokkaido University
Head, Research Center for Zoonosis Control
Head, OIE Reference Laboratory for Animal Influenza
Head, WHO Collaborating Centre for Zoonoses Control**

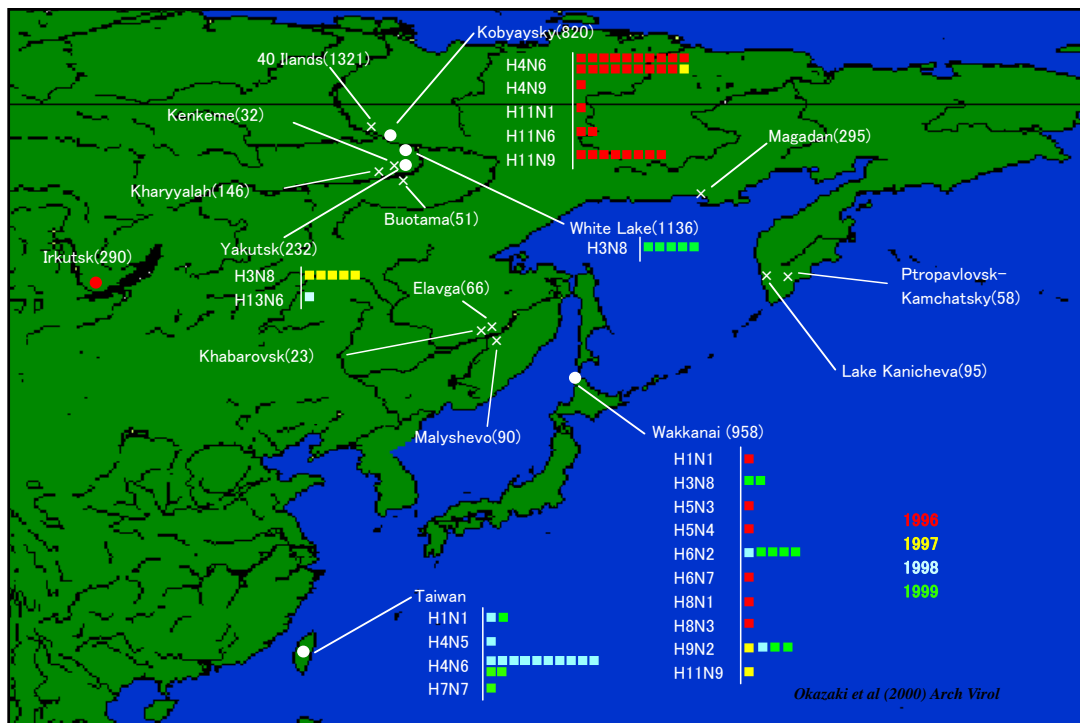
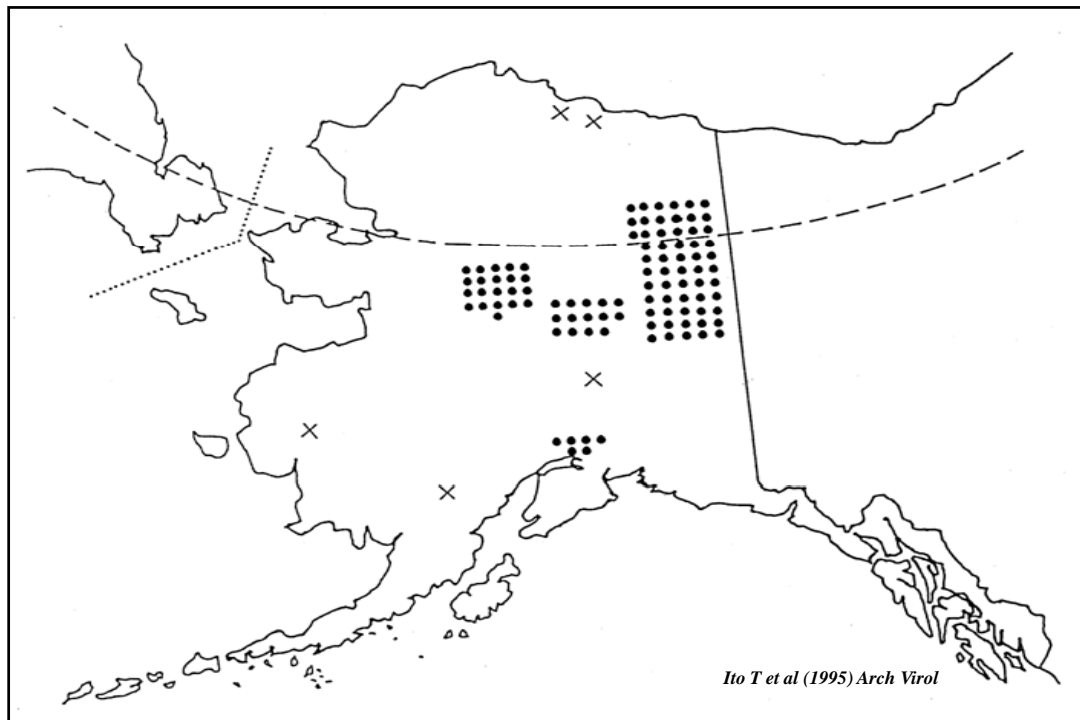
How to control avian influenza and how to prepare for pandemic influenza

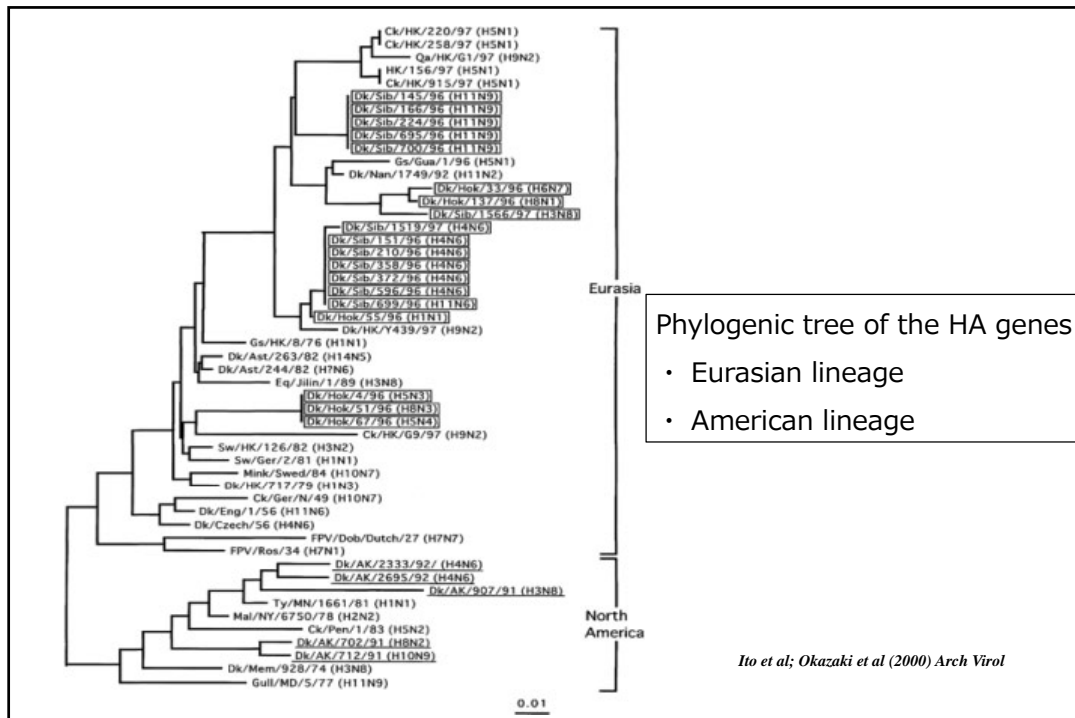
- 1. Why have the H5N1 HPAIVs persisted in poultry for 19 years and been antigenic variants selected ?**
Because of Misuse of Vaccine.
 - 2. Will the HPAIVs returned to migratory birds persist in nature ?**
Contamination of HPAIVs in the nesting lakes of migratory ducks must have occurred. Prompt eradication of the H5N1 HPAIVs from poultry in Asia is urgently needed.
 - 3. How should avian influenza be controlled ?**
For the containment and eradication of avian influenza viruses in the poultry flocks infected, enhanced surveillance, early detection, culling the flock, movement restriction, and strengthening hygiene without misuse of vaccine should be done.
Vaccine should be carefully used in addition to, not instead of stamping out.
 - 4. Will H5N1 HPAIV and H7N9 LPAIV cause pandemic influenza?**
It is unlikely to occur; direct transmission of AIV from birds only to specific humans who have receptor for avian strains, and thus human-human transmission may not occur, but may occur via pigs. H5N1 or H7N9 are not only candidates of pandemic strains.
 - 5. Are the measures for the control of seasonal flu satisfactory ?**
How to control pandemic influenza should be based on the measures for the control of seasonal influenza. Especially seasonal flu vaccines should be drastically improved since current split vaccines prepared by ether- or detergent-disruption are not immunogenic enough.
- ★ Global surveillance of avian, swine and human influenza, and drastic improvement of seasonal flu vaccines are of crucial importance.



Host range, and HA and NA subtypes of influenza A virus





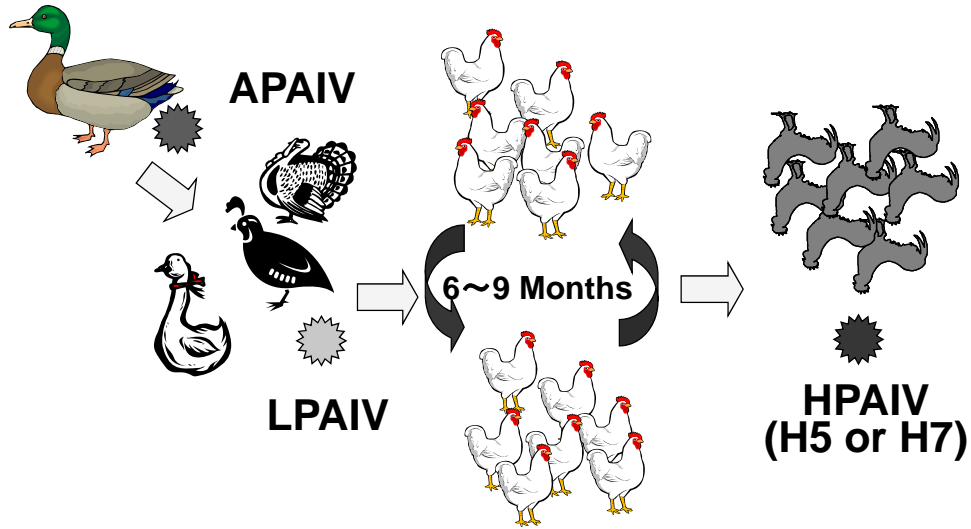


Duck influenza

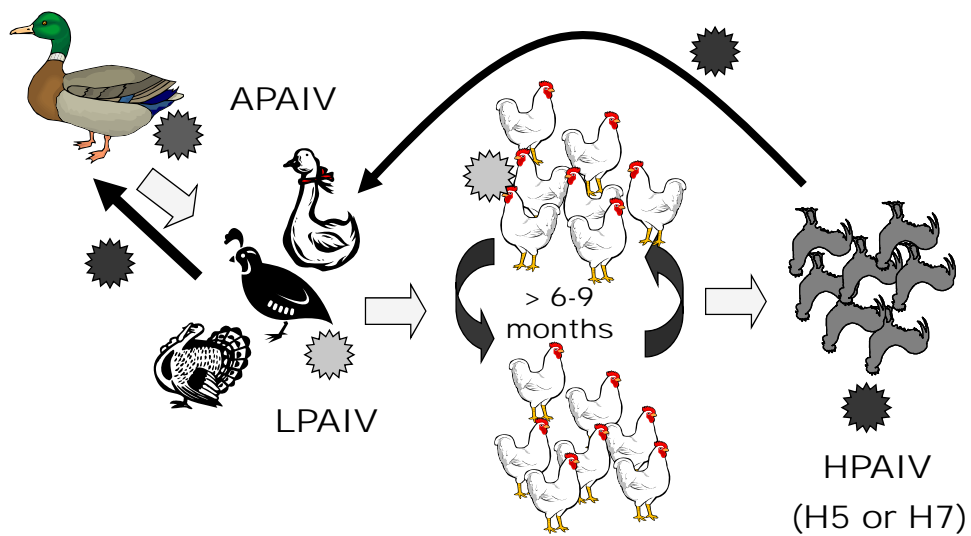
- Each of the known subtypes (H1-16, N1-9) of influenza A virus has been isolated from ducks.
- In ducks, viruses replicate in the colon, being shed with feces in a week, and non-pathogenic.
- Water-borne fecal-oral transmission
- Ducks carry and provide viruses during migration and overwintering.
- Influenza viruses circulating in ducks are antigenically and genetically highly stasis.

Migratory duck is the natural host of influenza A viruses.

Acquisition of pathogenicity of avian influenza viruses in chickens



Return of the HPAIV from domestic poultry to migratory water birds

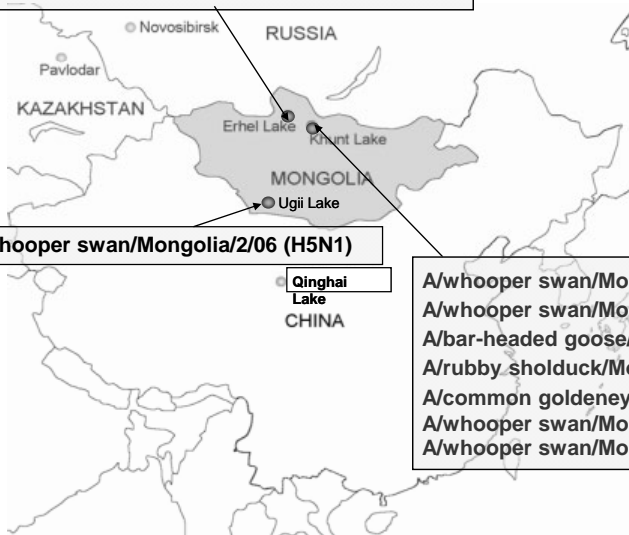


HPAI viruses isolated from wild birds in Mongolia

A/whooper swan/Mongolia/3/05 (H5N1)
A/bar-headed goose/Mongolia/1/05 (H5N1)
A/common goldeneye/Mongolia/12/06 (H5N1)



A/whooper swan/Mongolia/2/06 (H5N1)



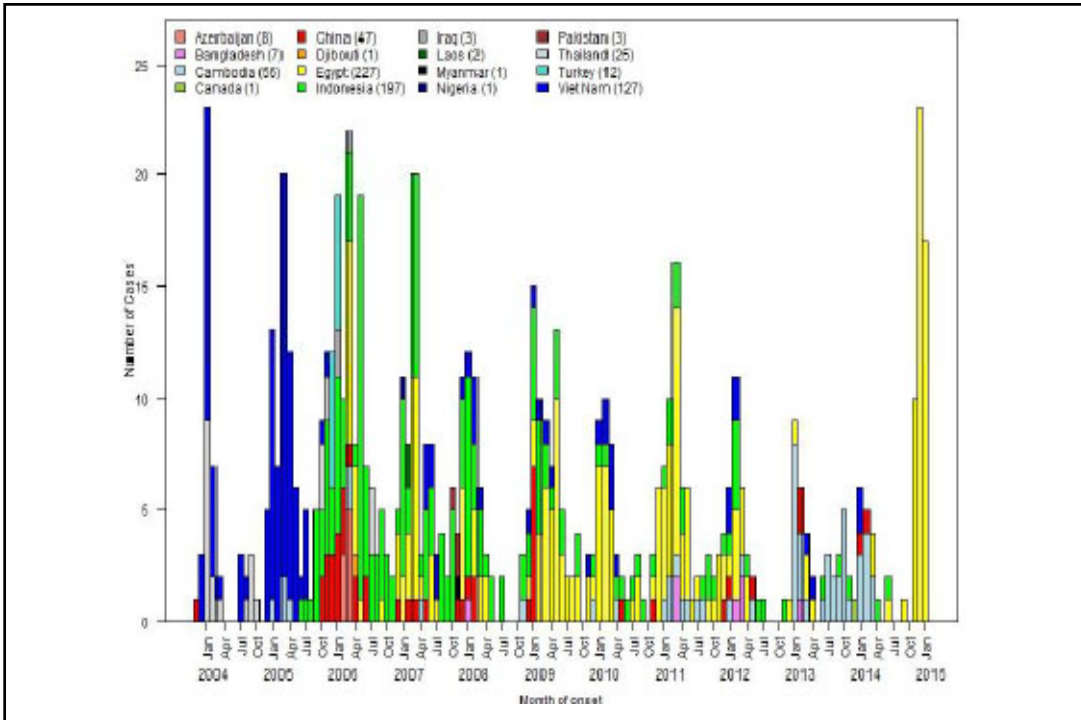
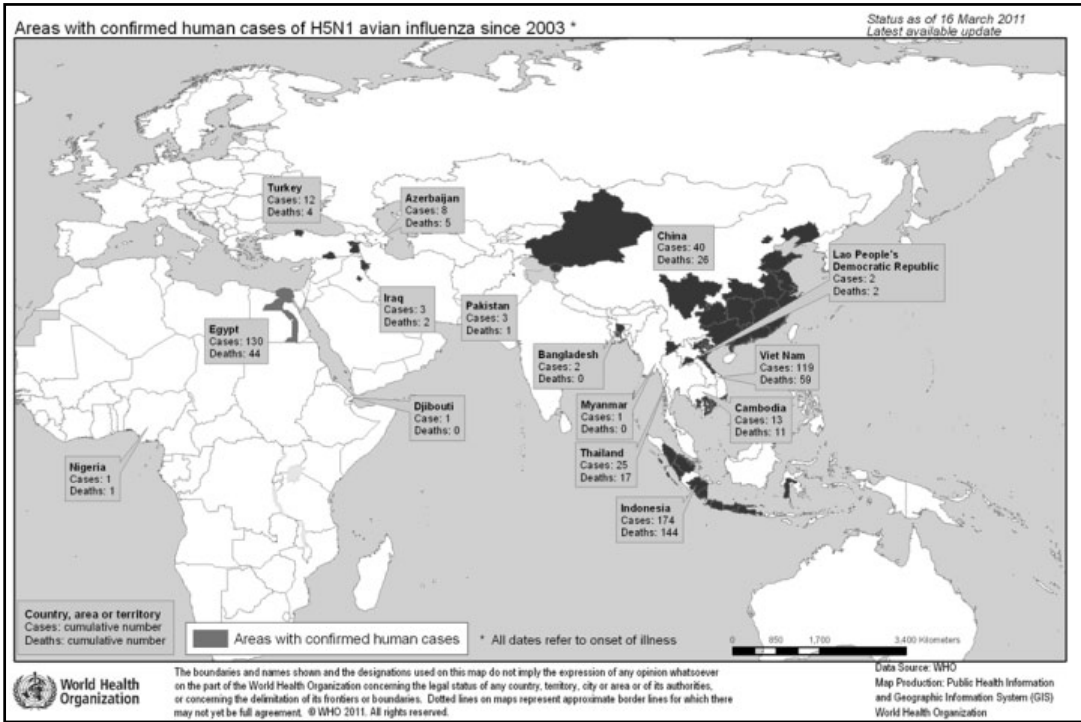
A/whooper swan/Mongolia/2/09 (H5N1)
A/whooper swan/Mongolia/9/09 (H5N1)
A/bar-headed goose/Mongolia/X53/09 (H5N1)
A/rubby sholduck/Mongolia/X42/2009 (H5N1)
A/common goldeneye/Mongolia/X60/09 (H5N1)
A/whooper swan/Mongolia/1/10 (H5N1)
A/whooper swan/Mongolia/7/10 (H5N1)

Areas reporting confirmed occurrence of H5N1 avian influenza in poultry and wild birds since 2003

Status as of 12 December 2009
 Latest available update



62 Countries where H5N1 HPAIV infections were reported in wild birds, poultry, and both Japan, Republic of Korea, China, Mongolia, Myanmar, Lao PDR, Thailand, Cambodia, Viet Nam, Malaysia, Indonesia, Bangladesh, India, Pakistan; Afghanistan, Iran, Azerbaijan, Georgia, Iraq, Kuwait, Saudi Arabia, Turkey, Israel; Russian Federation, Kazakhstan, Ukraine, Romania, Bulgaria, Albania, Serbia, Hungary, Slovakia, Czech Republic, Croatia, Poland, Slovenia, Bosnia & Herzegovina; Greece, Switzerland, Austria, France, Italy, Germany, Netherlands, Denmark, Sweden, Spain, England, Ireland; Djibouti, Gaza Strip, Egypt, Sudan, Nigeria, Niger, Cameroon, Burkina Faso, Cote d'Ivoire



Bird flu vaccines

Vietnam:
H5N2 and H5N1
(Adjuvant inactivated vaccines)

China:
H5N1 and recombinant NDV
(Reverse genetics inactivated vaccines)

Indonesia:
H5N1, H5N2, H5N9 and recombinant
H5N1
(inactivated vaccines)

Egypt: since 2006

Thailand:
Officially prohibited vaccination in 2006

As a stockpile,

Singapore:
H5N2
(Inactivated, adjuvanted vaccine)

Japan:
H5N1 and H7N7
(Oil-adjuvanted inactivated
vaccines)

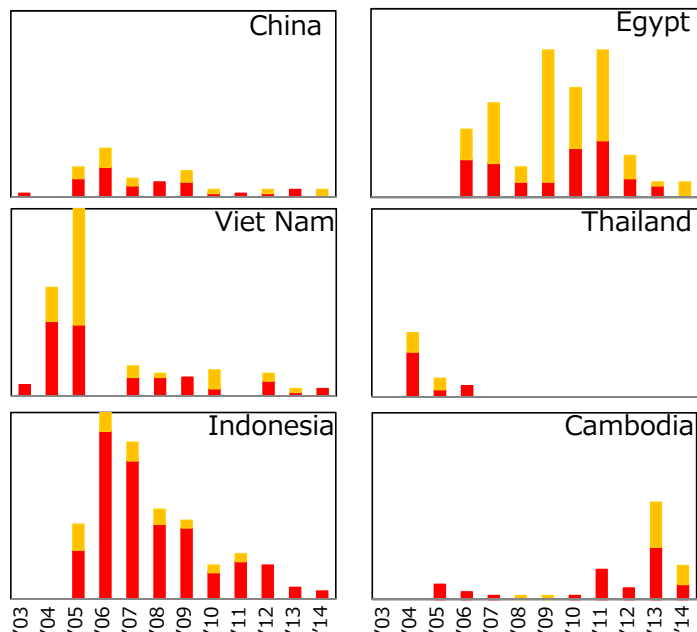
Pakistan:
H5N1, H5N2, H5N9, and H5N3
(Water based with alum hydroxide
and oil based with mineral oil)

Confirmed human cases of H5N1 HPAIV infection

Country	Deaths / Cases
China	30 / 47
Viet Nam	64 / 127
Indonesia	165 / 197
Egypt	63 / 173
Cambodia	37 / 56
Lao PDR	2 / 2
Thailand	17 / 25
Iraq	2 / 3
Azerbaijan	5 / 8
Turkey	4 / 12
Djibouti	0 / 1
Nigeria	1 / 1
Myanmar	0 / 1
Pakistan	1 / 3
Bangladesh	1 / 7
Canada	1 / 1
Total	393/688

As of 2 Oct. 2014

WHO (2014), Kuribayashi



Influenza Vaccine for bird flu

- may prevent manifestation of disease signs and decrease the amount of virus shed, but does not confer protective immunity from infection.
- “Stamping-out policy” is recommended for the control of avian influenza.
- Vaccination was not primarily recommended but later approved as one of the options applied only under DIVA based strategy.
- Country where vaccine is used is not designated as HPAI-free.

→ leads silent spread of virus.

26TH CONFERENCE OF THE OIE REGIONAL COMMISSION FOR ASIA, THE FAR EAST AND OCEANIA
Shanghai, People's Republic of China, 16-20 November 2009

RECOMMENDATION FOR THE CONTROL OF AVIAN INFLUENZA

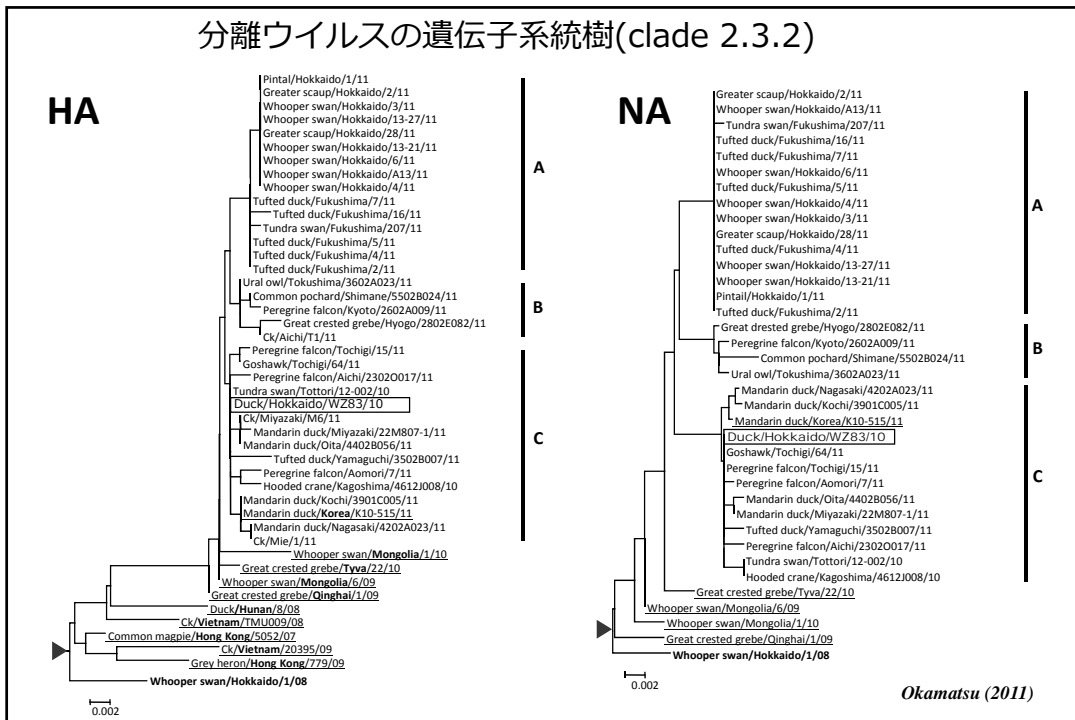
It is considered that;

- Highly pathogenic avian influenza H5N1 virus strains have persisted in domestic poultry for 14 years and antigenic variants have been selected mainly due to the misuse of vaccine.
- HPAI has been put under control in several countries.
- Stamping out policy has been the most effective measures for the control HPAI.
- Vaccine is used in 4 countries where HPAI has not been controlled.
- Vaccine is used instead of stamping out in 2 countries and in the other 2 countries, basically in addition to stamping out.
- Sentinel birds are put in the vaccinated poultry population in Viet Nam and not in the other 3 countries where vaccine is used.
- Compensation for livestock owners is done in most countries in case of stamping out.

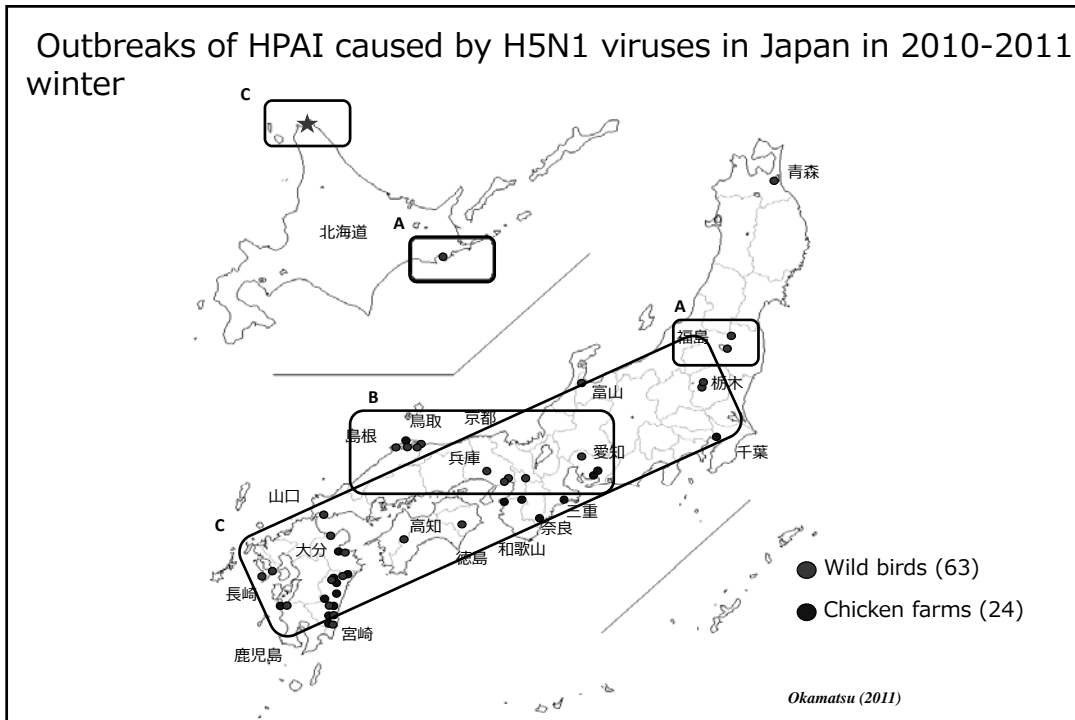
It is recommended that;

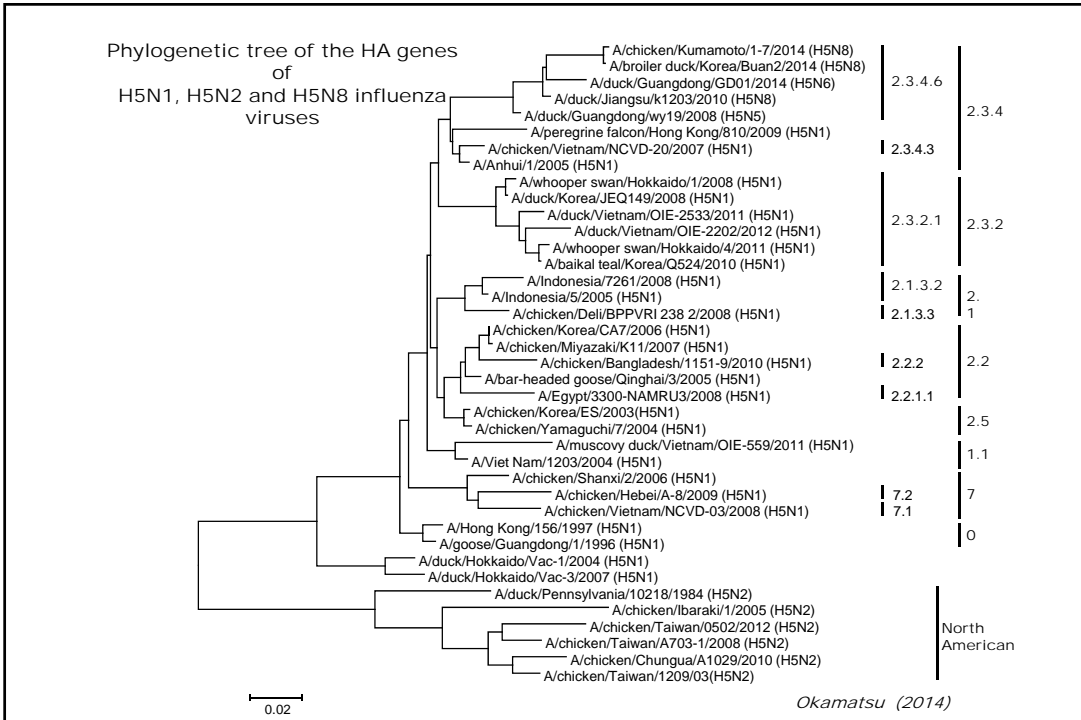
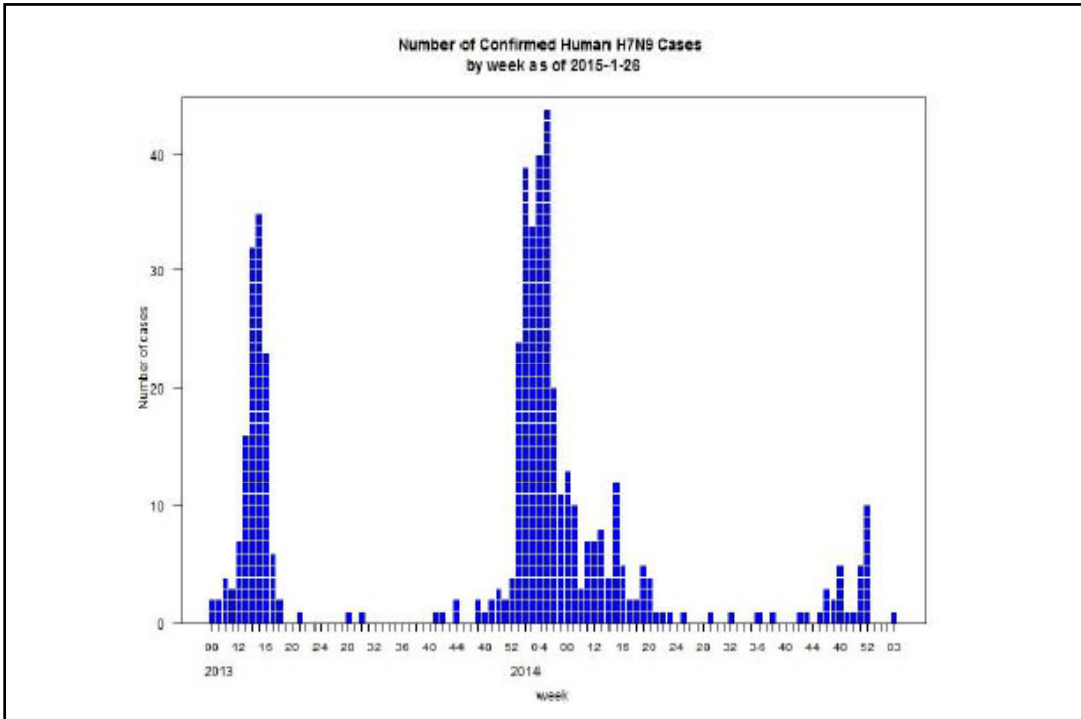
- Since stamping out is the best and ultimate measure for the control of HPAI, vaccine should be used
- The OIE should continue and develop standards on animal influenza surveillance, prevention and control.
- Surveillance of swine flu is crucial in the countries where avian flu has not been controlled.

分離ウイルスの遺伝子系統樹(clade 2.3.2)

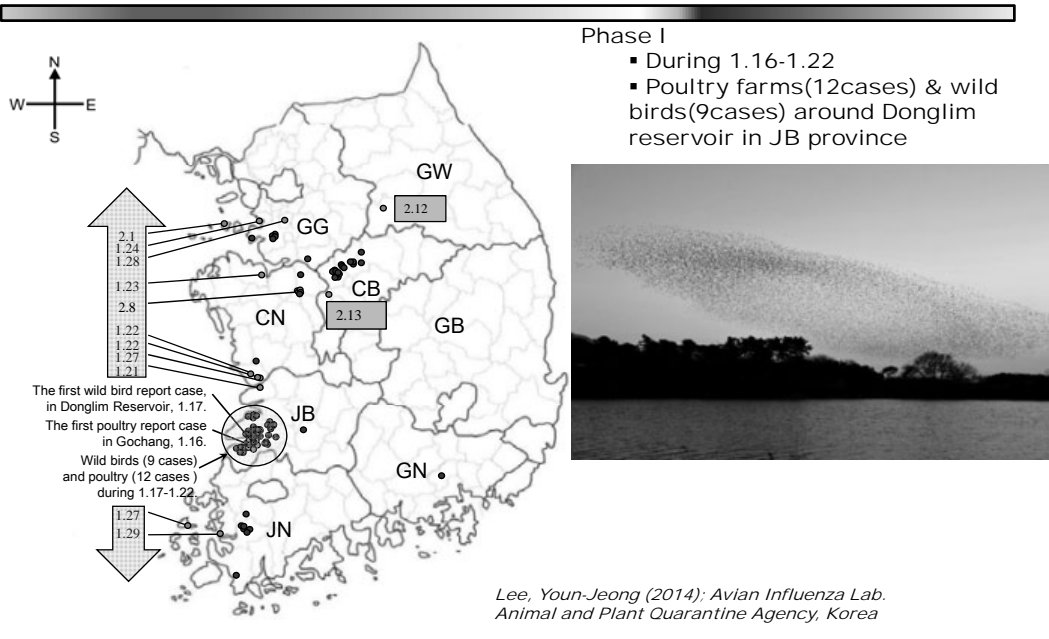


Outbreaks of HPAI caused by H5N1 viruses in Japan in 2010-2011 winter



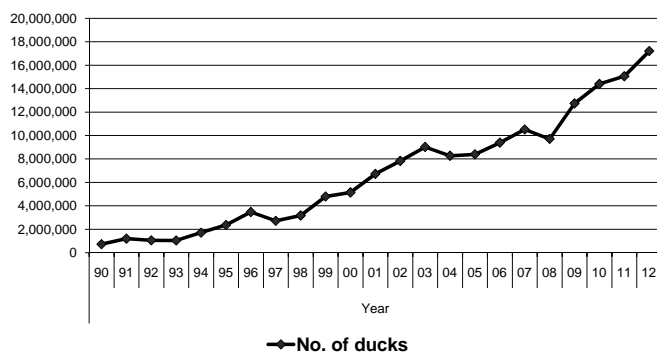


H5N8 HPAI outbreaks



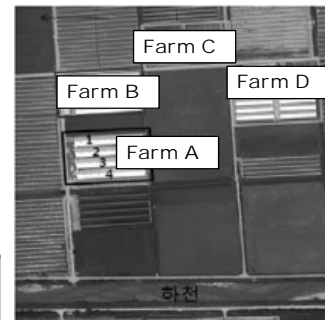
Domestic Duck Industry in Korea

- Duck industry have been sharply increased
- Biosecurity level is low
- Farms closely located with each other in the plain region
- High risk of transmission of virus: from wild birds to farm & farm to farm



Data: Korea Duck Association, 2014

Data: Epidemiological Division of QIA, 2014

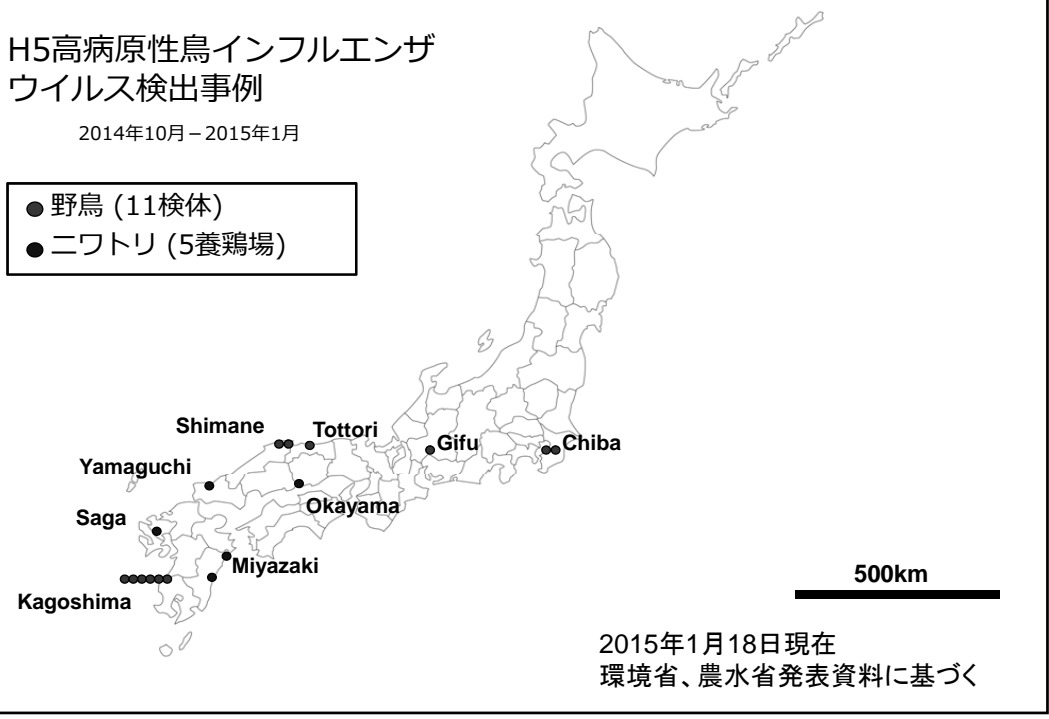


Lee, Youn-Jeong (2014); Avian Influenza Lab. Animal and Plant Quarantine Agency, Korea

H5高病原性鳥インフルエンザウイルス検出事例

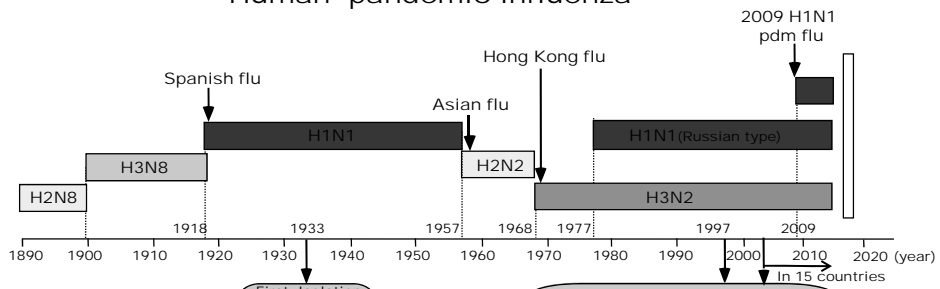
2014年10月 - 2015年1月

- 野鳥 (11検体)
- ニワトリ (5養鶏場)

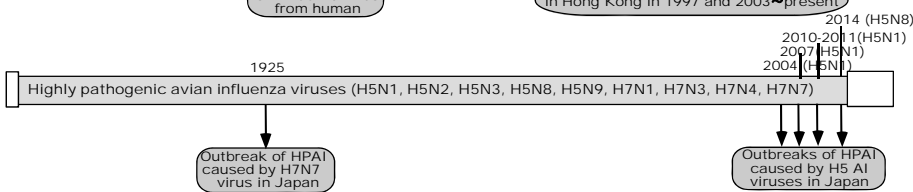


2015年1月18日現在
環境省、農水省発表資料に基づく

Human pandemic influenza



Highly pathogenic avian influenza



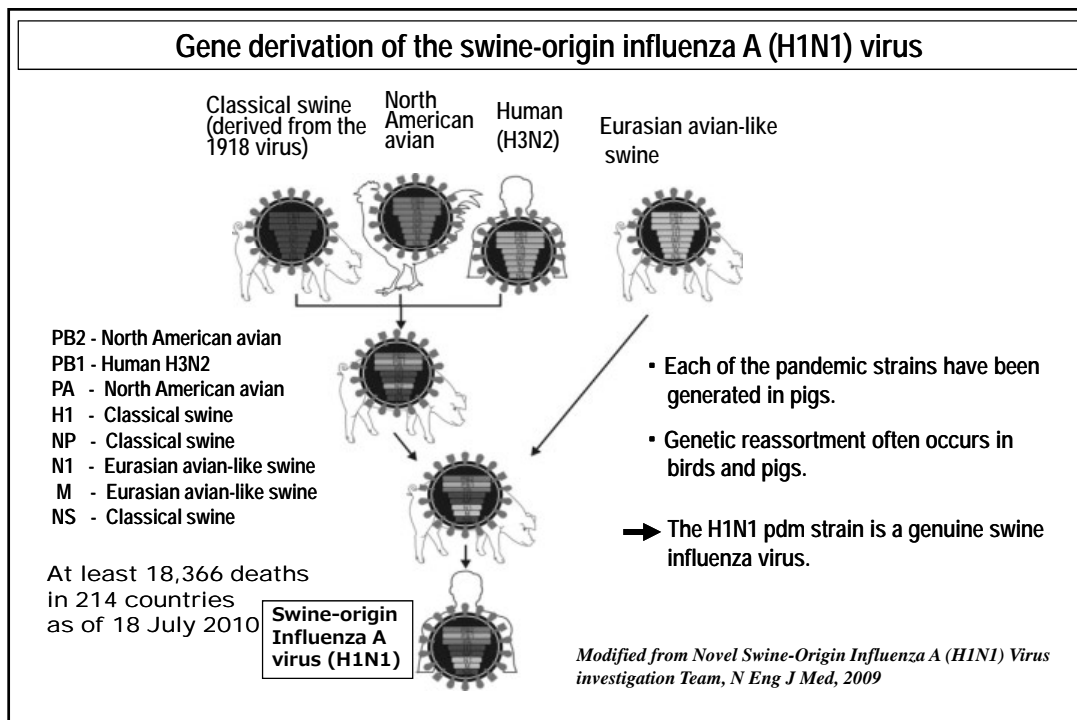
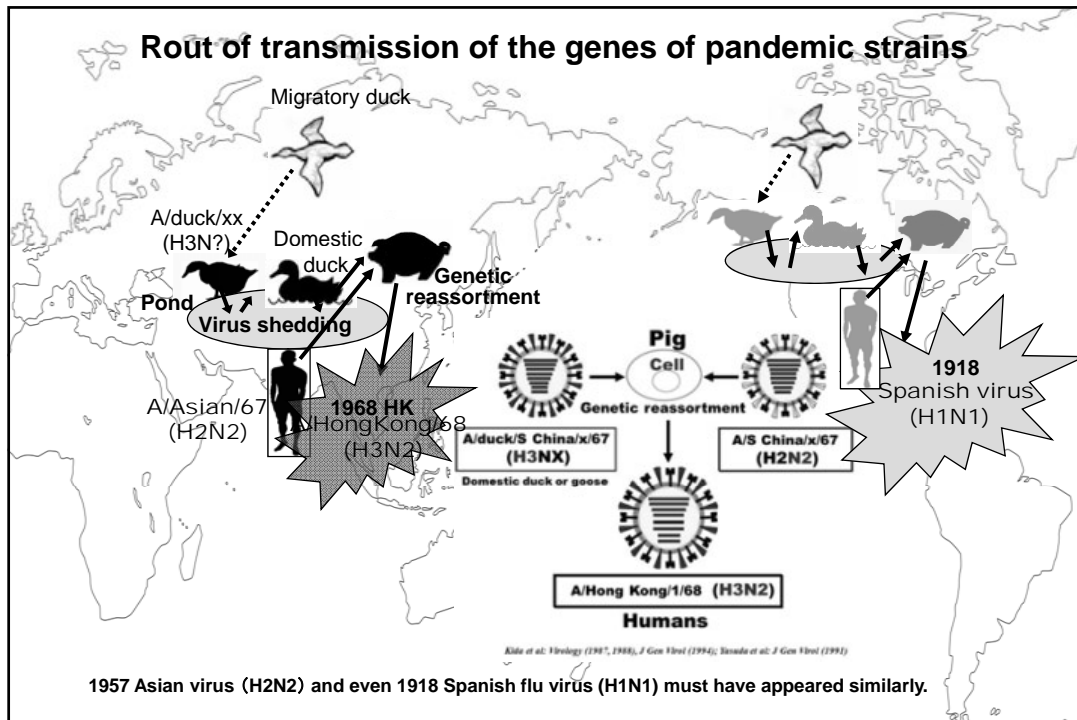
HAs of H3N2 viruses isolated from pigs in southern China

- ◊ Closely related with those of A/Hong Kong/68 (H3N2) and H3 viruses isolated from migratory ducks.
- ◊ Amino acid sequences at the receptor-binding site on the HA indicate either specificity to human or avian type receptors.
- ◊ Both types of receptor were found on the surface of the epithelial cells lining the upper respiratory tract of pigs.

KIDA et al (1988) Virology; Ito et al (1998) J Virol

Influenza viruses isolated from domestic ducks in southern China

- ◊ HAs of influenza viruses isolated from domestic ducks in southern China closely related with those of viruses isolated from migratory ducks, pigs, and A/Hong Kong/68 antigenically and genetically.
 - ◊ Each of the viruses was isolated on the Pacific Flyway of migratory ducks.
- **Route of transmission;**
Migratory duck → domestic duck → pig → humans



The role of pigs in the emergence of pandemic influenza virus strains

- ◆ Pigs are susceptible to infection with avian influenza viruses of each of the HA subtypes.
- ◆ Genetic reassortants were generated in the cells lining upper respiratory tract of pig upon concurrent infection with mammalian and avian strains.

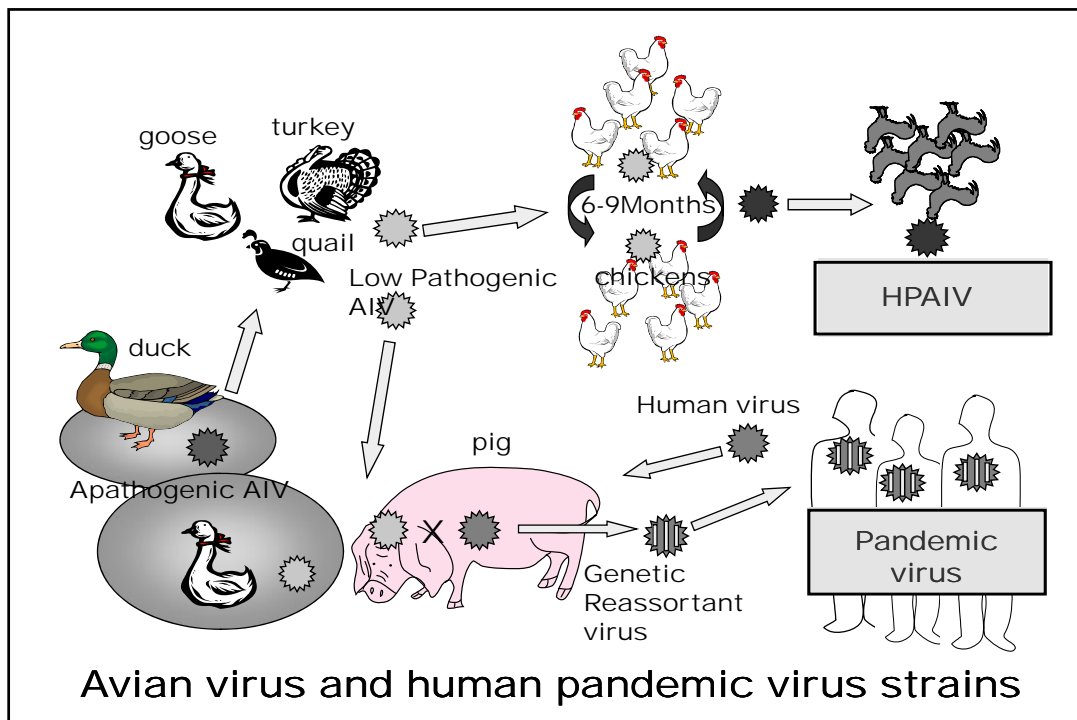
Kida H et al (1994) J Gen Virol

Candidates of future pandemic strain

- ◆ H1 to H16 and N1 to N9 subtypes of influenza A viruses perpetuate in the lakes where ducks nest in nature.
- ◆ 1957 H2N2, 1968 H3N2, even 1918 H1N1 and 2009 H1N1 pandemic viruses are reassortants between AIV and the preceding human strains.
- ◆ Pigs are susceptible to each of avian and mammalian influenza viruses, generating reassortants.

Avian viruses of any subtype can contribute genes for reassortants; None of the 16 HA and 9 NA subtypes can be ruled out as potential candidates for future pandemics.

➔ Global surveillance of swine flu as well as avian flu is important.



Library of vaccine strain candidates

	H1	H2	H3	H4	H5	H6	H7	H8	H9	H10	H11	H12	H13	H14	H15	H16
N1	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N2	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N3	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N4	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N5	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N6	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N7	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N8	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
N9	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Influenza viruses of 75 combinations of the HA and NA subtypes have been isolated from fecal samples of ducks in Alaska, Siberia, Mongolia, Taiwan, China, and Japan (black).

69 other combinations have been generated by genetic reassortment procedure in the lab (red)..

● Virus isolated from a waterfowl (75 combinations)
 ● Virus generated in the laboratory (69 combinations)

Jan 26, 2015

Thus, 2,000 avian influenza viruses of 144 combinations of HA and NA subtypes have been stocked as vaccine strain candidates. Their pathogenicity, antigenicity, genetic information and yield in chicken embryo have been analyzed, databased, and opened for Web site (<http://virusdb.czc.hokudai.ac.jp/vdbportal/view/index.jsp>).

How to prepare for pandemic influenza should be based upon how to control seasonal influenza

→ Drastic improvement of seasonal flu vaccine and biological standard

Short term goal:

1. Improvement of the immunological potency of seasonal flu vaccines ;
Clinical evaluation of inactivated vaccine of purified whole virus particles
Drastic revision of biological standard
2. Preemptive preparation of vaccine by forestall of antigenic variants on the basis of global surveillance and bioinformatics.
Good bye backward selection of vaccine strains.

Long term goal:

1. Development of effective and safe mucosal vaccines
2. Development of effective and safe adjuvants

Points:

1. Influenza is a typical acute infection.
2. Influenza is not eradicable, every year seasonal influenza must come.

Proposal of the development and practical use of seasonal influenza vaccines of global standard by the cooperation of industry, university, and government

Hiroshi Kida

Preclinical and clinical studies on seasonal influenza vaccines prepared from the inactivated whole virus particles

- 1) Each of 5 flu vaccine producers in Japan participates in the program (All Japan).
- 2) Comparison of immunogenicity and safety between whole virus particle vaccine and split vaccines.
Viruses, cultured in the cells or embryonated chicken eggs and purified are subjected to prepare whole particle vaccines and ether-disrupted split vaccines by each of the vaccine producers and Hokkaido University.
Vaccines prepared are subjected to immunological potency test and safety tests using in mice, ferrets, and monkeys for the preclinical tests, and humans for clinical tests.
担当：各製造所・社、北海道大学、新日本科学(株)(フェレット)、滋賀医科大学(サル)ほかが前臨床試験。
国立病院機構、国公私立大学病院、医師会、小児科医会、内科医会ほかが臨床試験。
- 3) Evaluation of the results of the tests.
担当：大学、学会、日本ワクチン産業協会、感染研ほか。
- 4) Drastic revision of biological standard for vaccines for human use.
担当：感染研、日本ワクチン産業協会、ワクチン学会、臨床ウイルス学会、インフルエンザ研究者交流の会ほか。
- 5) Each member studies on the route of inoculation of the vaccines and adjuvants for themselves.
- 6) Participants to this program:
Industries; 製造所・社; 北里第一三共、武田薬品、阪大微研会、化血研、デンカ生研
Universities; 北海道大学、メルボルン大学、ワクチン学会、ウイルス学会、臨床ウイルス学会、医師会ほか
Government; 感染研、厚生労働省、内閣府、文部科学省ほか。
- 7) Budget: 厚生労働科学研究費補助金、文部科学省・学術振興会科学研究費、JST、日本版 NIH (AMED) ほか。

How to control avian influenza and how to prepare for pandemic influenza

1. Why have the H5N1 HPAIVs persisted in poultry for 19 years and been antigenic variants selected ?
Because of Misuse of Vaccine.
 2. Will the HPAIVs returned to migratory birds persist in nature ?
Contamination of HPAIVs in the nesting lakes of migratory ducks must have occurred. Prompt eradication of the H5N1 HPAIVs from poultry in Asia is urgently needed.
 3. How should avian influenza be controlled ?
For the containment and eradication of avian influenza viruses in the poultry flocks infected, enhanced surveillance, early detection, culling the flock, movement restriction, and strengthening hygiene without misuse of vaccine should be done. Vaccine should be carefully used in addition to, not instead of stamping out.
 4. Will H5N1 HPAIV and H7N9 LPAIV cause pandemic influenza?
It is unlikely to occur; direct transmission of AIV from birds only to specific humans who have receptor for avian strains, and thus human-human transmission may not occur, but may occur via pigs. H5N1 or H7N9 are not only candidates of pandemic strains.
 5. Are the measures for the control of seasonal flu satisfactory ?
How to control pandemic influenza should be based on the measures for the control of seasonal influenza. Especially seasonal flu vaccines should be drastically improved since current split vaccines prepared by ether- or detergent-disruption are not immunogenic enough.
- ★ Global surveillance of avian, swine and human influenza, and drastic improvement of seasonal flu vaccines are of crucial importance.

**2015 International Symposium on
Avian Influenza Prevention and Control**

11 March 2015, Taipei, Taiwan

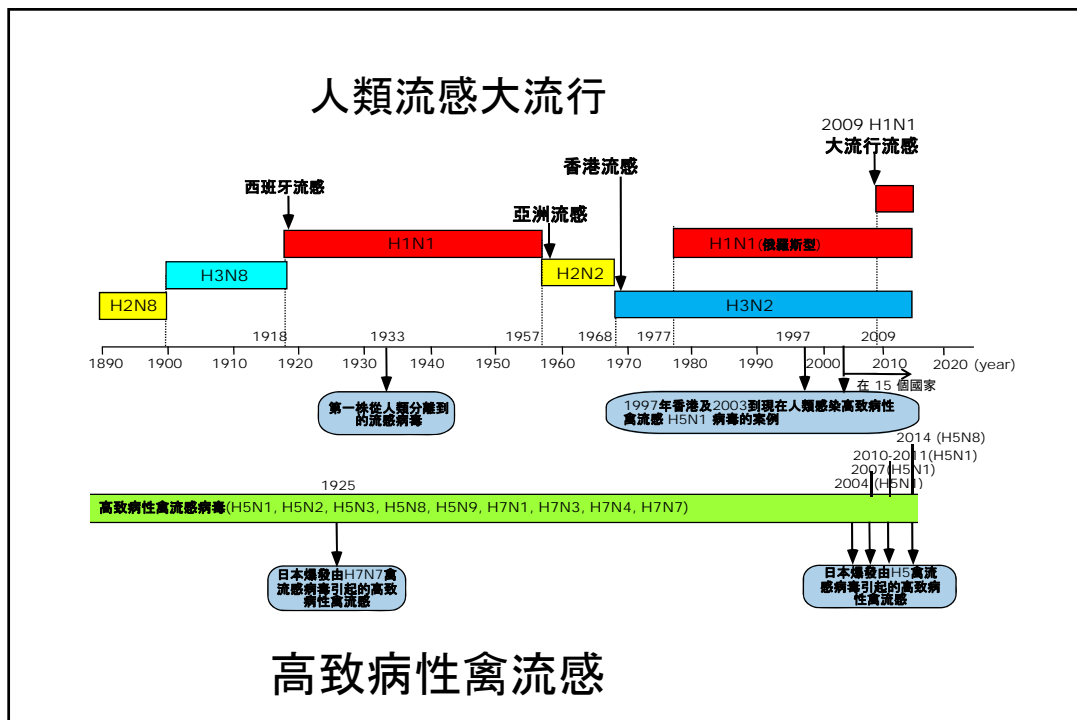
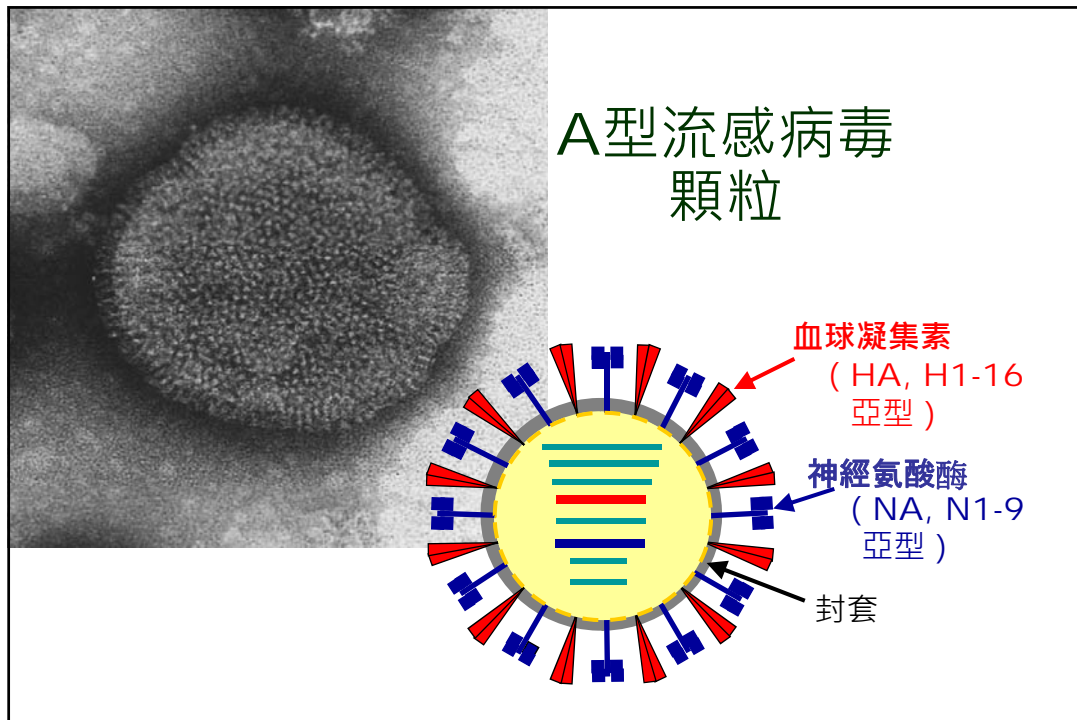
**如何控制禽流感及如何為流感大
流行做好準備**

Hiroshi Kida, DVM, PhD

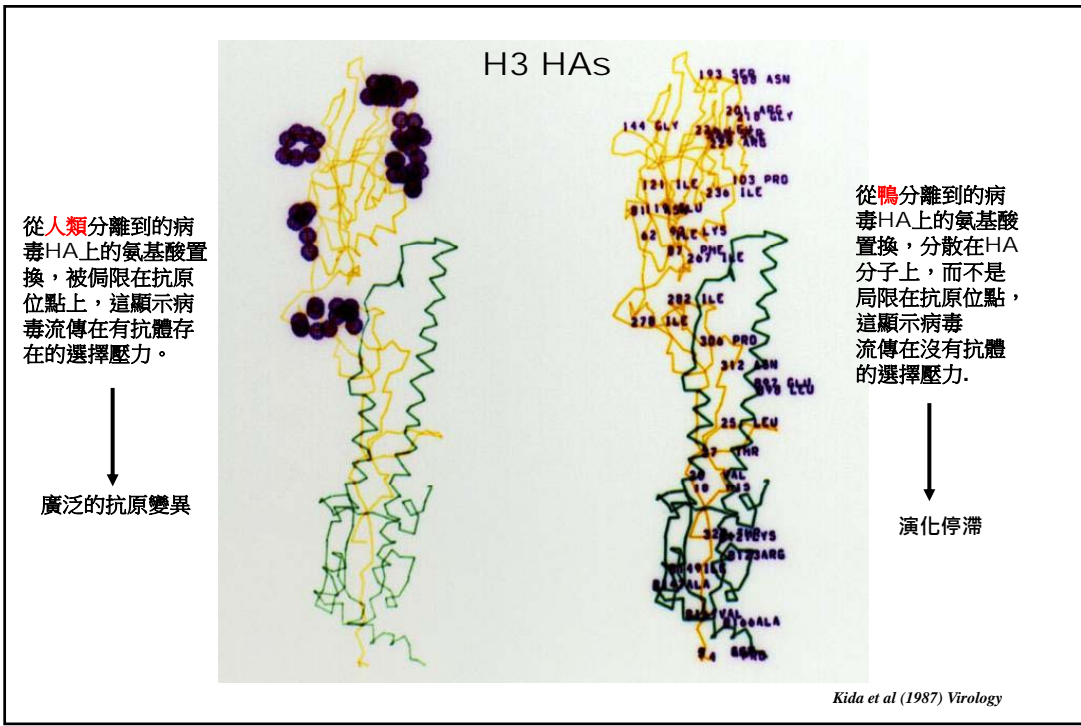
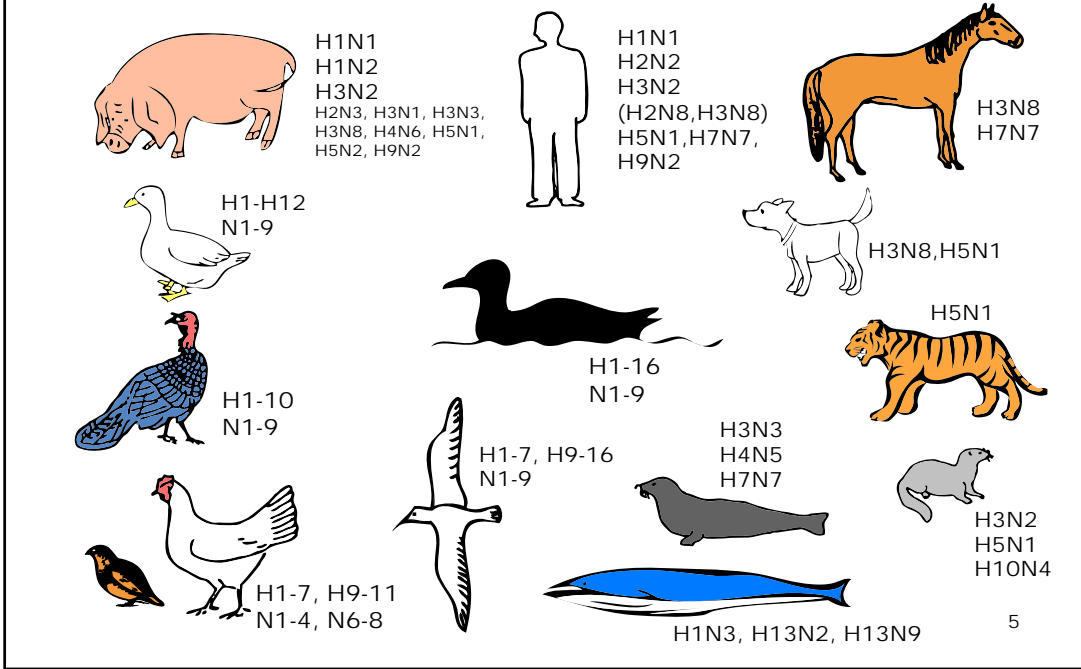
**Member of the Japan Academy
Specially Appointed Professor, Hokkaido University
Head, Research Center for Zoonosis Control
Head, OIE Reference Laboratory for Animal Influenza
Head, WHO Collaborating Centre for Zoonoses Control**

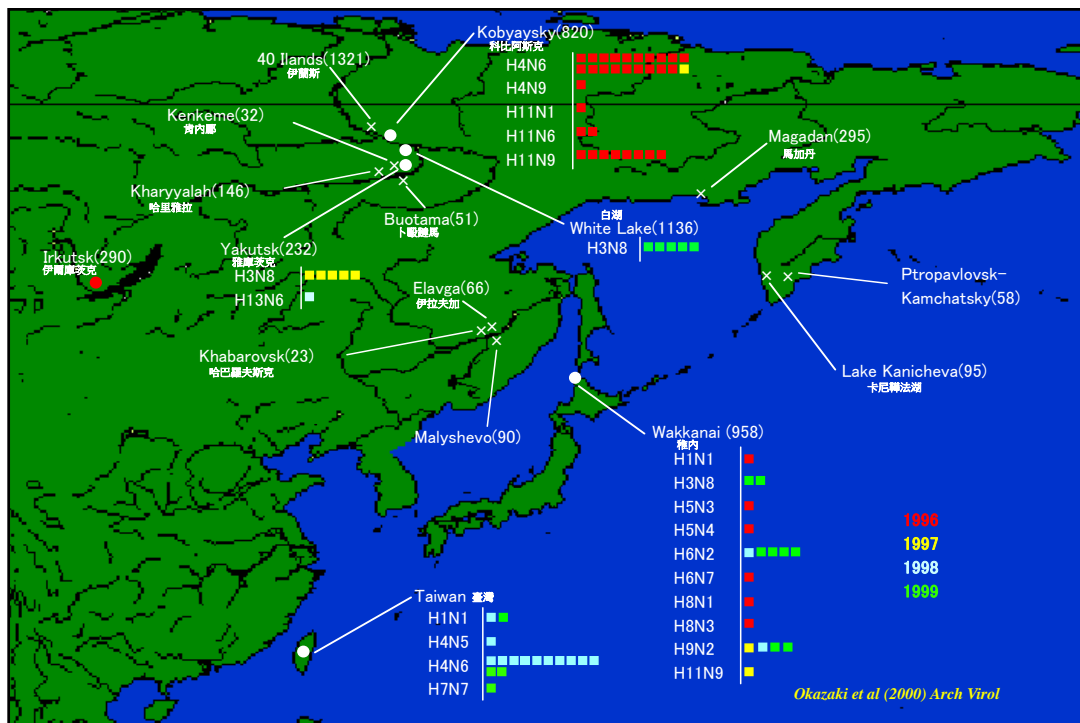
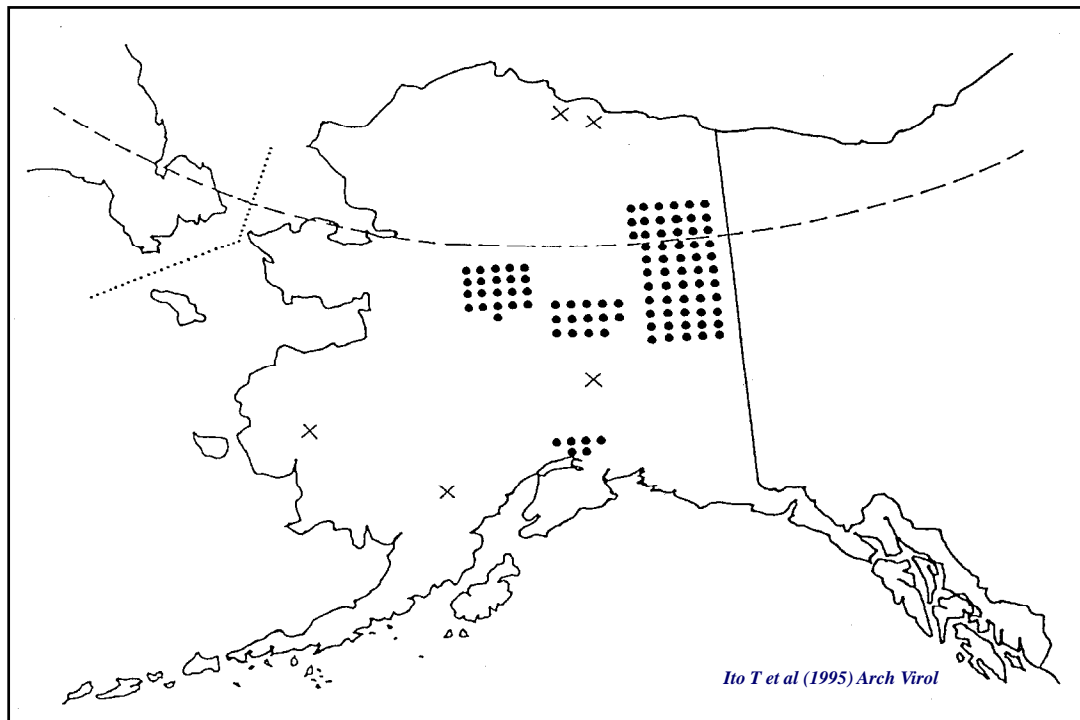
如何控制禽流感及如何為流感大流行做好準備

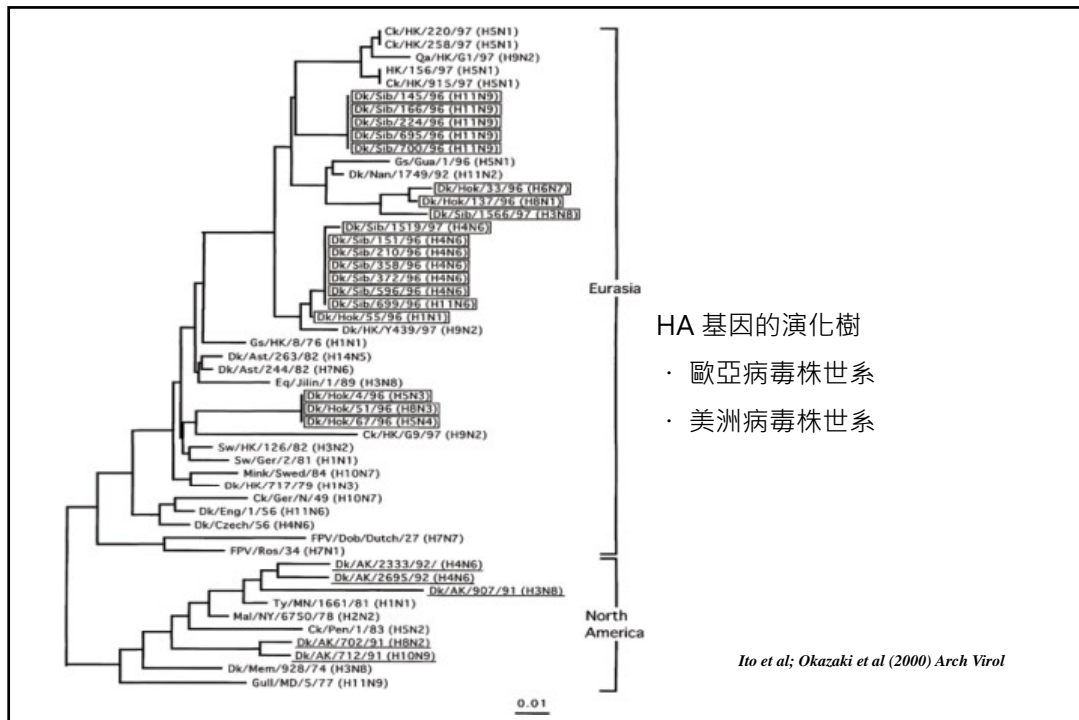
- 1. 為什麼有高致病性禽流感H5N1 病毒持續存在家禽19年, 且被選定抗原變異?**
因為誤用疫苗。
 - 2. 高致病性禽流感病毒是否會回到候鳥而持續存在於自然界?**
高致病性禽流感病毒污染遷徙鴨的湖泊巢穴則必然發生。
迅速的撲滅在亞洲家禽的高致病性禽流感H5N1病毒是迫切需要的。
 - 3. 應該如何禽流感方能得到控制?**
為了遏制和撲滅感染禽流感病毒的家禽，加強監測，及早發現，撲殺禽群，移動管制，並加強衛生及不誤用疫苗是應該做的。
除了疫苗應謹慎使用，也不能取代撲殺。
 - 4. 高致病性禽流感H5N1病毒及低致病性禽流感H7N9病毒會不會造成流感大流行?**
它是不太可能發生；禽流感病毒直接從鳥類傳播給人，只會對特定具有禽流感病毒接受體的人，因此人傳人可能不會發生，但經由豬可能會發生。H5N1或H7N9並不是大流行病毒株的唯一選項。
 - 5. 對於季節性流感的控制措施滿意嗎?**
如何控制大流行流感應基於季節性流感的控制措施。特別是季節性流感疫苗應大幅改善，因為當前裂解疫苗是以鹼或清潔劑破壞而製備，其免疫原性不足夠。
- ★全球監控家禽、豬和人流感，以及季節性流感疫苗的大幅改善是至關重要的。



宿主範圍, 及A型流感病毒的 HA 和 NA 亞型





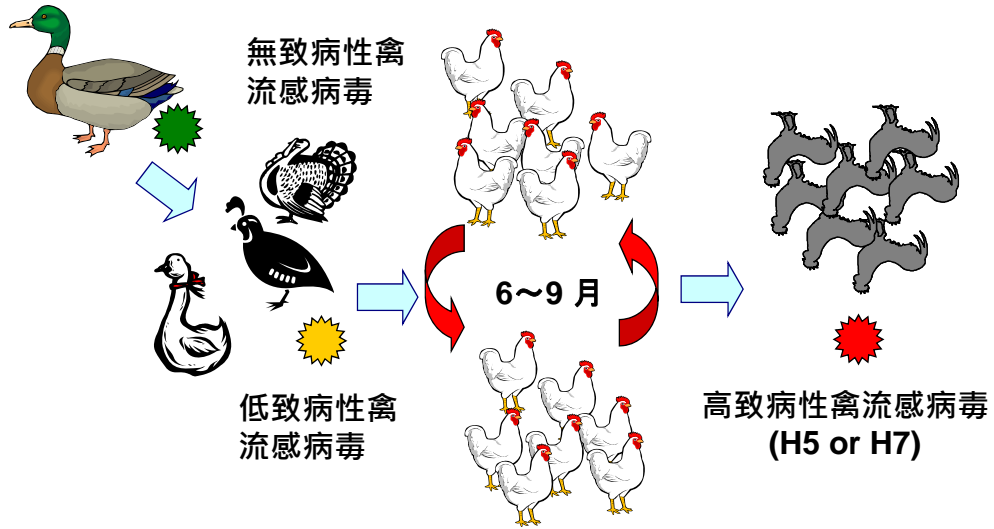


鴨流感

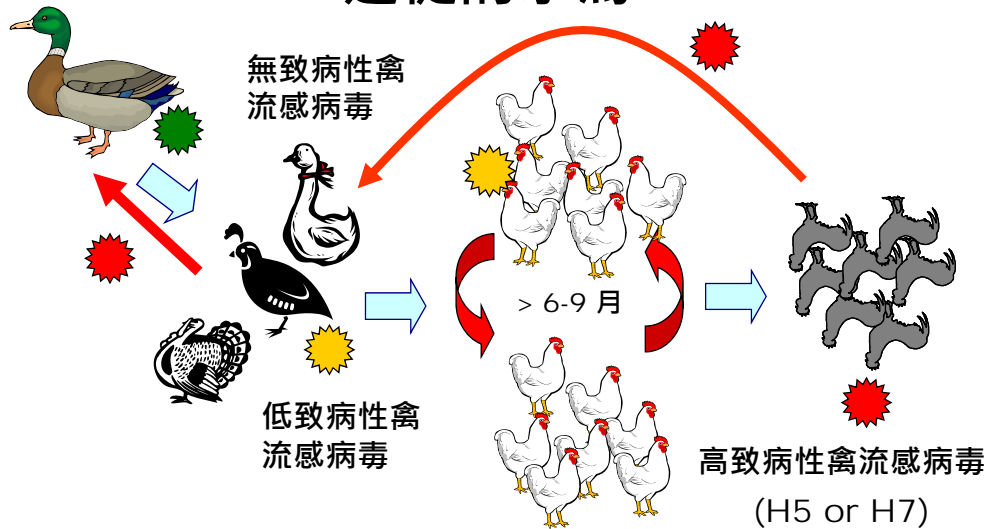
- 每個已知亞型(H1-16, N1-9)的流感病毒均已從鴨被分離到。
- 在鴨,病毒在結腸增殖,在一週就從糞便排出,無致病性。
- 水媒性的糞 - 口途徑傳播
- 在遷移過程與過冬期間,鴨子攜帶及提供病毒。
- 流傳在鴨子的流感病毒之抗原性和遺傳性均高度停滯。

→ 遷徙鴨是A型流感病毒的自然宿主。

雞隻禽流感病毒致病性的獲得



高致病性禽流感病毒從家禽回到 遷徙的水鳥



在蒙古從野鳥分離到的高致病性禽流感病毒

A/大天鵝/Mongolia/3/05 (H5N1)
 A/斑頭鵝/Mongolia/1/05 (H5N1)
 A/鵞鴨/Mongolia/12/06 (H5N1)

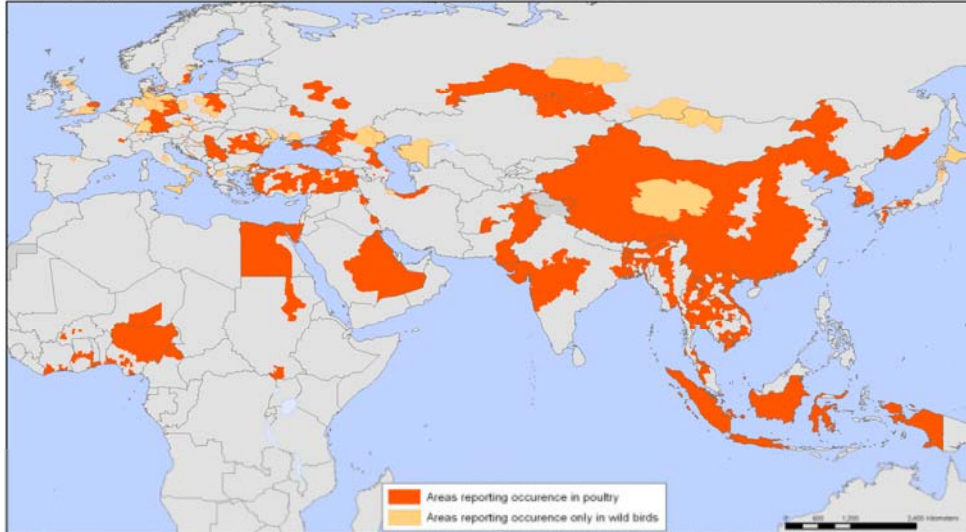
A/大天鵝/Mongolia/2/06 (H5N1)

A/大天鵝/Mongolia/2/09 (H5N1)
 A/大天鵝/Mongolia/9/09 (H5N1)
 A/斑頭鵝/Mongolia/X53/09 (H5N1)
 A/赤麻鴨/Mongolia/X42/2009 (H5N1)
 A/鵞鴨/Mongolia/X60/09 (H5N1)
 A/大天鵝/Mongolia/1/10 (H5N1)
 A/大天鵝/Mongolia/7/10 (H5N1)



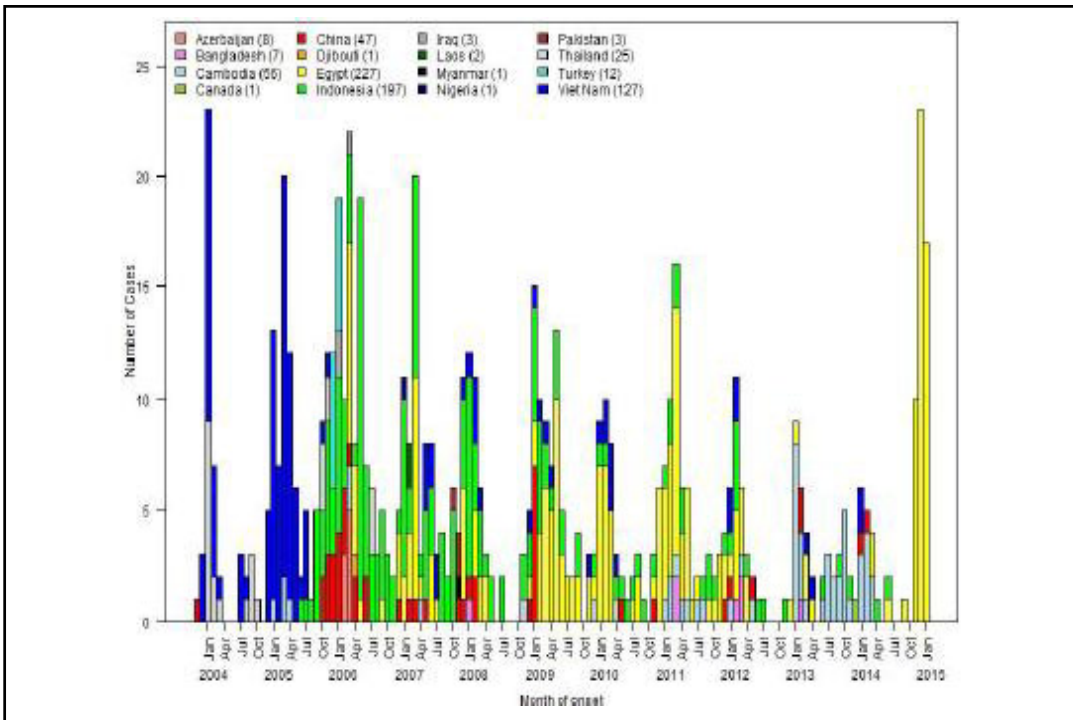
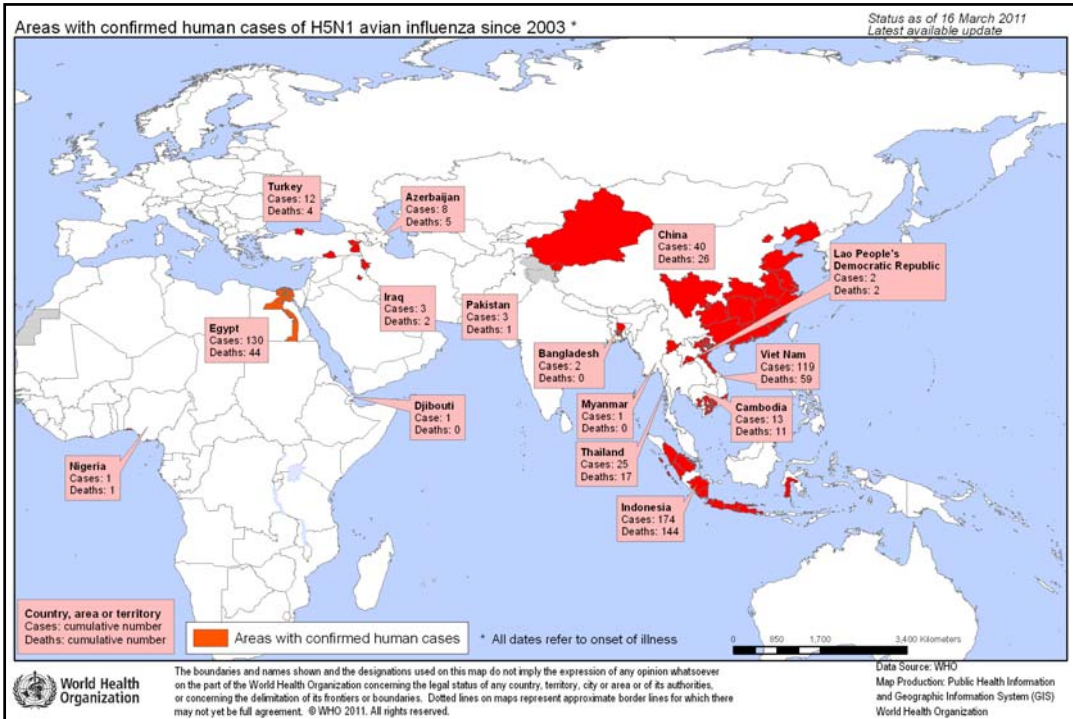
Areas reporting confirmed occurrence of H5N1 avian influenza in poultry and wild birds since 2003

Status as of 12 December 2006
 Latest available update



62 國通報高致病性禽流感H5N1病毒在野鳥、家禽及兩者的感染案例

Japan, Republic of Korea, China, Mongolia, Myanmar, Lao PDR, Thailand, Cambodia, Malaysia, Indonesia, Bangladesh, India, Pakistan; Afghanistan, Iran, Azerbaijan, Georgia, Iraq, Kuwait, Saudi Arabia, Turkey, Israel; Russian Federation, Kazakhstan, Ukraine, Romania, Bulgaria, Albania, Serbia, Hungary, Slovakia, Czech Republic, Croatia, Poland, Slovenia, Bosnia & Herzegovina; Greece, Switzerland, Austria, France, Italy, Germany, Netherlands, Denmark, Sweden, Spain, England, Ireland; Djibouti, Gaza Strip, Egypt, Sudan, Nigeria, Niger, Cameroon, Burkina Faso, Cote d'Ivoire



對禽流感的流感疫苗

- 可預防疾病臨床症狀的表現，降低病毒的排出數量，但並沒有賦予針對感染的保護性免疫。
- “撲殺政策”被推薦用於禽流感的控制。
- 施打疫苗不是首要的推薦，但後來批准為選項之一，但只適用於基於DIVA策略下。
- 使用疫苗的國家，就不被認定為無高致病性禽流感。

→ 導致病毒的沉默傳播。

OIE亞洲，遠東和大洋洲的區域委員會第26次會議

上海，中華人民共和國，2009年11月16-20日

建議禽流感的控制

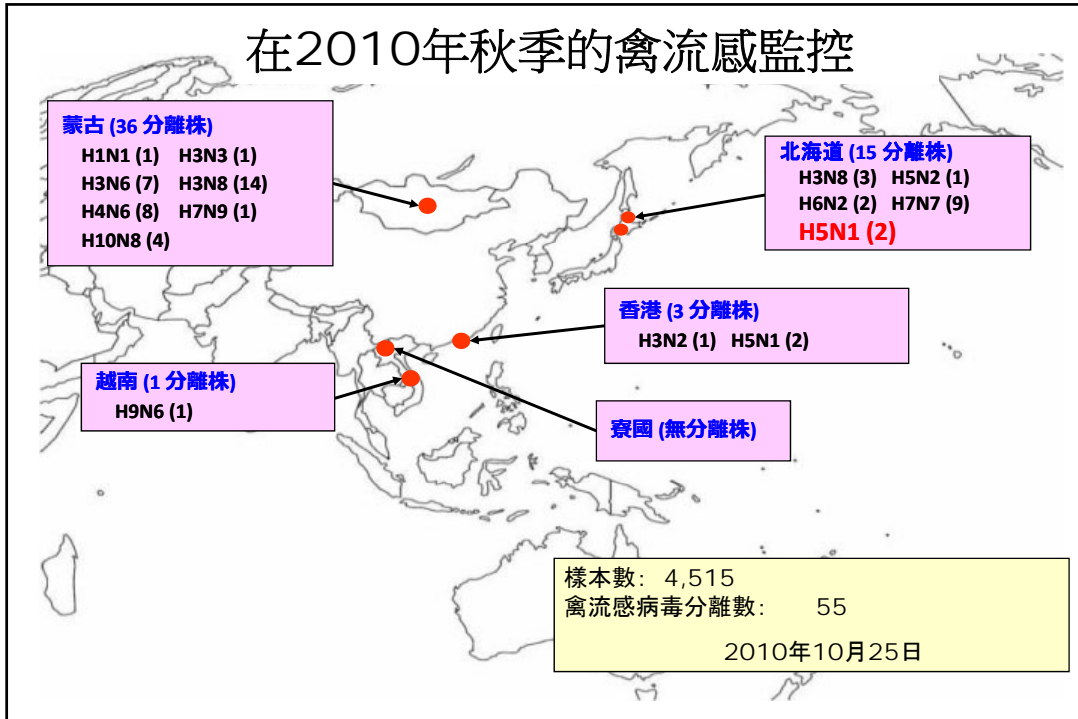
一致認為；

- 高致病性禽流感H5N1病毒株已經持續存在家禽14年，主要是由於疫苗的濫用造成抗原變異被選定。
- 高致病性禽流感在幾個國家已得到控制。
- 撲殺政策一直是控制高致病性禽流感最有效的措施。
- 4個國家使用疫苗，其高致病性禽流感還沒有得到控制。
- 2個國家以使用疫苗來代替撲殺，而在另外2個國家，基本上除了撲殺也使用疫苗。
- 在越南將哨兵禽放入接種疫苗的家禽族群中，而在其他3個使用疫苗的國家，則沒有放哨兵禽。
- 大多數國家在撲殺後，都對畜主做補償。

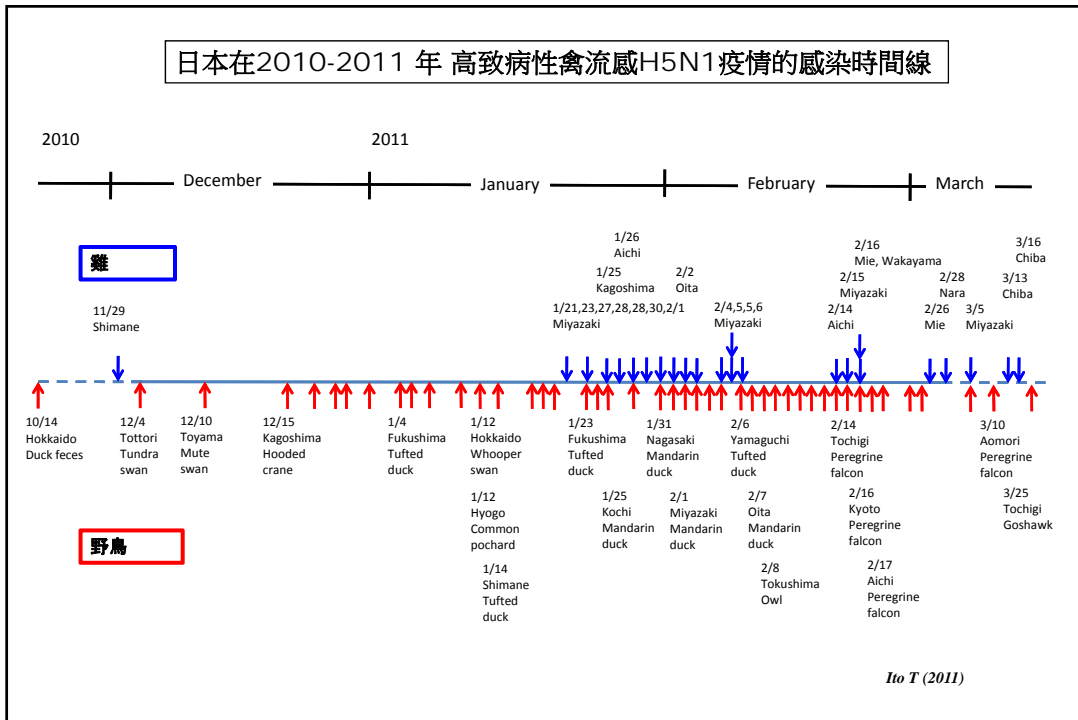
建議；

- 由於撲殺是控制高致病性禽流感的最好的和最終的措施，疫苗的使用，不能取代撲殺。
- 世界動物衛生組織應繼續並發展對動物流感監測，預防和控制的標準。
- 豬流感的監測在禽流感一直沒有得到控制的國家是至為重要。

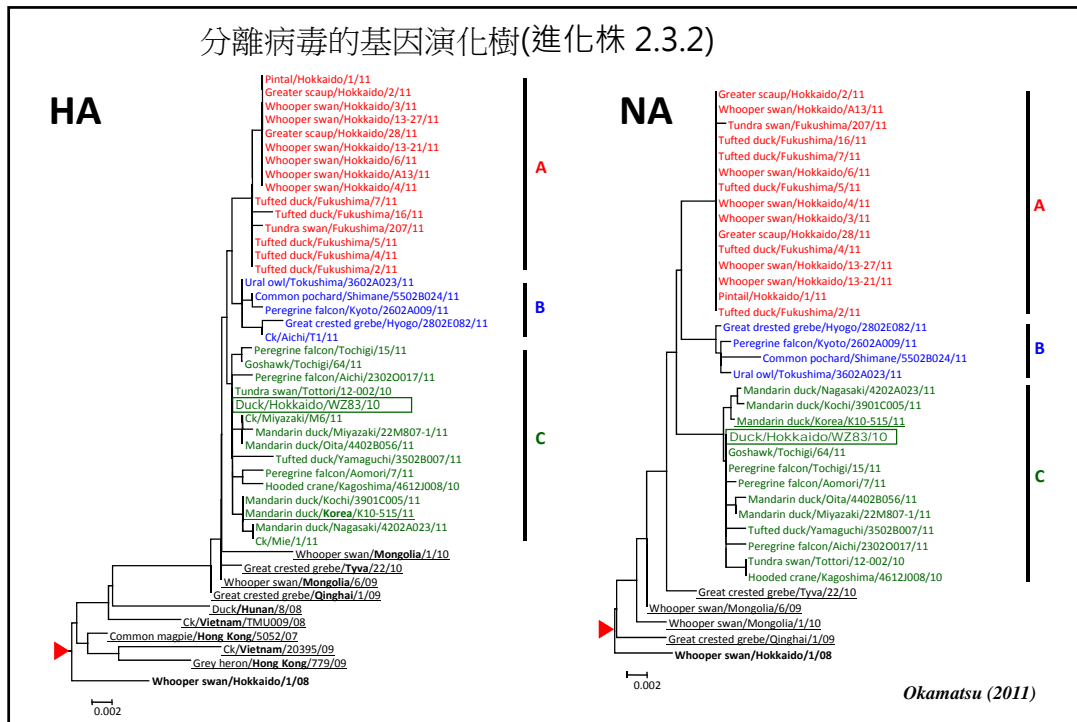
在2010年秋季的禽流感監控



日本在2010-2011 年 高致病性禽流感H5N1 疫情的感染時間線

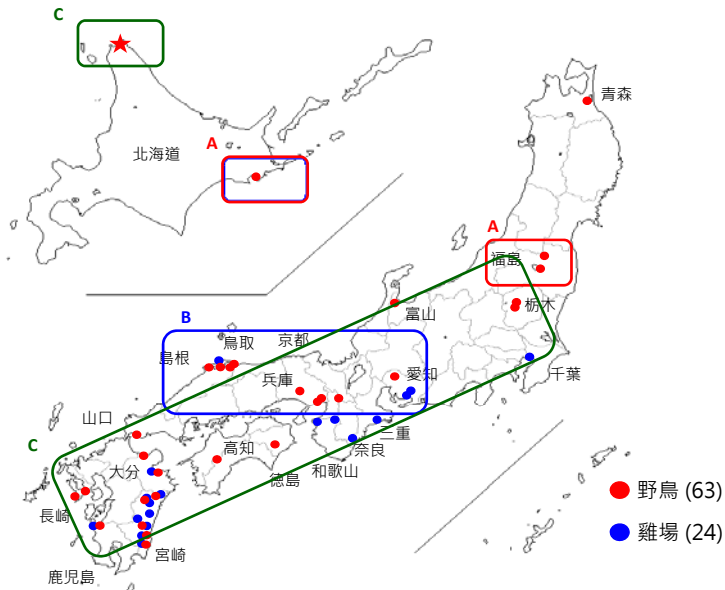


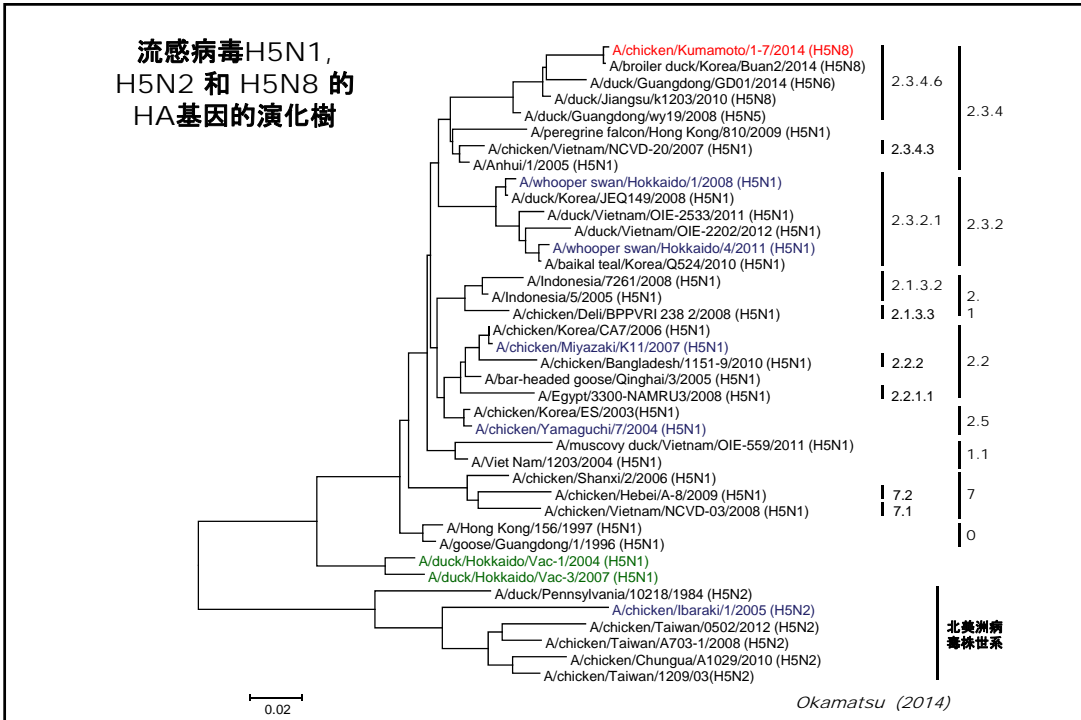
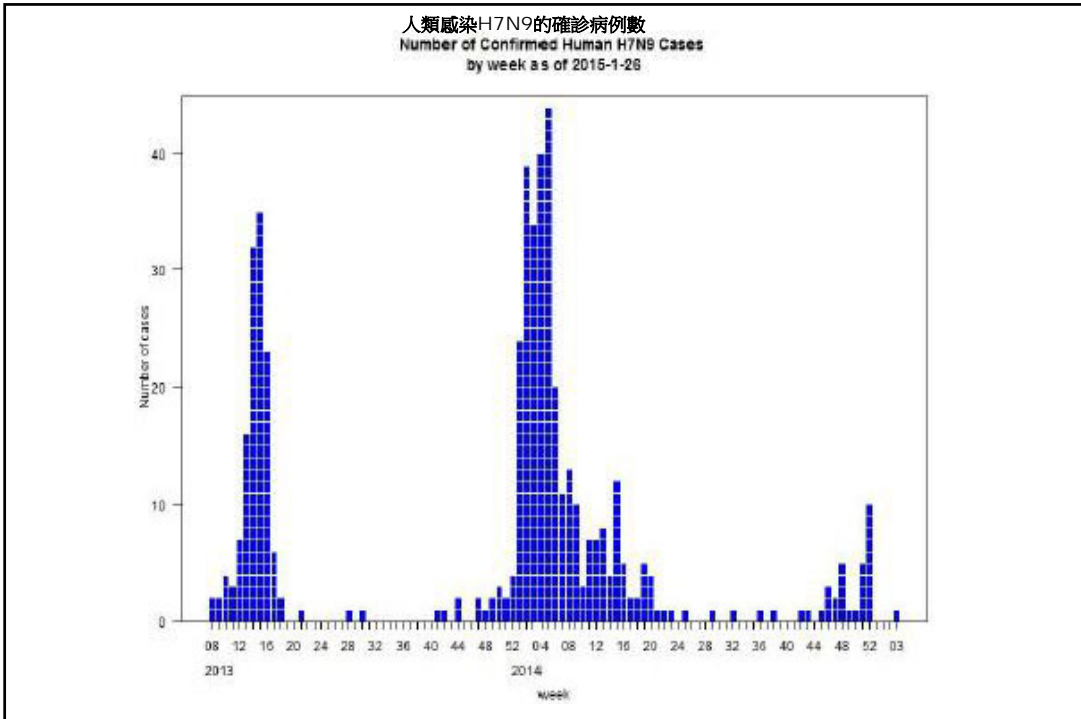
分離病毒的基因演化樹(進化株 2.3.2)



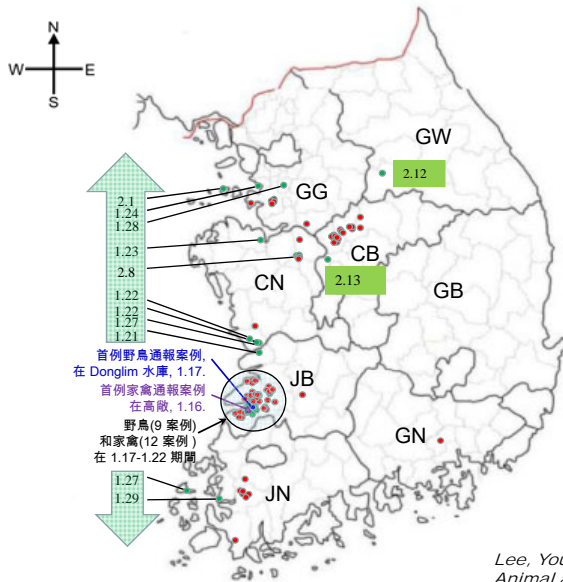
在日本2010-2011年H5N1病毒引起高致病性禽流感的爆發

水





H5N8高致病性禽流感疫情



階段 I

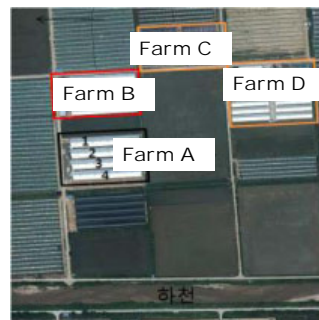
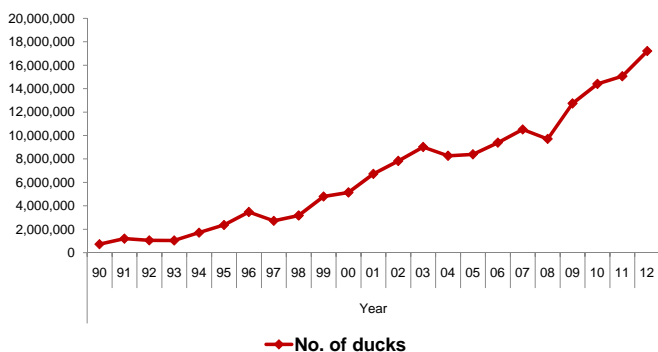
- 在 1.16-1.22 期間
- 家禽場(12 案例) 和野鳥(9 案例) 在 JB 省Donglim水庫附近



Lee, Youn-Jeong (2014); Avian Influenza Lab. Animal and Plant Quarantine Agency, Korea

在韓國國內鴨產業

- 養鴨業已經大幅上升
- 生物安全級別為低
- 在平原地區農場彼此位置很靠近
- 病毒傳播的風險高：從野鳥到農場，或農場與農場之間



資料: 韓國養鴨協會, 2014

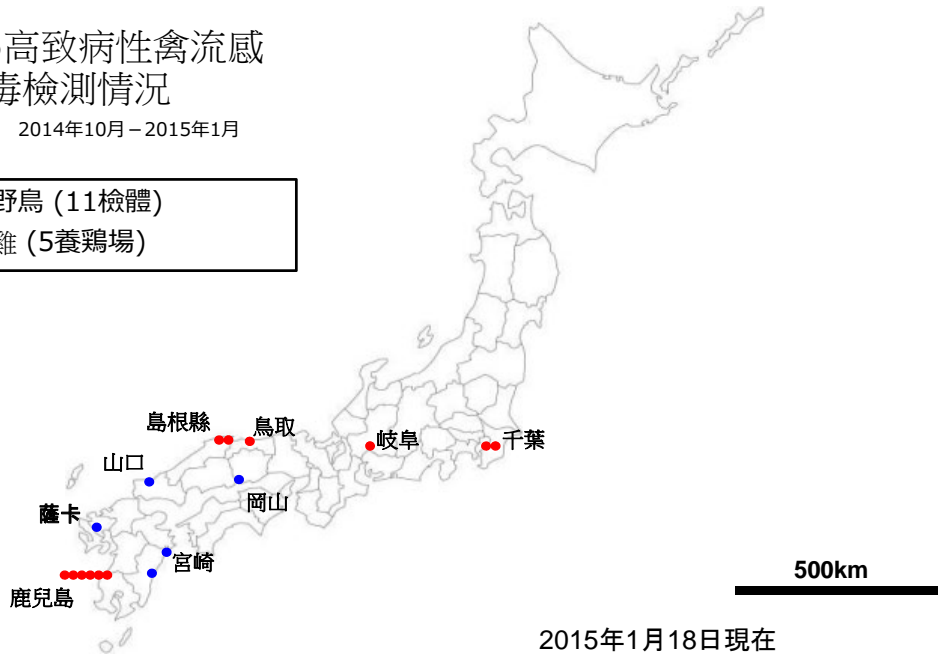
資料: QIA, 疫學組 2014

Lee, Youn-Jeong (2014); Avian Influenza Lab. Animal and Plant Quarantine Agency, Korea

H5高致病性禽流感病毒檢測情況

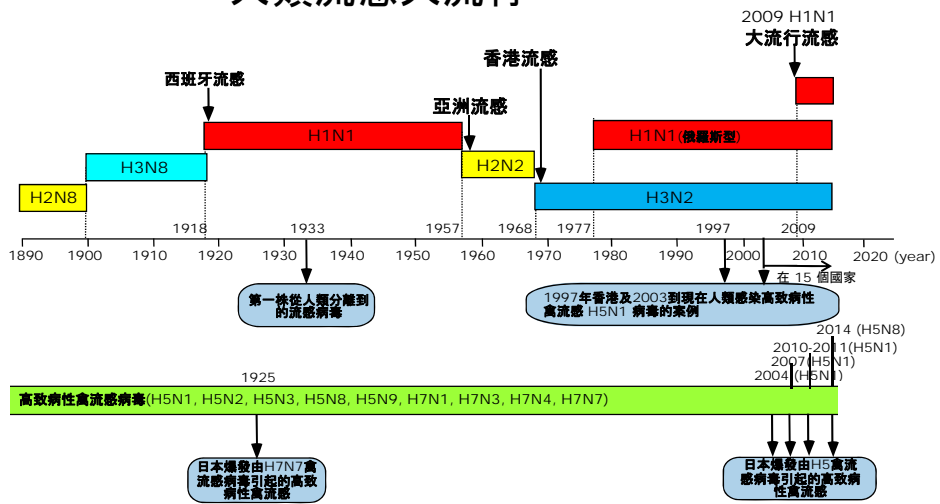
2014年10月 - 2015年1月

- 野鳥 (11檢體)
- 雞 (5養雞場)



2015年1月18日現在
環境省、農水省発表資料に基づく

人類流感大流行



高致病性禽流感

從中國南部豬隻分離到的H3N2病毒的HA基因

- 與A /香港/68 (H3N2) 和從遷徙鴨分離的H3病毒的HA基因有密切相關。
- 在接受體結合位點上的HA的氨基酸序列，顯示不是對人的接受體具專一性就是對禽類接受體具專一性。
- 這兩種類型的接受體被發現存在於豬的上呼吸道的表面上的上皮細胞襯。

KIDA et al (1988) Virology; Ito et al (1998) J Virol

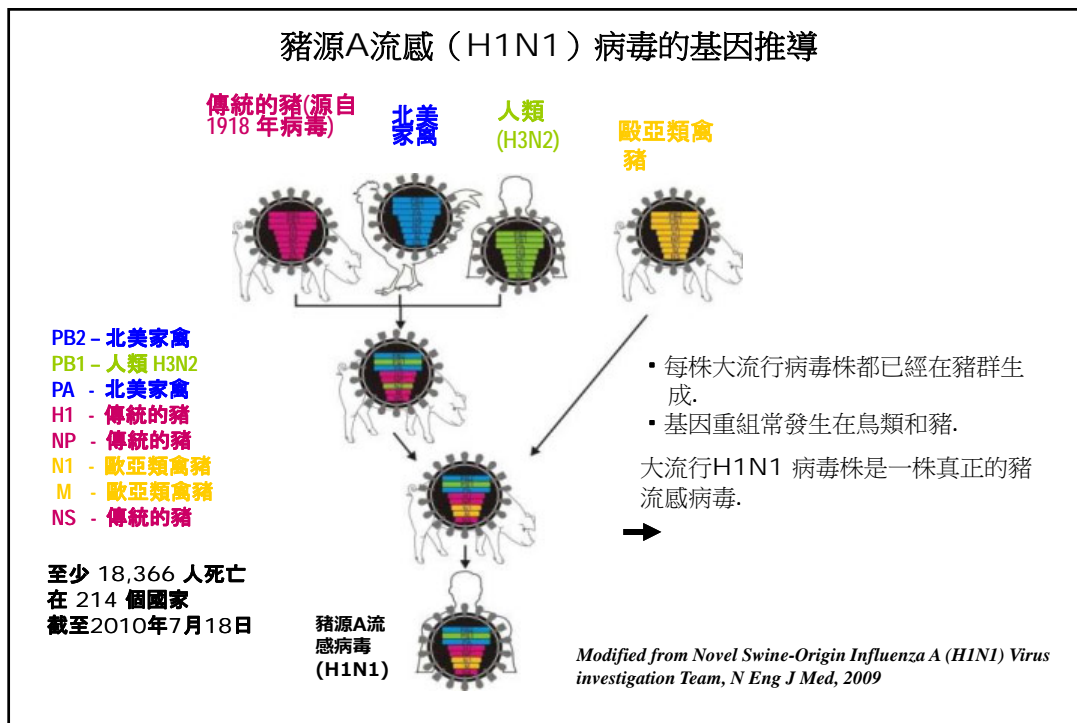
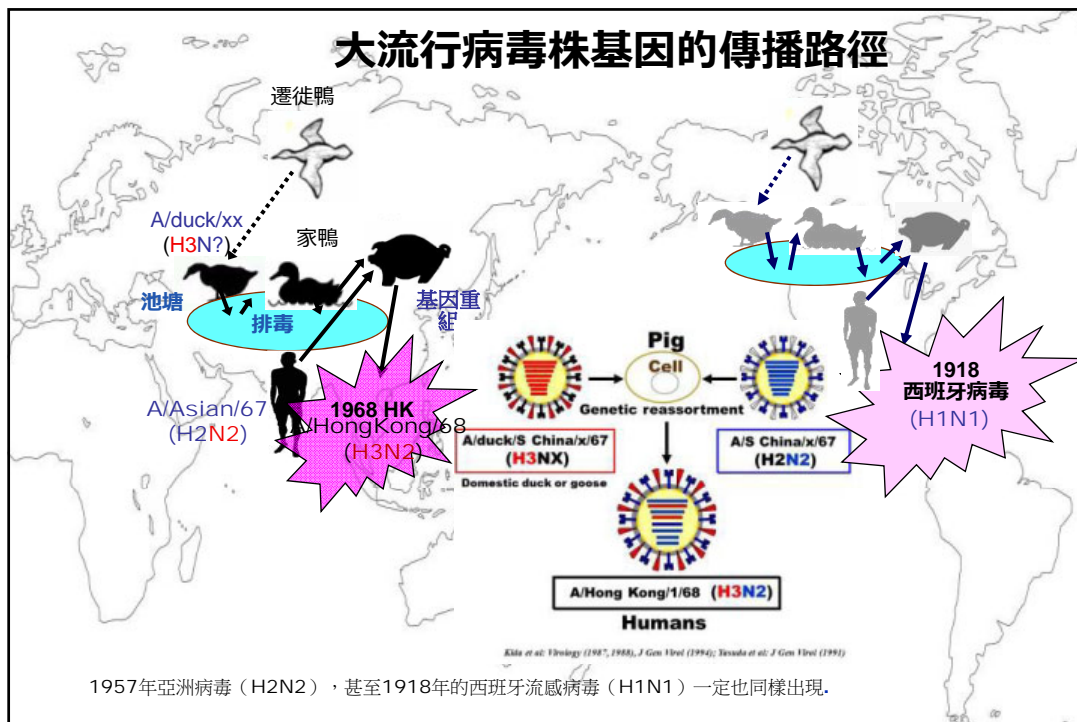
在中國南部家鴨分離到的流感病毒

- 在中國南部家鴨分離到的流感病毒的HA基因的抗原性及遺傳性與分離自遷徙鴨, 豬, 和 A/香港/68 關係密切。
- 每一株病毒都從太平洋飛行路徑上的遷徙鴨所分離到。

→ 傳播路徑;

遷徙鴨 → 家鴨 → 豬 → 人類

Yasuda et al (1991) J Gen Virol



豬在出現大流行流感病毒株的角色

- ◆ 豬對每種HA亞型的禽流感病毒都容易受到感染。
- ◆ 基因重組是發生在豬的上呼吸道的上皮細胞襯中，當豬隻同時感染哺乳動物和鳥類的病毒株。

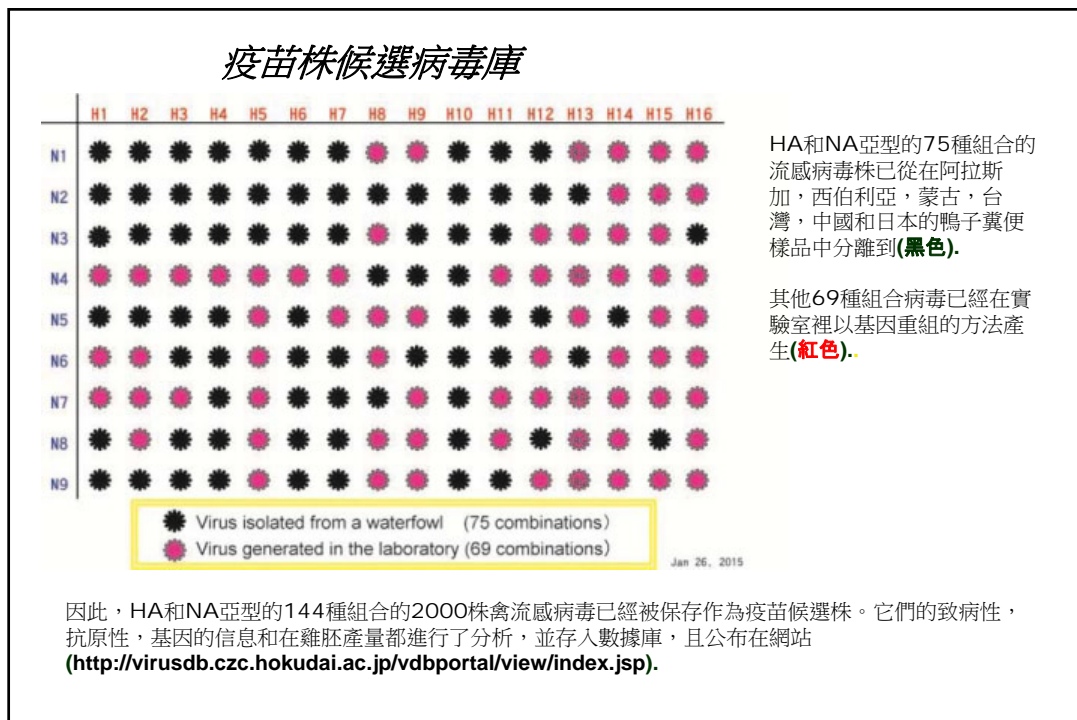
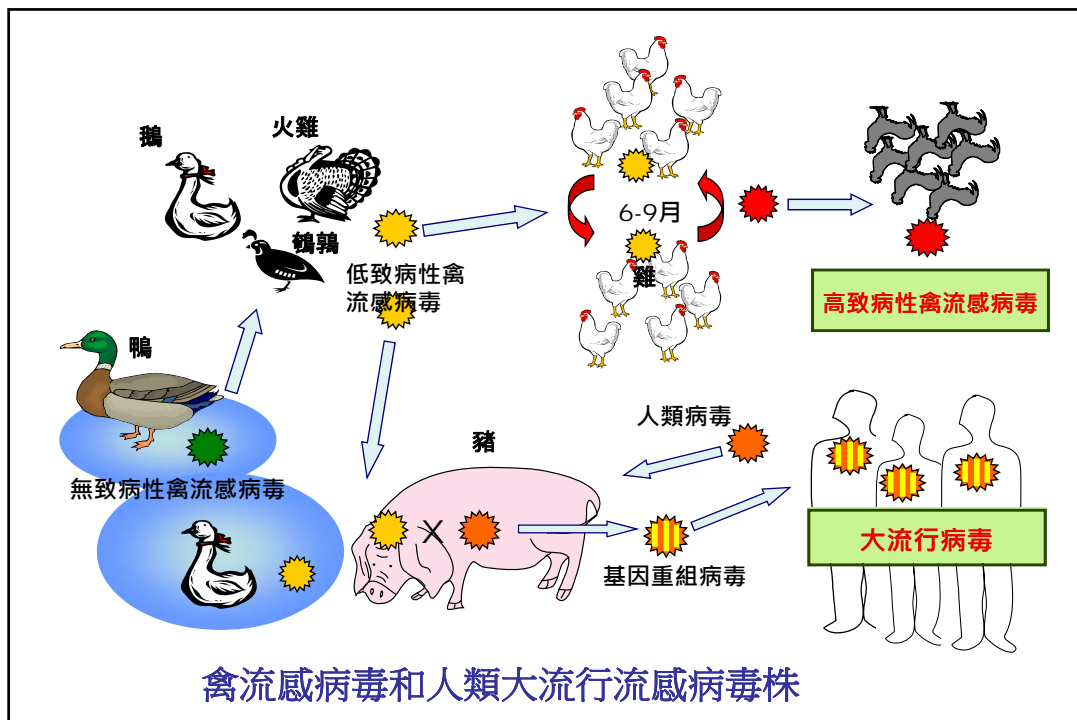
Kida H et al (1994) J Gen Virol

未來流感大流行的候選病毒株

- ◆ A型流感H1到H16和N1到N9的亞型病毒在自然狀況下永久存在於鴨築窩的湖泊中。
- ◆ 1957年H2N2，1968年H3N2，甚至1918年H1N1和2009年H1N1流感大流行的病毒都是禽流感病毒與先前的人類病毒株進行基因重組的病毒株。
- ◆ 豬很容易接受各種禽流感病毒和哺乳動物流感病毒，並產生重組。

任何亞型的禽流感病毒都可以貢獻重組所需的基因；因此，16種HA和9種NA的任何亞型都無法排除是未來流感大流行的潛在候選病毒株。

→ 豬流感和禽流感的全球監測是非常重要的。



如何為流感大流行做好準備，應根據如何控制季節性流感 →季節性流感疫苗和生物標準需大幅改善

短期目標:

1. 季節性流感疫苗的免疫效力的改善;純化全病毒顆粒的滅活疫苗的臨床評價;生物標準的大幅修改
2. 以全球監測和生物信息學為基礎研判抗原變異, 並據以搶先準備疫苗, 擇別落後的疫苗株選擇。

長期目標:

1. 開發有效的以及安全的黏膜疫苗
2. 開發有效的以及安全的佐劑

特點:

1. 流感是典型的急性感染。
2. 流感是無法撲滅, 每年季節性流感一定會來。

透過產業, 大學和政府的合作, 建議季節性流感疫苗的開發和實用化的全球標準

Hiroshi Kida

以不活化全病毒顆粒製備季節性流感疫苗的臨床前和臨床研究

- 1) 在日本的5個流感疫苗生產商, 每個都參加這個計畫(全都是日本)。
- 2) 全病毒顆粒疫苗和裂解疫苗之間免疫原性和安全性的比較。
病毒, 在細胞或雞胚培養, 經純化後由各疫苗生產商和北海道大學製備全病毒顆粒的疫苗和
醃-破裂的裂解疫苗。
製備的疫苗使用小鼠, 雪貂和猴子進行包括免疫效力試驗和安全性試驗的臨床前試驗, 之後再針對人進行臨床試驗。
聯繫方式: 每個生產設施和公司, 北海道大學, 新日本生物製藥有限公司(醃), 醫學(猴)的滋賀大學除了臨床前研究。
國立醫院機構, 公共和私人大學醫院, 醫學協會, 兒科醫生協會, 醫生滿足其他的臨床試驗。。
- 3) 試驗結果的評價。
聯繫方式: 大學, 學會, 日本疫苗產業協會, 傳染病等國家研究所。
- 4) 人用疫苗生物標準的大幅修改。
聯繫方式: 國家傳染病研究所, 日本疫苗產業協會, 疫苗協會, 臨床病毒學會, 流感研究人員交流等會議。
- 5) 每位成員都針對疫苗接種路徑及適合疫苗之佐劑進行研究。
- 6) 計畫參與者:
產業; 製造所·社; 北里第一三共, 武田藥品, 阪大微研會, 化血研, 登卡精研
大學; 北海道大學, 墨爾本大學, 疫苗協會, 病毒學學會, 病毒學臨床學會, 增加醫學會
政府; 國立感染症研究所, 衛生部, 勞動和福利, 內閣辦公室, 教育部, 文化部, 體育等。
- 7) 預算: 厚生労働科学研究費補助金、文部科学省・學術振興会科学研究費、JST、日本版 NIH(AMED)其他。

如何控制禽流感及如何為流感大流行做好準備

1. 為什麼有高致病性禽流感H5N1 病毒持續存在家禽19年, 且被選定抗原變異?

因為誤用疫苗。

2. 高致病性禽流感病毒是否會回到候鳥而持續存在於自然界?

高致病性禽流感病毒污染遷徙鴨的湖泊巢穴則必然發生。

迅速的撲滅在亞洲家禽的高致病性禽流感H5N1病毒是迫切需要的。

3. 應該如何禽流感方能得到控制?

為了遏制和撲滅感染禽流感病毒的家禽，加強監測，及早發現，撲殺禽群，移動管制，並加強衛生及不誤用疫苗是應該做的。

除了疫苗應謹慎使用，也不能取代撲殺。

4. 高致病性禽流感H5N1病毒及低致病性禽流感H7N9病毒會不會造成流感大流行?

它是不太可能發生；禽流感病毒直接從鳥類傳播給人，只會對特定具有禽流感病毒接受體的人，因此人傳人可能不會發生，但經由豬可能會發生。H5N1或H7N9並不是大流行病毒株的唯一選項。

5. 對於季節性流感的控制措施滿意嗎?

如何控制大流行流感應基於季節性流感的控制措施。特別是季節性流感疫苗應大幅改善，因為當前裂解疫苗是以醚或清潔劑破壞而製備，其免疫原性不足夠。

★全球監控家禽、豬和人流感，以及季節性流感疫苗的大幅改善是至關重要的。

Epidemiology and Prevention Strategies of Highly Pathogenic Avian Influenza (H5N8) in Korea

Jida Choi, D.V.M., Ph.D

**Veterinary Researcher
Veterinary Epidemiology Division
Animal and Plant Quarantine Agency, Korea**



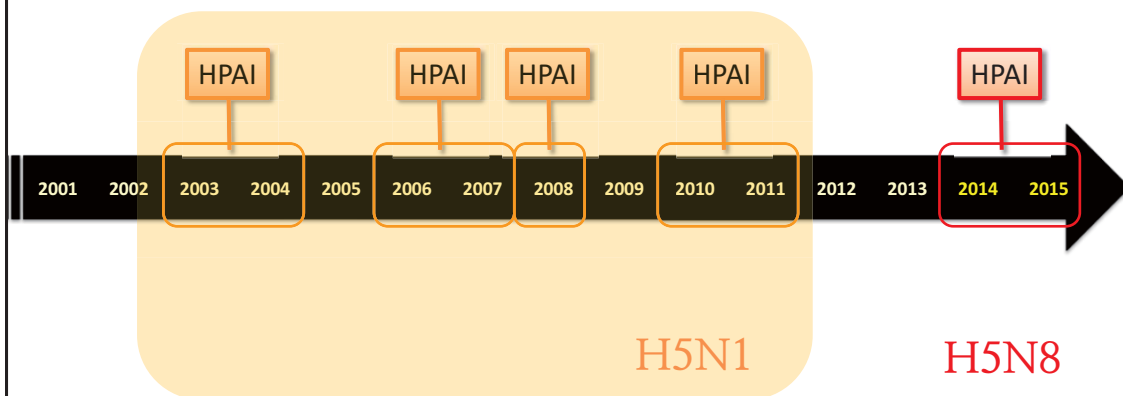
Contents

1. Highly Pathogenic Avian Influenza Epidemics (2003–2014)
2. Epidemiology and control measures of H5N8 HPAI outbreaks
3. Prevention Strategies for HPAI
4. Conclusion

I

Highly Pathogenic Avian Influenza Epidemics (2003–2014)

History of HPAI outbreaks in Korea



Epidemics of HPAI in Korea (2003 – 2011)

Year	2003/04	2006/07	2008	2010/11
Outbreak Period	Winter (03.12.10~'04.3.20) (102 days)	Winter ('06.11.22~'07.3.6) (104 days)	Spring ('08.4.1~5.12) (42 days)	Winter ('10.12.29~'11.5.6.) (139 days)
Outbreak Region	10 districts 19case (Chicken 10, Duck 9)	5 districts 7case (Chicken 4, Duck 2, Quail 1)	19 districts 33case (Chicken 21, Duck 6, Mix 6)	25 districts 53case (Chicken 18, Duck 33, Quail 1, Pheasant 1)
Subtype	H5N1 (clade 2.5)	H5N1 (clade 2.2)	H5N1 (clade 2.3.2)	H5N1 (clade 2.3.2)
Disease burden (\$)	13.6 Million	5.1 million	27 Million \$	71.5 million
Origin of introduction	Wild migratory birds			

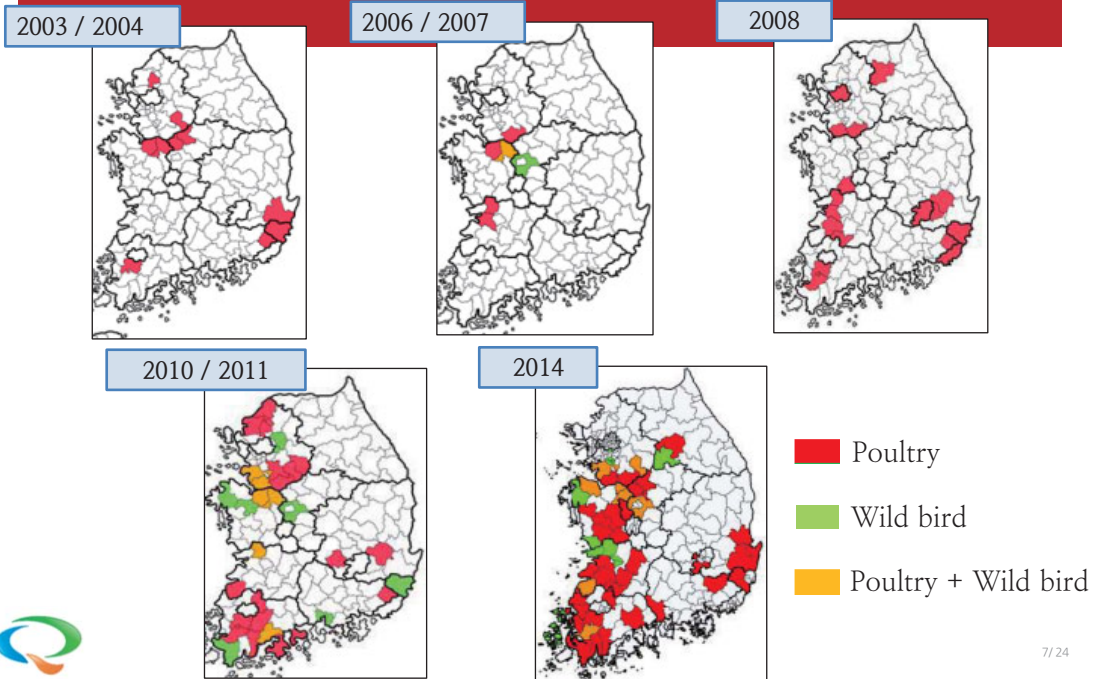


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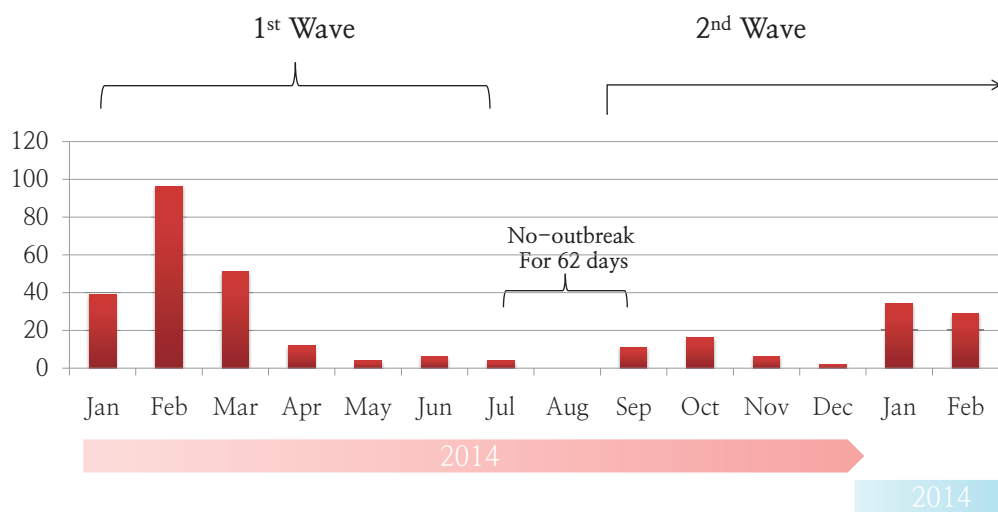
H5N1 vs. H5N8

	'03/'04	'06/'07	'08	'10/'11	'14	
Serotype	H5N1	H5N1	H5N1	H5N1	H5N8	
Clade	2.5	2.2	2.3.2.1	2.3.2.1	2.3.4.6	
Intravenous pathogenicity index (IVPI)	3.0	3.0	3.0	3.0	3.0	
Pathogenicity in chicken	Mortality(%)	100	100	100	100	
	Lethal time	2days	3days	2days	3days	
	Virus shedding	10 ^{4.0} (2days)	10 ^{5.0} (3days)	10 ^{5.5} (2days)	10 ^{5.2} (3days)	10 ^{5.6} (4-5days)
	Transmission	2/2(4days)	3/3(4days)	-	-	2/3(10.5days)
Pathogenicity in duck	Mortality(%)	0	0	100	100	
	Lethal time	0	0	4.6days	6.8days	
	Virus shedding	10 ^{1.0} (4days)	10 ^{2.2} (4days)	10 ^{3.8} (6days)	10 ^{2.6} (7days)	10 ^{4.5} (7days)
	Transmission	-	-	3/3(9days)	2/2(10days)	3/3(7days)
Pathogenicity in mallard	Mortality(%)	-	0	-	0	
	Virus shedding	-	10 ^{1.0} (3days)	-	10 ^{1.3} (3days)	10 ^{2.5} (5days)
	Transmission	-	2/2(3days)	-	2/2(3days)	2/2(6days)

Geographical Distribution of HPAI outbreaks



2014/2015 HPAI in Korea



II

Epidemiology and control measures of H5N8 HPAI outbreaks in Korea

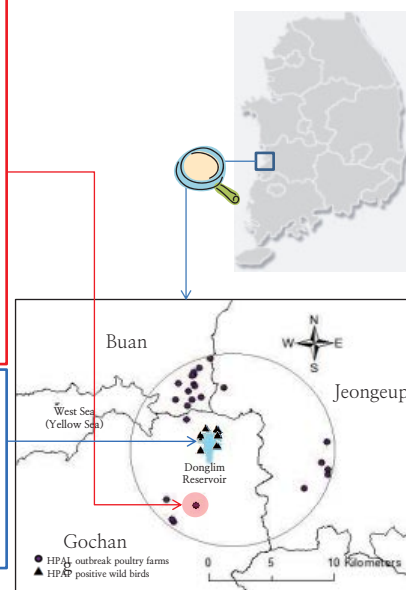
Index case of H5N8 HPAI

Poultry

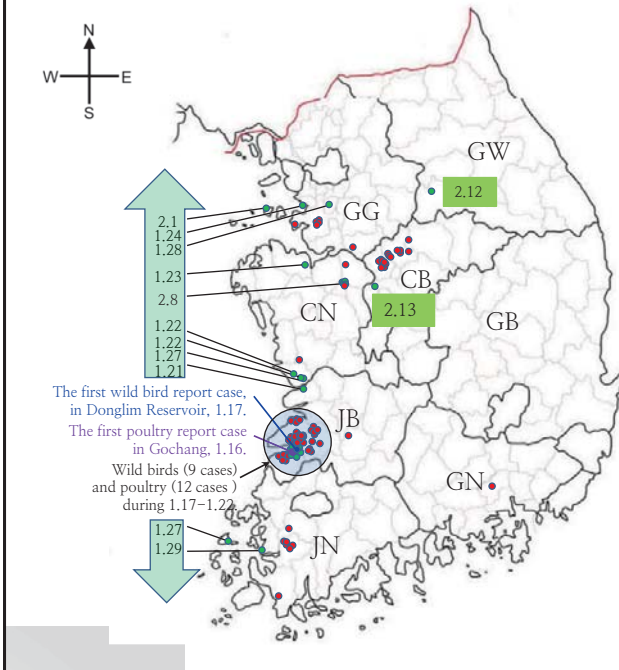
- Date: 2014. 1. 16.
- Region: Gochang in Jeonbuk(JB) province
- Farm: duck breeder farm
 - 20-53 week-old breeder ducks
 - 16,000 birds
- Reporting: farmer → regional veterinary office → QIA
- Clinical signs:
 - Decrease of egg production (above 50%)
 - Increase of death (1-2 birds/day → 7 birds/day)
 - Depression

Wild birds

- Date: 2014. 1. 17.
- Region: Donglim reservoir near by index case's farm
- Reporting: QIA team for epidemiological investigation
- A hundred of dead Baikal Teal in Donglim reservoir



H5N8 HPAI outbreak



Phase I

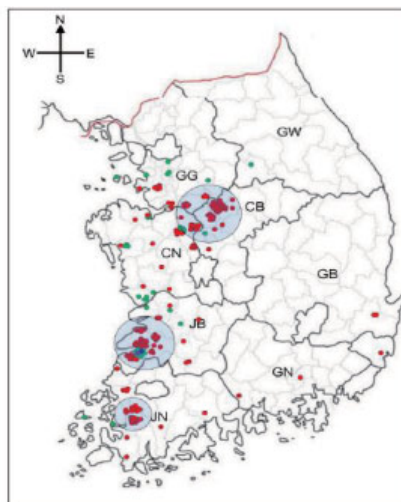
- During 1.16-1.22
- Poultry farms(12cases) & wild birds(9cases) around Donglim reservoir in JB province



Phase II

- Since 1.22
- Spread to North and South region in Western part of Korea

Spatio-temporal Evolution of 2014 H5N8 Epidemic



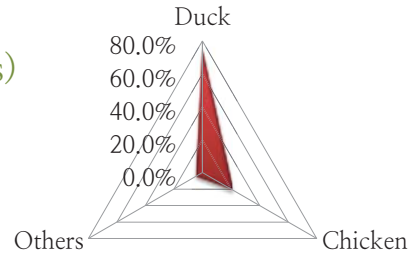
- H5N8 isolate in wild birds
- H5N8 isolate in poultry



Affected Population (Poultry)

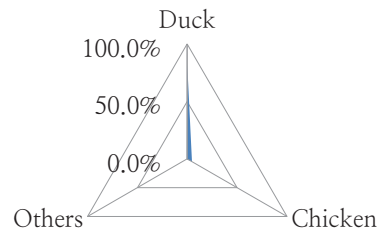
1st Wave

- H5N8 viruses from poultry (212 cases)
 - Duck (159): 75%
 - Chicken (44): 21%
 - Others (9): 4%



2nd Wave

- H5N8 viruses from poultry (91cases)
 - Duck (80): 81.6%
 - Chicken (10): 4.7%
 - Others (1): 0.5%



Clinical Manifestation

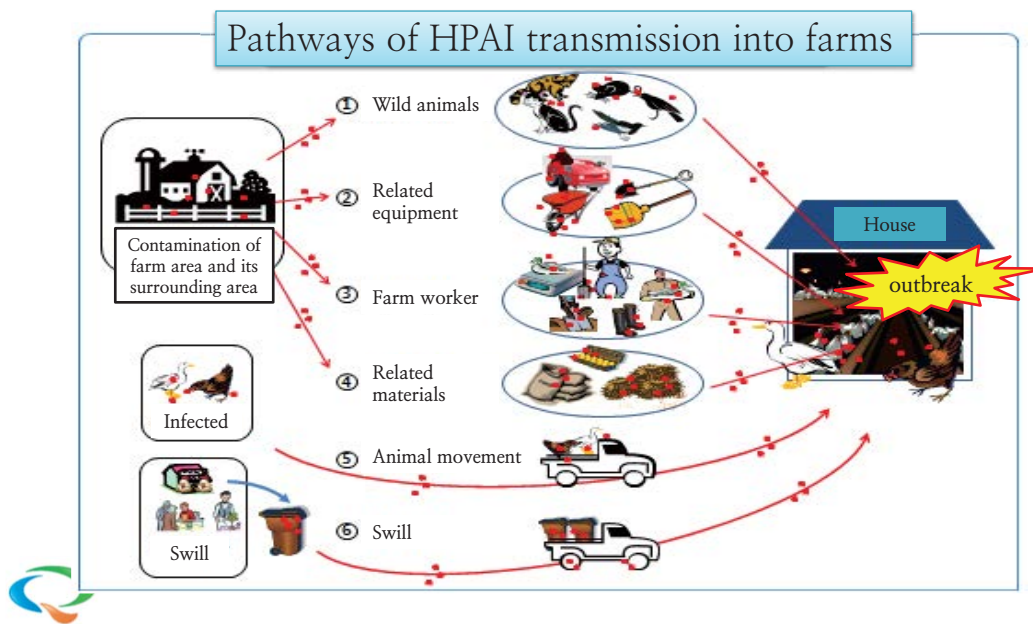
Species	No. outbreak farms	Asymptomatic	Symptomatic								
			Mortality Increase	Intake Reduction	Drinking Increase	Drowsiness Decrease vitality	Decrease egg laying	Cyanosis	Ataxia	Neurological signs (lameness, Wry neck)	
Ducks	Breeder	42	7 (17%)	19	20	-	13	31	4	6	6
	Meat	117	56 (48%)	56	28	1	31	-	7	9	15
	Sub-total	159	63 (40%)	75	48	1	44	31	11	15	21
Chicken	Layer	27	2 (7%)	25	1	1	7	6	1	3	-
	Breeder	12	1 (8%)	11	3	-	3	3	2	1	-
	Korean Native (Broiler)	5	1 (20%)	3	-	-	2	-	-	-	-
	Sub-total	44	4 (9%)	39	4	1	12	9	3	4	-
Others	Ostrich	1	-	-	1	-	1	-	-	-	-
	Goose	2	-	2	1	-	1	-	-	-	2
	Mallard	1	-	-	-	-	-	1	-	-	-
	Quail	1	-	1	-	-	-	-	-	-	-
	Goose	1	-	1	1	-	1	-	-	-	1
	Mixed	3	-	3	1	-	-	-	-	-	-
	Sub-total	9	-	7	4	-	3	1	-	-	3
Total	212	67(32%)	121	56	2	59	41	14	19	24	

Clinical signs in duck farms



- A. Mortality increase
- B. Neurological sign
- C. Decrease egg laying
- D. Diarrhea

Spreading of HPAI infection between farms



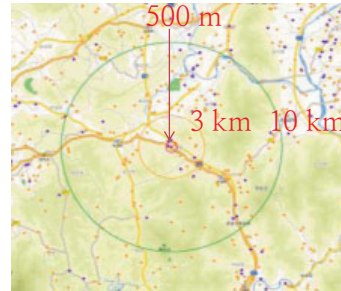
Control measures of HPAI in Korea

- Stamping-out policy (culling)

- Prompt depopulation : infected farm, farms within 500m radius
- Pre-emptive culling : within 3 km radius, dangerous contact

- Zoning and movement restriction

- 500 m radius : contaminated zone
- 500m – 3 km : protection zone
- 3 km – 10km : surveillance zone



- Vaccination prohibited

- Movement restriction were lifted 30 days after the last culling



III

Prevention Strategies for HPAI

National Animal Disease Control System for HPAI in Korea

1. Legislation

- ▶ Act for Prevention of Livestock Epidemics
 - Enforcement Decree, Enforcement Ordinance

- ▶ Directive for Animal Diseases Control Guidelines
 - FMD, AI, CSF, ND, TB & BR etc.(13 Types)

- ▶ HPAI Emergency Action plan



Current scheme of surveillance for avian influenza for different types of poultry farms and wild birds

: number of tests, estimated prevalence, and sensitivity of detection

Type	Current scheme		Current scheme					Suggestion (with 95% confidence)			
	No. specimens		Prevalence**_ % (estimated)		Sensitivity (estimated)†_ %			No. specimens		Sensitivity (expected)	
	Individual	Farm*	Individual	Farm	Individual	Farm	Overall	Individual	Farm	Individual	Farm
To detect Highly pathogenic avian influenza											
Breeder ducks	20/40*	All(105)	0.04	1.8 7	0.8/1.6	86.2	1.4	50feces	All(105)	2.0	1.7
Meat ducks	20	All(784)	0.24	1.3 8	4.7	100	4.7	50	All(784)		
Birds in live animal market	20	All(310)	5.08	23. 20	11.0	100	11.0	20	All(310)		
Source farm of birds on the live animal market	20	Traced 80 (expected)	11.15	45. 98	90.6	100	90.6	20	Traced 80 (expected)	Identical to the current scheme	
Quails, turkeys, and others	20	Sample (162)	0.04	0.5 4	0.8	58.4	0.5	20	Sample (162)		
Wild birds	700/250*	-	0.85	-	99.7/88.2	-	0.85	700/250	-		
Wild birds (Captured)	1,000*	-	-	-	100	-	-	2,000	-	100	-
To detect low pathogenic avian influenza (H5, H7 types)											
Grandparent chicken	10	10	0.03	2.29	0.3	20.7	0.1	20	All(10)	0.6	0.1
Breeder chicken	20	330	0.001	0.10	0.02	26.2	0.01	20	All(330)		
Layer chickens	20	284	0.002	0.0 5	0.04	13.2	0.01	20	12	Identical to the current scheme	
Korean native chicken	20	280	0.02	0.41	0.4	68.3	0.3	20	12		



IV

Conclusion

Conclusion

- ✓ Since first outbreak of January 16, 2014, the HPAI (H5N8) outbreak has had serious impact to poultry industry.
- ✓ Novel reassortant influenza A (H5N8) viruses were isolated from wild birds and domestic poultry at the same time on Jan, 2014.
- ✓ It is assumed that the virus was introduced into Korea through migratory birds which fly from high latitudes during the winter.



Conclusion

- ✓ The major transmission routes between farms were the movement of farmers, visitors, vehicles and materials.
- ✓ In comparison with previous H5N1 outbreaks, H5N8 virus has lower fatality and longer period of time to death, causing notification to be delayed.
- ✓ Standard Operation Procedure validated for H5N1, not for H5N8 (Lack of understand about epidemiology of H5N8). Thus we changed the SOP and Surveillance program.



Thank you

韓國高致病性禽流感的流 行病學和預防策略 (H5N 8)

Jida Choi, D.V.M., Ph.D

獸醫研究員
獸醫疫學組
韓國動植物檢疫局



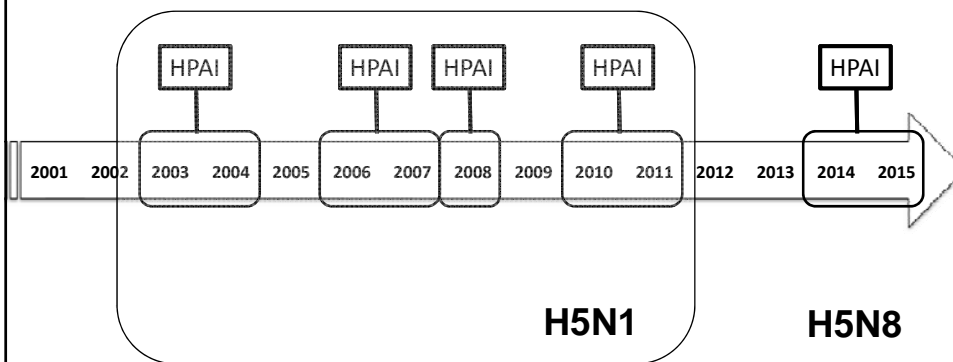
內容大綱

1. 高致病性禽流感疫情(2003-2014)
2. 高致病性禽流感H5N8疫情的流行病學和控制措施
3. 高致病性禽流感的預防策略
4. 結論

I

高致病性禽流感疫情(2003-2014)

韓國高致病性禽流感的流行史



韓國高致病性禽流感疫情 (2003 – 2011)

年	2003/04	2006/07	2008	2010/11
爆發期間	冬季 (03.12.10~'04.3.20) (102 天)	冬季 ('06.11.22~'07.3.6) (104 天)	春季 ('08.4.1~5.12) (42 天)	冬季 ('10.12.29~'11.5.6.) (139 天)
爆發區域	10 區 19 案例 (雞 10, 鴨 9)	5 區 7 案例 (雞 4, 鴨 2, 鵝 1)	19 區 33 案例 (雞 21, 鴨 6, 混合 6)	25 區 53 案例 (雞 18, 鴨 33, 鵝 1, 雉 1)
亞型	H5N1 (分化枝 2.5)	H5N1 (分化枝 2.2)	H5N1 (分化枝 2.3.2)	H5N1 (分化枝 2.3.2)
疾病負擔(\$)	13.6 百萬	5.1 百萬	27 百萬 \$	71.5 百萬
病毒來源	遷徙的候鳥			

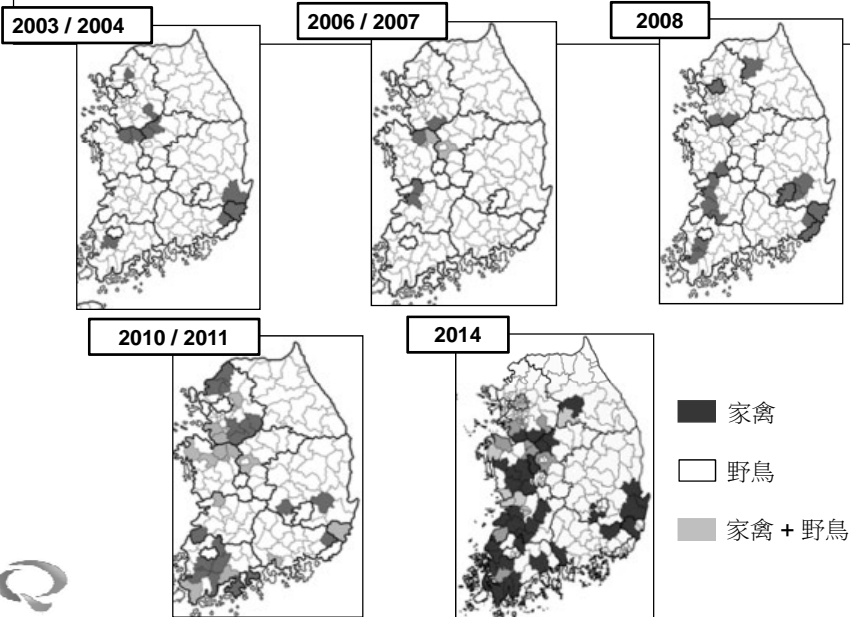


5

H5N1 vs. H5N8

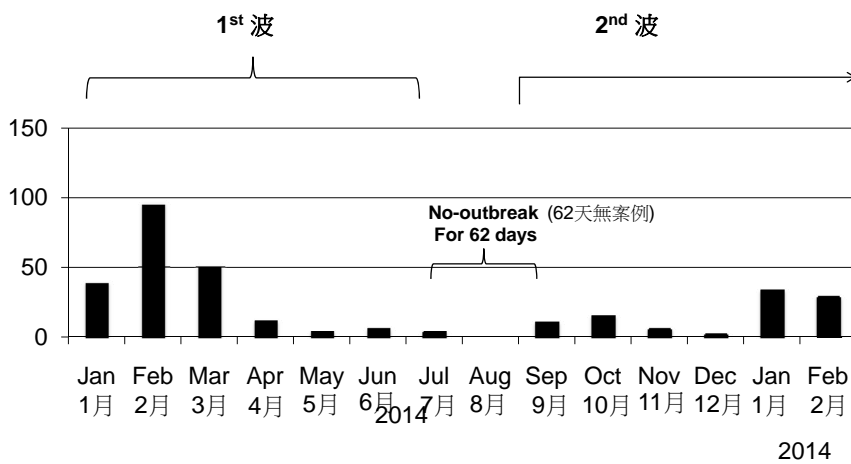
	'03/'04	'06/'07	'08	'10/'11	'14	
亞型	H5N1	H5N1	H5N1	H5N1	H5N8	
分化枝	2.5	2.2	2.3.2.1	2.3.2.1	2.3.4.6	
靜脈注射致病性指數 (IVPI)	3.0	3.0	3.0	3.0	3.0	
對雞之致病性	死亡率(%)	100	100	100	100	
	致死時間	2 天	3 天	2 天	3 天	4.5 天
	排毒	10 ^{4.0} (2 天)	10 ^{5.0} (3 天)	10 ^{5.5} (2 天)	10 ^{5.2} (3 天)	10 ^{5.6} (4-5 天)
	傳播	2/2(4 天)	3/3(4 天)	-	-	2/3(10.5 天)
對鴨之致病性	死亡率(%)	0	0	100	100	0-20
	致死時間	0	0	4.6 天	6.8 天	11 天
	排毒	10 ^{1.0} (4 天)	10 ^{2.2} (4 天)	10 ^{3.8} (6 天)	10 ^{2.6} (7 天)	10 ^{4.5} (7 天)
	傳播	-	-	3/3(9 天)	2/2(10 天)	3/3(7 天)
對綠頭鴨之致病性	死亡率(%)	-	0	-	0	0
	排毒	-	10 ^{1.0} (3 天)	-	10 ^{1.3} (3 天)	10 ^{2.5} (5 天)
	傳播	-	2/2(3 天)	-	2/2(3 天)	2/2(6 天)

高致病性禽流感疫情的地理分佈



7/24

2014/2015 韓國高致病性禽流感



8/24

II

高致病性禽流感H5N8疫情的 流行病學和控制措施

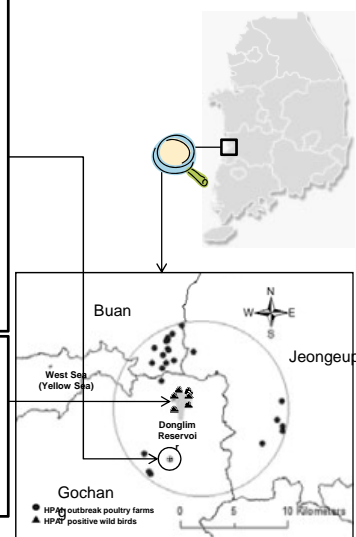
高致病性禽流感H5N8的指標案例

家禽

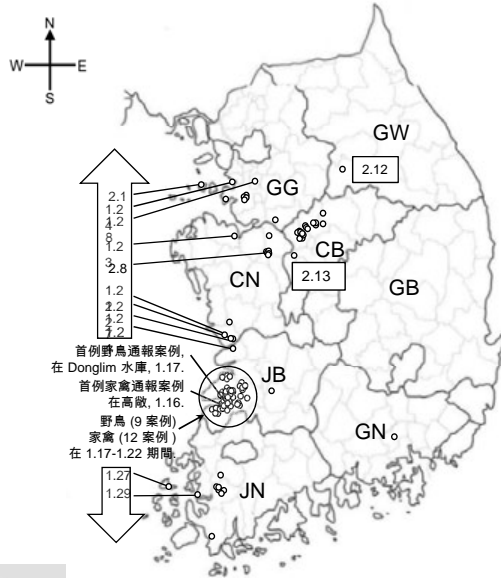
- 日期: 2014. 1. 16.
- 區域: 全羅北道 (JB) 省高敞
- 農場: 種鴨場
 - 20-53 週齡種鴨
 - 16,000 隻
- 通報: 畜主 → 區域獸醫辦公室 → QIA
- 臨床症狀:
 - 產蛋下降 (50% 以上)
 - 增加死亡 (1-2 隻/天 → 7 隻/天)
 - 精神鬱抑

野鳥

- 日期: 2014. 1. 17.
- 區域: 靠近指標案例場的Donglim水庫
- 通報: QIA 團隊進行流行病學調查
- 在Donglim水庫有一百隻死巴鴨



高致病性禽流感 H5N8 疫情



階段 I

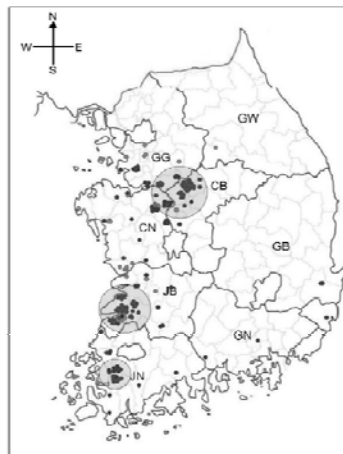
- 期間 1.16-1.22
- 家禽場(12 案例) & 野鳥(9 案例) 在全羅北道 (JB) 省 Donglim 水庫周圍



階段 II

- 自 1.22 開始
- 蔓延至韓國西部的北區和南區

2014年H5N8疫情的時空演化



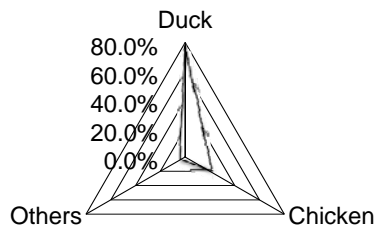
- H5N8 分離自野鳥
- H5N8 分離自家禽



受影響的族群（家禽）

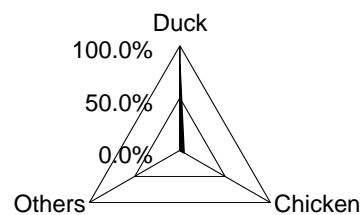
1st 波

- 從212件家禽案例的H5N8病毒
 - 鴨 (159): 75%
 - 雞 (44): 21%
 - 其他 (9): 4%



2nd 波

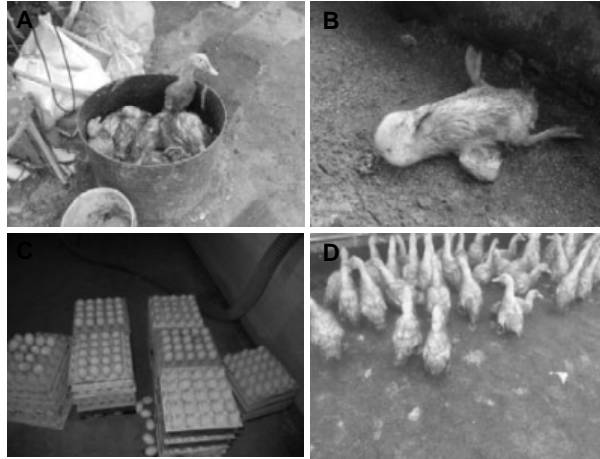
- 從91件家禽案例的H5N8病毒
 - 鴨 (80): 81.6%
 - 雞 (10): 4.7%
 - 其他 (1): 0.5%



臨床表現

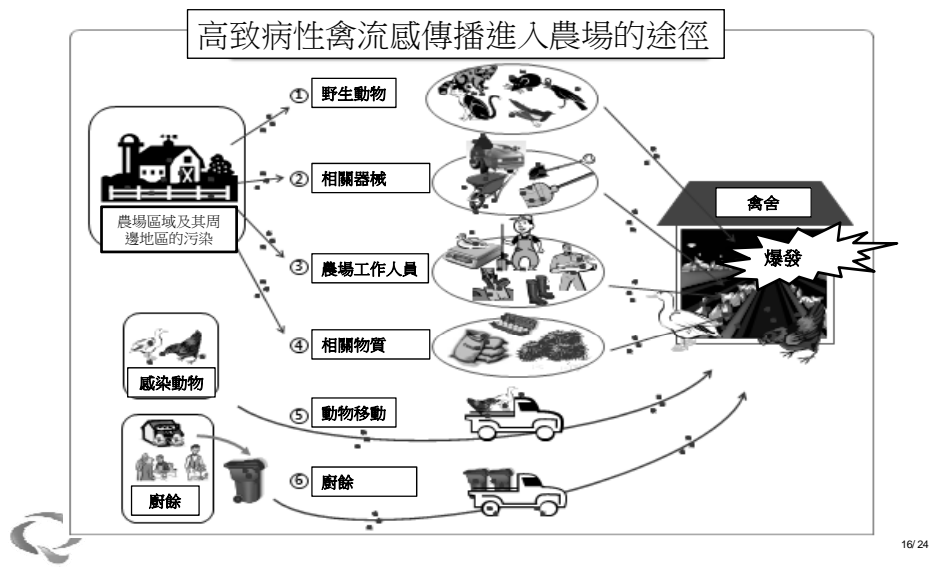
動物種類	爆發場數	無症狀的	症狀								
			增加死亡率	減少攝食	增加飲水	嗜睡 活力下降	產蛋下降	發紺	運動失調	神經症狀 (跛行、歪脖子)	
鴨	種鴨	42	7 (17%)	19	20	-	13	31	4	6	6
	肉鴨	117	56 (48%)	56	28	1	31	-	7	9	15
	小計	159	63 (40%)	75	48	1	44	31	11	15	21
雞	蛋雞	27	2 (7%)	25	1	1	7	6	1	3	-
	種雞	12	1 (8%)	11	3	-	3	3	2	1	-
	韓國本土 (肉雞)	5	1 (20%)	3	-	-	2	-	-	-	-
	小計	44	4 (9%)	39	4	1	12	9	3	4	-
其他	駝鳥	1	-	-	1	-	1	-	-	-	-
	鵝	2	-	2	1	-	1	-	-	-	2
	綠頭鴨	1	-	-	-	-	-	1	-	-	-
	鸚鵡	1	-	1	-	-	-	-	-	-	-
	鵪鶉	1	-	1	1	-	1	-	-	-	1
	混合	3	-	3	1	-	-	-	-	-	-
小計	9	-	7	4	-	3	1	-	-	3	
合計	212	67(32%)	121	56	2	59	41	14	19	24	

鴨場的臨床症狀



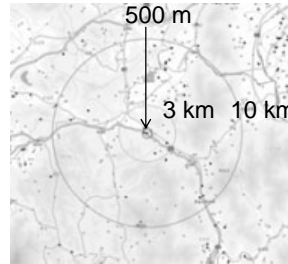
- A. 死亡率增加
- B. 產蛋下降
- C. 下痢

農場之間傳播高致病性禽流感的感染



韓國高致病性禽流感的控制措施

- 撲殺政策（撲殺）
 - 迅速清場：感染農場半徑500公尺範圍內的農場
 - 預防性撲殺：半徑3公里範圍內的危險接觸場
- 分區和移動管制
 - 半徑500公尺：汙染區
 - 半徑500公尺 - 3公里：保護區
 - 半徑3公里 - 10公里：監控區
- 禁止施打疫苗
- 撲殺最後場的30天後，解除移動管制



III

高致病性禽流感的預防策略

韓國高致病性禽流感的國家動物疾病控制系統

1. 立法

- ▶ 預防畜禽疫情法案
 - 強制令，強制執行條例

- ▶ 指示動物疾病控制指導方針
 - 口蹄疫，禽流感，豬瘟，新城病，結核病和牛鼻氣管炎等。(13 種)

- ▶ 高致病性禽流感緊急行動計劃



對不同類型的家禽場和野鳥禽流感的現行監控計劃： 測試數量，估計盛行率和檢測敏感性

型態	現行計畫							建議 (真 95% 查獲度)			
	樣本數		盛行率** (% (估計))		檢感性 (估計計畫)			樣本數		檢感性 (預期)	
	個別	農場*	個別	農場	個別	農場	全體	個別	農場	個別	農場
檢測高致病性禽流感											
種物	20/40*	全部(105)	0.04	1.8 7	0.8/1.6	86.2	1.4	50農場	全部(105)	2.0	1.7
肉類	20	全部(784)	0.24	1.3 8	4.7	100	4.7	50	全部(784)		
活禽市場的家禽	20	全部(310)	5.08	23. 20	11.0	100	11.0	20	全部(310)		
活禽市場家禽的來源場	20	追蹤的 80 (指期)	11.15	45. 98	90.6	100	90.6	20	追蹤的 80 (指期)	與現行計畫完全相同	
鴨、火雞、和其他	20	樣本 (162)	0.04	0.5 4	0.8	58.4	0.5	20	樣本 (162)		
野鳥	700/250*	-	0.85	-	99.7/88.2	-	-	700/250	-	-	-
野鳥 (持續)	1,000*	-	-	-	100	-	0.85	2,000	-	100	-
除測低致病性禽流感(H5, H7 亞型)											
肉雞	10	10	0.03	2.29	0.3	20.7	0.1	20	全部(10)	0.6	0.1
種雞	20	330	0.001	0.10	0.02	26.2	0.01	20	全部(330)		
蛋雞	20	284	0.002	0.0 5	0.04	13.2	0.01	20	12	與現行計畫完全相同	
韓國本土雞	20	280	0.02	0.41	0.4	68.3	0.3	20	12		



IV 結論

結論

- ✓ 自2014年1月16日的第一次爆發，高致病性禽流感（H5N8）疫情已嚴重影響家禽業。
- ✓ 在2014年1月新型重組A型流感（H5N8）病毒同時從野鳥和家禽被分離到。
- ✓ 據推測，該病毒係在冬季經由在高緯度飛行的候鳥引入韓國。



結論

- ✓ 農場之間的主要傳播途徑是農民，訪客，車輛和物資的流動.
- ✓ 與以前的H5N1疫情相比，H5N8病毒具有較低的死亡率和死亡時間週期較長，導致通報延遲.
- ✓ 標準操作程序(SOP)驗證了H5N1，不是H5N8（缺乏對H5N8流行病學的了解）。因此，我們改變了SOP和監控計畫.



謝謝聆聽

Characteristics of new avian influenza virus strains isolated from avian in Taiwan

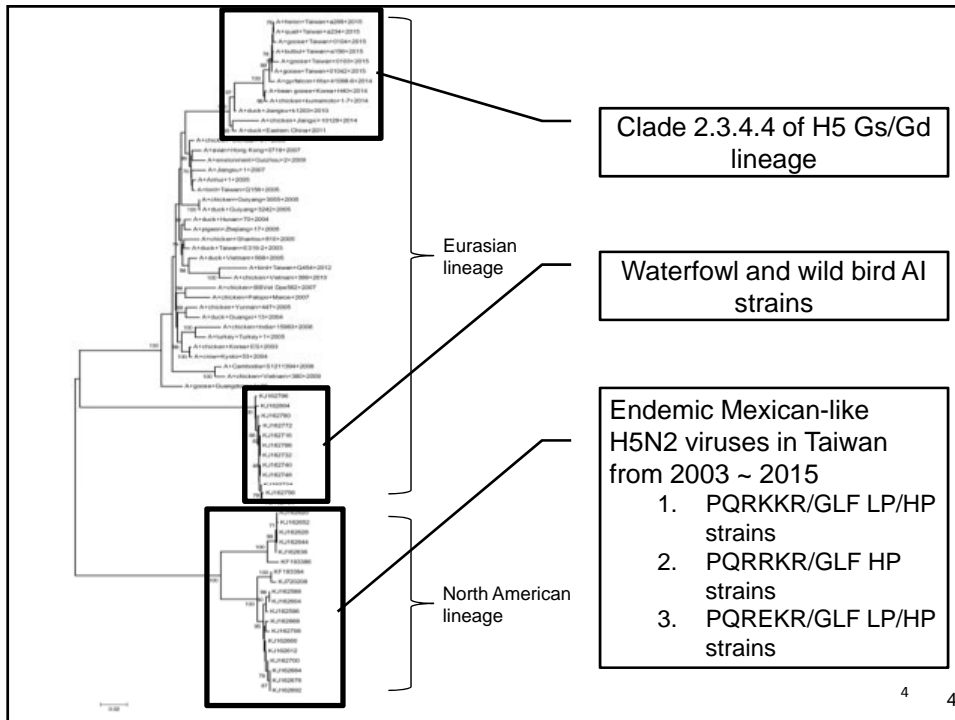
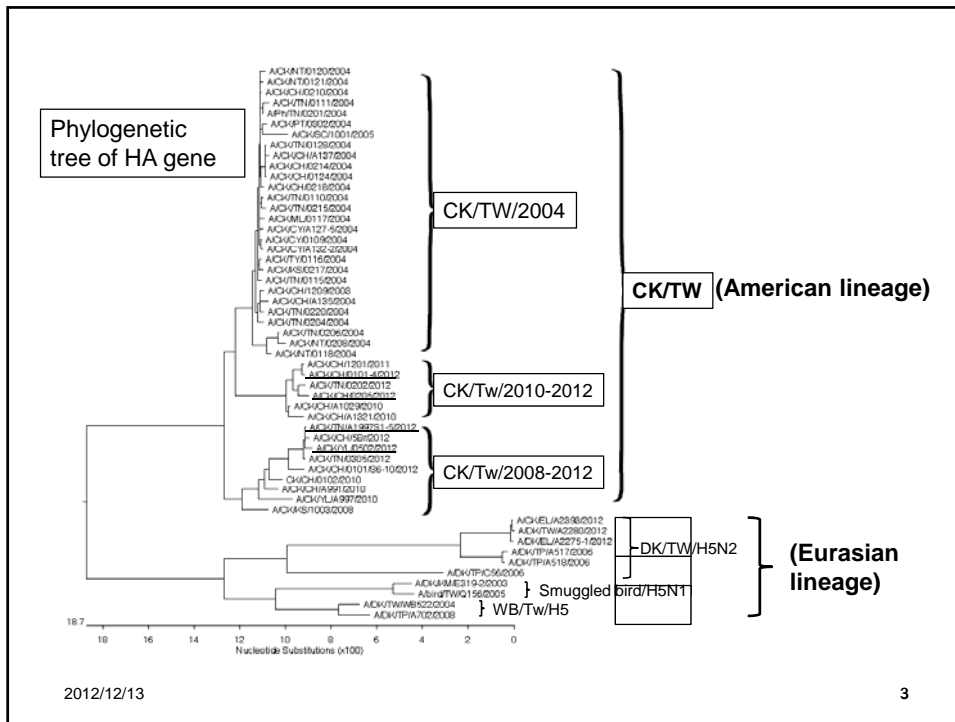
Hsiang-Jung Tsai
Animal Health Research Institute
Taiwan

1

Before 2015

- A Mexican-like H5N2 viruses has caused several outbreaks in chicken population in Taiwan since 2003.
- The HA gene of H5 viruses isolated from domestic duck and wild duck in Taiwan cluster together and belong to Eurasian lineage and differ with the gene of H5N2 viruses from chicken.

2



Outbreaks of three novel H5 AIV in Taiwan in 2015

- In Jan. 9, an outbreak of the new H5N2 strain at 4 goose farms in Yunlin County and a duck egg farm in Pingtung County was confirmed by AHRI.
- We also confirmed an outbreak of H5N8 avian flu at a goose farm in Chiayi County.
- In Jan 16, additional outbreaks of H5N3 strain in a goose farm in Pingtung County and a goose farm in Kaoshung County was confirmed by AHRI.

5

- The H5 sequence of the new H5N2 strain was 99 percent similar to that of the H5N8 flu virus that attacked South Korea in 2014, while the N2 sequence was 96 percent similar to the virus that hit China's Jilin Province in 2011.
- The H5 sequence of the H5N8 virus was 99 percent similar to the Korean strain, while the N8 sequence is 98 percent similar to the Korean strain.
- The H5 sequence is 99 percent the same as one seen in South Korea, while the N3 is 98 percent similar to the H1N3 found in Thai ducks in 2011, the H2N3 found in Mongolian mallards in 2010, and the H5N3 found in wild ducks in Kaohsiung in 2013.

6

The virus types of the infected poultry farms

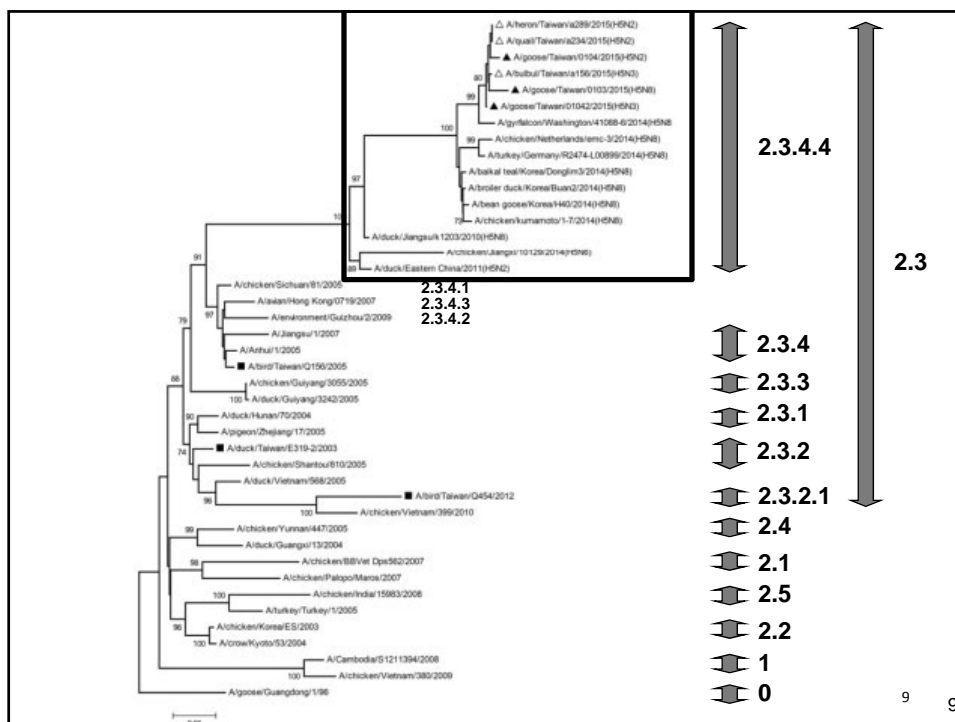
- From Jan. 9 to March 2, total of 874 poultry farms were diagnosed to be infected with H5 AIV.
- H5N8 (PLRERRRKR/GLF): 222 farms
- H5N2 (PLRERRRKR/GLF): 470 farms
- H5N2+H5N8 (PLRERRRKR/GLF): 67 farms
- H5N3 (PLRERRRKR/GLF): 25 farms
- H5N2+H5N3 (PLRERRRKR/GLF): 2 farms
- H5N2 (PQREKR/GLF or PQRKR/GLF): 63 farms
- H5(N?) (PLRERRRKR/GLF): 25 farms

Multi-basic cleavage sites of new HPAI viruses

	Cleavage site	Critical basic aa	Phenotype
A/Goose/Taiwan/0103 (H5N8)	PLRERRRKR/GLF	5	HP
A/Goose/Taiwan/0104 (H5N2)	PLRERRRKR/GLF	5	HP
A/Goose/Taiwan/01042 (H5N3)	PLRERRRKR/GLF	5	HP

Table 1: Multi-basic cleavage sites of recently circulating Goose/Guangdong-lineage HPAI H5N1 viruses.

Sub-type	Clade ¹	no. of sequences 2009-2013	Cleavage site consensus ²	critical basic aa ³	Size of insert
H5	LP	199	PORETR/GLF	1	0
H5N1	Gs/Gd-lineage	979	PORERRRKR/GLF	6	4
	Clade 1	73	PQREGRKKR/GLF	5	4
	Clade 2.1	12	PQESRRKR/GLF	4	3
	Clade 2.2	436	PQGERRRKR/GLF	6	4
	Clade 2.3.1	20 ⁴	PQRERRRKR/GLF	5	3
	Clade 2.3.2	361	PQRERRRKR/GLF	5	3
	Clade 2.3.3	30 ⁴	PQRERRRKR/GLF	5	3
	Clade 2.3.4	73	PLRERRRKR/GLF	5	3
	Clade 2-like	8 ⁴	PQRERRRKR/GLF	6	4
	Clade 7	5	PQIEGRKKR/GLF	5	4



Characteristic amino acids of the three novel influenza A (H5N8, H5N2, H5N2) viruses

Viral protein	Amino acid position	Goose/Taiwan/0103 (H5N8)	Goose/Taiwan/0104 (H5N2)	Goose/Taiwan/1042 (H5N3)	Comments
PB2	627	E	E	E	E627K: adaptation to mammalian host
HA	138	A	A	A	S138A: increased binding to human-type receptors
	160	A	A	A	T160A: N-glycosylation loss and increased binding to human-type receptors
	226	Q	Q	Q	Q226L: increased binding to human-type receptors
	228	G	G	G	G228S: increased binding to human-type receptors
M1	30	D	D	D	N30D: increased pathogenesis in mice
	215	A	A	A	T215A: increased pathogenesis in mice
M2	31	N	N	N	S31N: resistance to amantadine and rimantadine
NS1	42	S	S	S	P42S: increased pathogenesis in mice

Sequence comparison between A/Gs/Taiwan/0103
and other H5N8 viruses

	PB2	PB1	PA	HA
A/gyrfalcon/Washington/4 1088-6/2014	99.6	91.5	99.4	98.9
A/bean_goose/Korea/H40 /2014	99.4	91.7	99.4	98.5
A/chicken/kumamoto/1- 7/2014	99.2	91.5	99.0	98.5
A/duck/Jiangsu/k1203/20 10	98.1	92.4	96.4	96.4

11 11

Sequence comparison between A/Gs/Taiwan/0103
and other H5N8 viruses

	NP	NA	M	NS
A/gyrfalcon/Washington/4 1088-6/2014	92.8	98.9	99.8	99.8
A/bean_goose/Korea/H40 /2014	92.9	98.7	99.8	99.6
A/chicken/kumamoto/1- 7/2014	92.8	98.5	99.9	99.5
A/duck/Jiangsu/k1203/20 10	93.5	96.8	97.5	91.6

12 12

Sequence homology of three different NA subtypes of Taiwan novel H5 influenza viruses

	PB2	PB1	PA	HA	NP	NA	M	NS
H5N8 H5N2	87.4	95.1	92.3	99.3	97.6	59.5	99.8	94.6
H5N8 H5N3	87.0	95.4	99.8	99.5	97.8	57.4	99.8	99.9
H5N2 H5N3	92.3	94.3	92.3	99.7	98.3	57.9	99.8	94.5

13 13

Virus reassortant in Taiwan

- These strains get additional constellations through reassortment with the viruses from wild birds
 - A/Goose/Taiwan/0103 (H5N8): 2 of the 8 gene segments (PB1, NP) match wild bird sequences
 - A/Goose/Taiwan/0104 (H5N2): 6/8 (PB2, PB1, PA, NP, NA, NS)
 - A/Goose/Taiwan/01042 (H5N3): 4/8 (PB2, PB1, NP, NA)
- These data showed that all three H5 Taiwan strains were distinct from the viruses circulating in Europe, which all 8 gene segments match South Korean lineages.

14 14

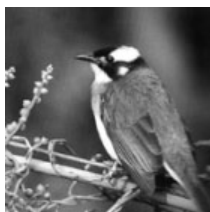
Comment by ProMED Mods.AS/CRD

- The situation in Taiwan, with 4 HPAI strains circulating simultaneously, may reflect the global spreading capability of the HPAI H5 clade 2.3.4 and its apparent inherent instability, expressed in the appearance of several recombinant strains.
- Since mid-November 2014, HPAI H5 strains have been reported from 4 continents: Europe (Germany, Netherlands, England, Italy, Russia), Asia (China, Japan, S. Korea, Vietnam, India, Taiwan), North America (USA, Canada), Africa (Nigeria, Libya) and the Middle East (Egypt, Israel). These outbreaks were caused by various strains (H5N1, H5N2, H5N3, H5N6, H5N8). Do they all share the same HPAI H5 clade 2.3.4.4?

15

Novel highly pathogenic avian influenza virus isolated from wild birds

- During this epidemic, we had isolated three novel HPAI viruses from birds
 - A/bulbul/Taiwan/a156/2015 (H5N3)
 - A/quail/Taiwan/a234/2015 (H5N2)
 - A/heron/Taiwan/a289/2015 (H5N2)



16 16

	A/heron/Taiwan/a289/2015 (H5N2) vs A/goose/Taiwan/0104/2015 (H5N2)	
PB2	99.8 %	EA
PB1	99.9 %	EA
PA	99.9 %	EA
H5	99.6 %	EA
NP	99.7 %	EA
N2	99.4 %	EA
MP	99.8 %	EA
NS	99.8 %	EA

17

	A/bulbul/Taiwan/a156/2015 (H5N3) vs A/goose/Taiwan/01042/2015(H5N3)	
PB2	99.7 %	EA
PB1	99.8 %	EA
PA	99.7 %	EA
H5	99.8 %	EA
NP	99.8 %	EA
N3	99.6 %	EA
MP	99.5 %	EA
NS	99.7 %	EA

18

	A/quail/Taiwan/a234/2015 (H5N2) vs A/goose/Taiwan/0104/2015(H5N2)	
PB2	99.9 %	EA
PB1	99.6 %	EA
PA	99.8 %	EA
H5	99.8 %	EA
NP	99.9 %	EA
N2	99.7 %	EA
MP	99.9 %	EA
NS	99.7 %	EA

19

Novel highly pathogenic avian influenza virus isolated from wild birds

- Sequence analysis showed that all sequences of 8 genes of these three viruses had highly sequence similarity with viruses from poultry

20

Pathological study on three novel HPAI in domestic waterfowl and poultry

21

Gross lesions of geese, ducks and chickens

- Cutaneous hemorrhage of beak, feet and eyelid
- Subcutaneous edema of the head, neck and feet
- Hemorrhage of conjunctival and nasal mucosa
- Brain: meningeal congestion and brain swelling
- Heart: hydropericardium and myocardial degeneration and necrosis
- Liver and spleen: swelling and multiple white spots
- Lung: edema
- Kidney: swelling and uric acid crystal deposition
- Pancreas: multiple white necrotic spots with hemorrhage
- Ovary: multifocal follicular and intrafollicular hemorrhage and congestion with follicular atresia

22

Histopathology of geese, ducks and chickens

- Nonsuppurative meningoencephalitis
- Myocarditis
- Hepatic necrosis
- Splenic necrosis
- Parabronchitis
- Renal tubular necrosis
- Pancreatic necrosis

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Distribution of viral antigen (IHC) (new viral strains)

	Brain		Heart		Liver		Spleen		Lung		Kidney		Pancreas		Intestine	
	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]
Goose	++	+++	+++	++	+++	+++	+++	+++	++	++	+	++	+++	+++	-	++
Duck	++	+++	+++	++	++	+++	++	+++	++	++	+	+	+++	+++	-	+++
Turkey	++	+++	+++	++	++	++	++	++	++	+	+++	++	+++	+++	-	+
Chicken	++	+++	+++	++	++	++	++	++	++	+	+++	+++	+++	+++	-	+
H5N2 AIV bearing 4 a.a. (old viral strains)																
Chicken	+++	+++	++	++	-	+	-	+	+	+	+++	+++	+++	+++	-	-

His. = histopathology; IHC = immunohistochemistry

* - = no; + = mild; ++ = moderate; +++ = severe lesion.

§ - = rare; + = seldom; ++ = common; +++ = widespread.

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Conclusion

- The new strains of HPAI H5 viruses can caused severe disease, clinical signs and mortality in geese, ducks, chickens and turkeys in Taiwan.
- These new viruses had the neurotropism and broad tissue infectivity.
- The level of viral replication in tissues, especially in brain and heart, determine the manifestation of clinical disease and mortality in AI-infected poultries and waterfowls.

台灣高病原性家禽流行性感冒 新病毒株之特徵

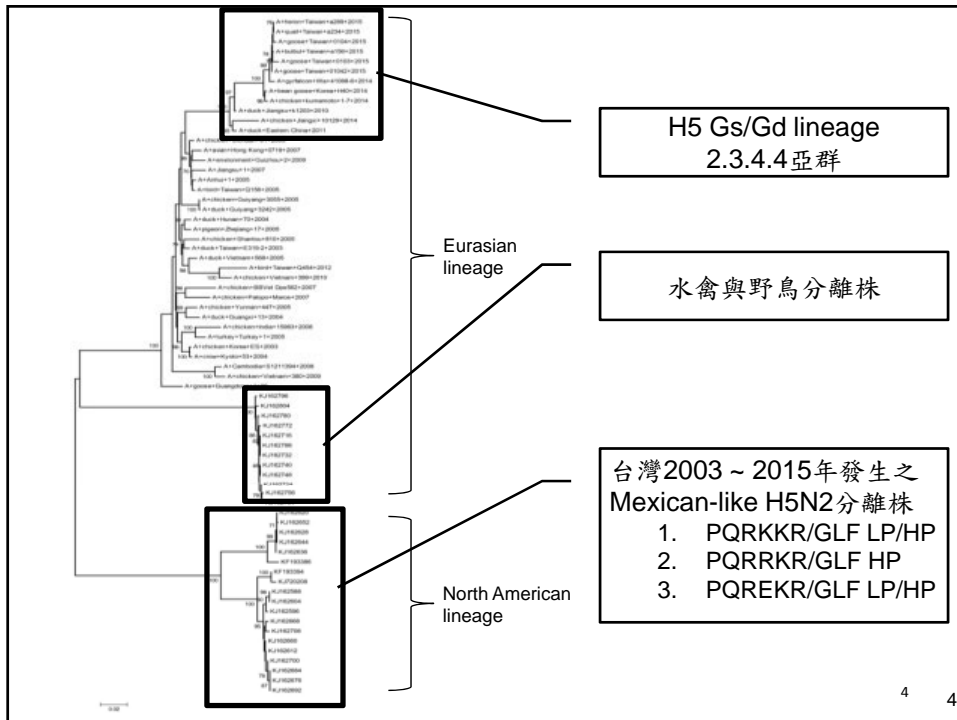
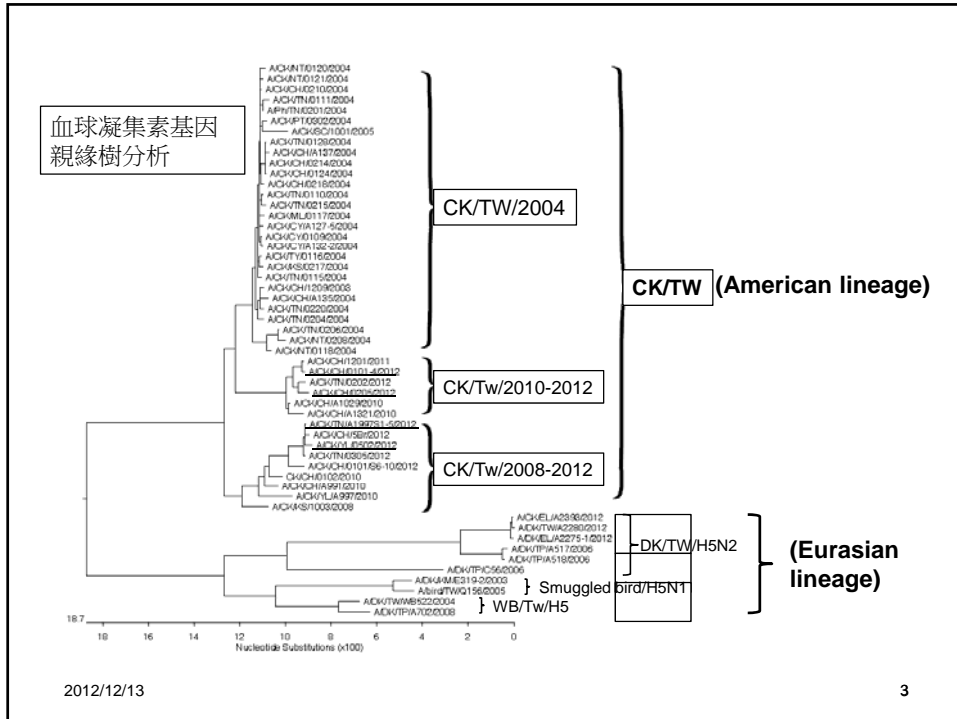
蔡向榮
家畜衛生試驗所

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2015年之前台灣禽流感病毒

- Mexican-like H5N2亞型病毒於2003年開始在台灣養雞業發生數次之疫情
- 在台灣養鴨場及野鳥所分離到的H5亞型病毒，血球凝集素基因均歸屬於Eurasian lineage，不同於養雞場所分離到的H5N2亞型病毒

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2015年台灣三株新型H5亞型病毒

- 1月9日在雲林4場鵝場及屏東1蛋鴨場病例中，家畜衛生試驗所確診為新型H5N2
- 同時在嘉義的鵝場也證實H5N8的疫情
- 1月16日在屏東及高雄鵝場病例中，家畜衛生試驗所確診為新型H5N3

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- 新型H5N2病毒的血球凝集素基因與2014年韓國爆發的H5N8病毒相似性為99%；神經胺酸酶N2則與2011年中國吉林省所分離到的病毒最相近為96%
- 台灣H5N8病毒的血球凝集素與神經胺酸酶基因與韓國H5N8病毒株相似性分別為99%與98%
- H5N3病毒的血球凝集素基因仍與韓國H5N8最相近為99%，N3基因則和2011年泰國鴨隻H1N3病毒、2010年蒙古野鳥H2N3病毒與2013台灣高雄野鳥H5N3病毒具最高之相似性為98%

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養禽場病毒鑑定結果

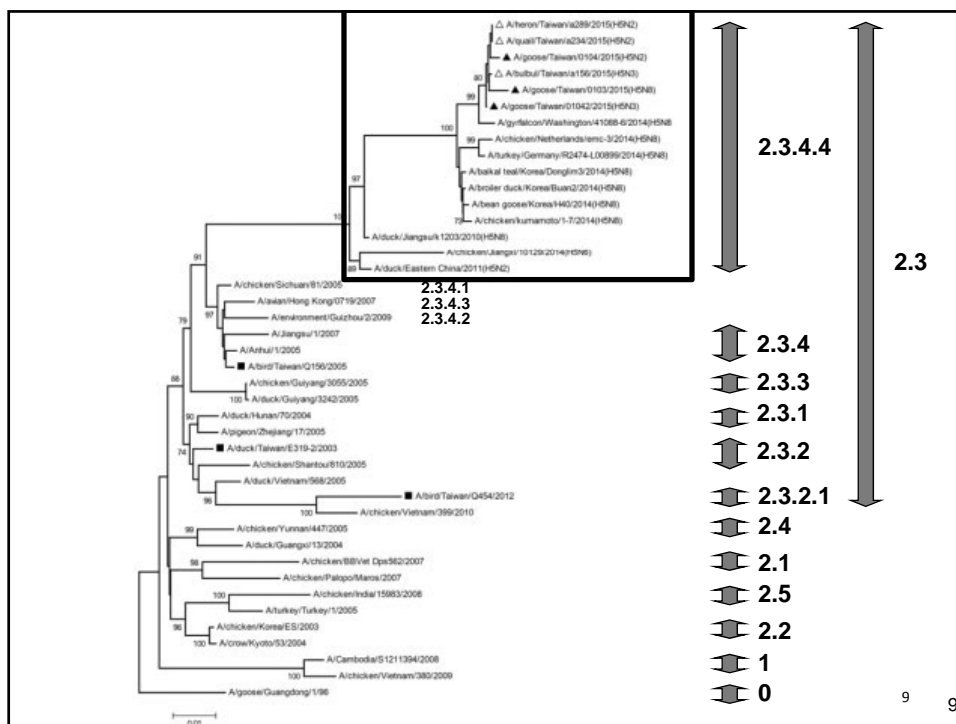
- 1月9日到3月2日間總共874場確診為H5亞型流感病毒
- H5N8 (PLRERRRKR/GLF): 222場
- H5N2 (PLRERRRKR/GLF): 470場
- H5N2+H5N8 (PLRERRRKR/GLF): 67場
- H5N3 (PLRERRRKR/GLF): 25場
- H5N2+H5N3 (PLRERRRKR/GLF): 2場
- H5N2 (PQREKR/GLF or PQRKR/GLF): 63場
- H5(N?) (PLRERRRKR/GLF): 25場

台灣新型H5亞型病毒之切割位序列

	Cleavage site	Critical basic aa	Phenotype
A/Goose/Taiwan/0103 (H5N8)	PLRERRRKR/GLF	5	HP
A/Goose/Taiwan/0104 (H5N2)	PLRERRRKR/GLF	5	HP
A/Goose/Taiwan/01042 (H5N3)	PLRERRRKR/GLF	5	HP

Table 1: Multi-basic cleavage sites of recently circulating Goose/Guangdong-lineage HPAI H5N1 viruses.

Sub-type	Clade ¹	no. of sequences 2009-2013	Cleavage site consensus ²	critical basic aa ³	Size of insert
H5	LP	199	PQRETR/GLF	1	0
H5N1	Gs/Gd-lineage	979	PQRERRRKR/GLF	6	4
	Clade 1	73	PQREGRKR/GLF	5	4
	Clade 2.1	12	PQRESRRK/GLF	4	3
	Clade 2.2	436	PQGERRRKR/GLF	6	4
	Clade 2.3.1	20 ⁴	PQRERRRR/GLF	5	3
	Clade 2.3.2	361	PQRERRRR/GLF	5	3
	Clade 2.3.3	30 ⁴	PQRERRRR/GLF	5	3
	Clade 2.3.4	73	PLRERRRKR/GLF	5	3
	Clade 2-like	8 ⁴	PQRERRRKR/GLF	6	4
	Clade 7	5	PQIEGRRKR/GLF	5	4



台灣新型H5亞型病毒各基因之胺基酸特性

Viral protein	Amino acid position	Goose/Taiwan/0103 (H5N8)	Goose/Taiwan/0104 (H5N2)	Goose/Taiwan/0102 (H5N3)	Comments
PB2	627	E	E	E	E627K: adaptation to mammalian host
HA	138	A	A	A	S138A: increased binding to human-type receptors
	160	A	A	A	T160A: N-glycosylation loss and increased binding to human-type receptors
	226	Q	Q	Q	Q226L: increased binding to human-type receptors
	228	G	G	G	G228S: increased binding to human-type receptors
M1	30	D	D	D	N30D: increased pathogenesis in mice
	215	A	A	A	T215A: increased pathogenesis in mice
M2	31	N	N	N	S31N: resistance to amantadine and rimantadine
NS1	42	S	S	S	P42S: increased pathogenesis in mice

台灣A/Gs/Taiwan/0103病毒株與其他國家H5N8病毒株之基因相似性

	PB2	PB1	PA	HA
A/gyrfalcon/Washington/41088-6/2014	99.6	91.5	99.4	98.9
A/bean_goose/Korea/H40/2014	99.4	91.7	99.4	98.5
A/chicken/kumamoto/1-7/2014	99.2	91.5	99.0	98.5
A/duck/Jiangsu/k1203/2010	98.1	92.4	96.4	96.4

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台灣A/Gs/Taiwan/0103病毒株與其他國家H5N8病毒株之基因相似性

	NP	NA	M	NS
A/gyrfalcon/Washington/41088-6/2014	92.8	98.9	99.8	99.8
A/bean_goose/Korea/H40/2014	92.9	98.7	99.8	99.6
A/chicken/kumamoto/1-7/2014	92.8	98.5	99.9	99.5
A/duck/Jiangsu/k1203/2010	93.5	96.8	97.5	91.6

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台灣三株H5亞型病毒之基因相似性

	PB2	PB1	PA	HA	NP	NA	M	NS
H5N8 H5N2	87.4	95.1	92.3	99.3	97.6	59.5	99.8	94.6
H5N8 H5N3	87.0	95.4	99.8	99.5	97.8	57.4	99.8	99.9
H5N2 H5N3	92.3	94.3	92.3	99.7	98.3	57.9	99.8	94.5

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病毒重組

- 台灣所分離到之新型H5亞型病毒為野鳥之重組病毒
 - A/Goose/Taiwan/0103 (H5N8): 兩段基因(PB1, NP) 與野鳥病毒所帶有之基因相吻合
 - A/Goose/Taiwan/0104 (H5N2): 六段基因(PB2, PB1, PA, NP, NA, NS)
 - A/Goose/Taiwan/01042 (H5N3): 四段基因(PB2, PB1, NP, NA)
- 結果顯示台灣所分離到之三株H5亞型病毒特性顯著不同於歐洲所發生之South Korean lineages H5N8病毒

14 14

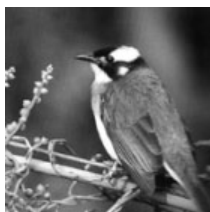
ProMED Mods.AS/CRD 之評論

- 台灣目前有四種HPAI病毒同時流行，也許是反映全球的HPAI H5 clade 2.3.4病毒傳播，而且結果顯示病毒仍處於不穩定的狀態，因而同一時間內有多株重組病毒之產生
- 從2014年11月中以來，HPAI H5亞型病毒已於全球四大洲造成疫情，包括歐洲（德國、荷蘭、英國、義大利及俄羅斯）、亞洲（中國、日本、南韓、越南、印度及台灣）、美洲（美國及加拿大）、非洲（奈及利亞及利比亞）以及中東的埃及與以色列。這些疫情由多種病毒亞型包括H5N1、H5N2、H5N3、H5N6、H5N8所造成，是否均歸屬為相同的HPAI H5 clade 2.3.4.4，仍待探討。

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鳥類分離之HPAI病毒

- 在疫情流行期間，我們於鳥類分離到三株病毒
 - A/bulbul/Taiwan/a156/2015 (H5N3)
 - A/quail/Taiwan/a234/2015 (H5N2)
 - A/heron/Taiwan/a289/2015 (H5N2)



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	A/heron/Taiwan/a289/2015 (H5N2) vs A/goose/Taiwan/0104/2015 (H5N2)	
PB2	99.8 %	EA
PB1	99.9 %	EA
PA	99.9 %	EA
H5	99.6 %	EA
NP	99.7 %	EA
N2	99.4 %	EA
MP	99.8 %	EA
NS	99.8 %	EA

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	A/bulbul/Taiwan/a156/2015 (H5N3) vs A/goose/Taiwan/01042/2015(H5N3)	
PB2	99.7 %	EA
PB1	99.8 %	EA
PA	99.7 %	EA
H5	99.8 %	EA
NP	99.8 %	EA
N3	99.6 %	EA
MP	99.5 %	EA
NS	99.7 %	EA

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	A/quail/Taiwan/a234/2015 (H5N2) vs A/goose/Taiwan/0104/2015(H5N2)	
PB2	99.9 %	EA
PB1	99.6 %	EA
PA	99.8 %	EA
H5	99.8 %	EA
NP	99.9 %	EA
N2	99.7 %	EA
MP	99.9 %	EA
NS	99.7 %	EA

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鳥類分離之HPAI病毒

- 序列分析顯示野鳥分離株與家禽分離株之八段基因有極高之相似性

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病理變化

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感染HPAVI雞、鴨、鵝及火雞之肉眼病變

- 喙、腳鱗皮膚及眼瞼皮下出血
- 顏面、頸部及腳皮下水腫
- 結膜及鼻腔黏膜出血
- 腦腫大及腦膜鬱血
- 心囊積水及心肌變性壞死
- 肝及脾腫大及多發壞死斑
- 肺水腫
- 腎腫大及尿酸鹽沉積
- 胰臟多發壞死及出血斑
- 卵巢濾泡出血及/或鬱血，卵泡萎縮及變性

雞、鴨、鵝及火雞之組織病變

- 非化膿性腦膜腦炎
- 心肌變性壞死及心肌炎
- 肝多發壞死
- 脾多發壞死
- 旁支氣管炎
- 腎小管壞死
- 胰臟多發壞死

Distribution of viral antigen (IHC) (new viral strains)																
	Brain		Heart		Liver		Spleen		Lung		Kidney		Pancreas		Intestine	
	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]	His.*	IHC [§]
Goose	++	+++	+++	++	+++	+++	+++	+++	++	++	+	++	+++	+++	-	++
Duck	++	+++	+++	++	++	+++	++	+++	++	++	+	+	+++	+++	-	+++
Turkey	++	+++	+++	++	++	++	++	++	++	+	+++	++	+++	+++	-	+
Chicken	++	+++	+++	++	++	++	++	++	++	+	+++	+++	+++	+++	-	+
H5N2 AIV bearing 4 a.a. (old viral strains)																
Chicken	+++	+++	++	++	-	+	-	+	+	+	+++	+++	+++	+++	-	-

His. = histopathology; IHC = immunohistochemistry
 * - = no; + = mild; ++ = moderate; +++ = severe lesion.
 § - = rare; + = seldom; ++ = common; +++ = widespread.