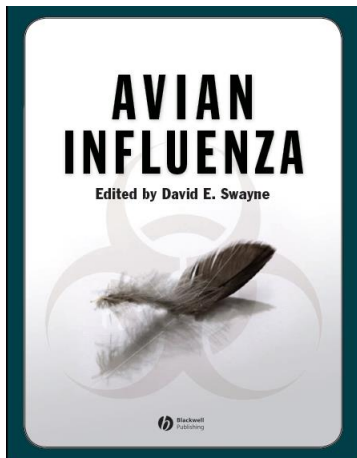




Avian Influenza: 禽流感:

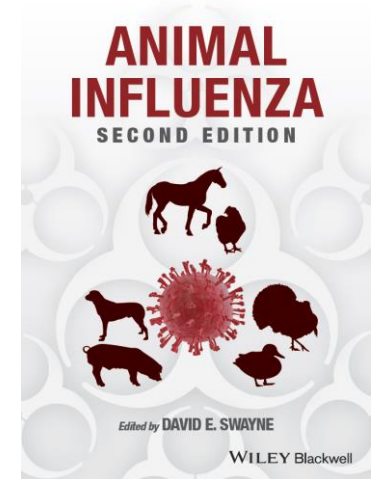
The Virus, Disease, Global Outlook and Impact

病毒、疾病、全球展望和影响



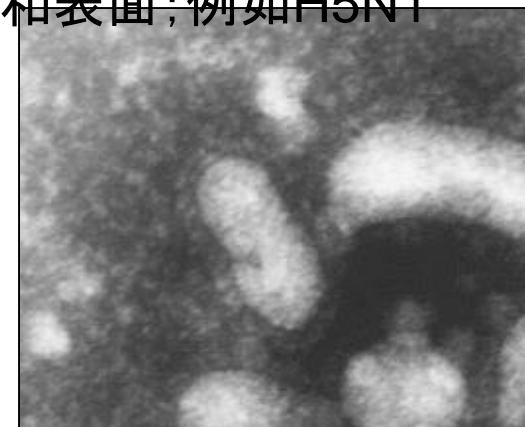
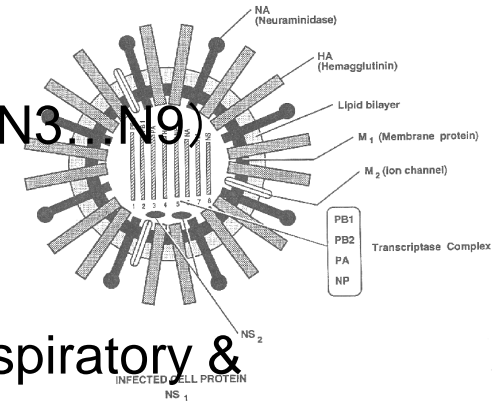
David E Swayne

Southeast Poultry Research Laboratory, U.S. National Poultry Research Center, USDA/Agricultural Research Service, Athens, Georgia;



1. Avian Influenza Virus 禽流感病毒

- **Orthomyxovirus with protein projections on the surface:** 表面有囊膜的正粘病毒
- 16 hemagglutinin subtypes (i.e. H1-H16) 16个血凝素亚型(即H1-H16)
- 9 neuraminidase subtypes (i.e. N1, N2, N3...N9) 9种神经氨酸酶亚型(即N1、N2、N3...N9)
- Thus named: H5N1, H9N2, H5N2, etc. 由此命名为H5N1、H9N2、H5N2等。
- Vary in disease production (chickens): 疾病生产的不同(鸡):
- Low pathogenicity (LP): local - mild respiratory disease and egg drop – virus in respiratory & digestive organs/tissues, surface of eggs; e.g. H9N2 LPAIV (H1-16)
- 低致病性(LP): 局部轻度呼吸道疾病和产蛋下降-呼吸道和消化器官/组织, 卵表面; 例如H9N2-LPAIV(H1-16)
- High pathogenicity (HP): systemic - deadly disease (some H5 & H7) – virus in all organs/tissues & inside and on surface of eggs; e.g. H5N1 HPAIV (Only H5 & H7)
- 高致病性(HP): 全身性致死性疾病(一些H5和H7)-病毒在所有器官/组织, 卵的内部和表面; 例如H5N1 HPAIV(仅H5和H7)
- Can infect a variety of poultry and wild birds species, depending on virus strain
- 可根据病毒株感染多种家禽和野生鸟类



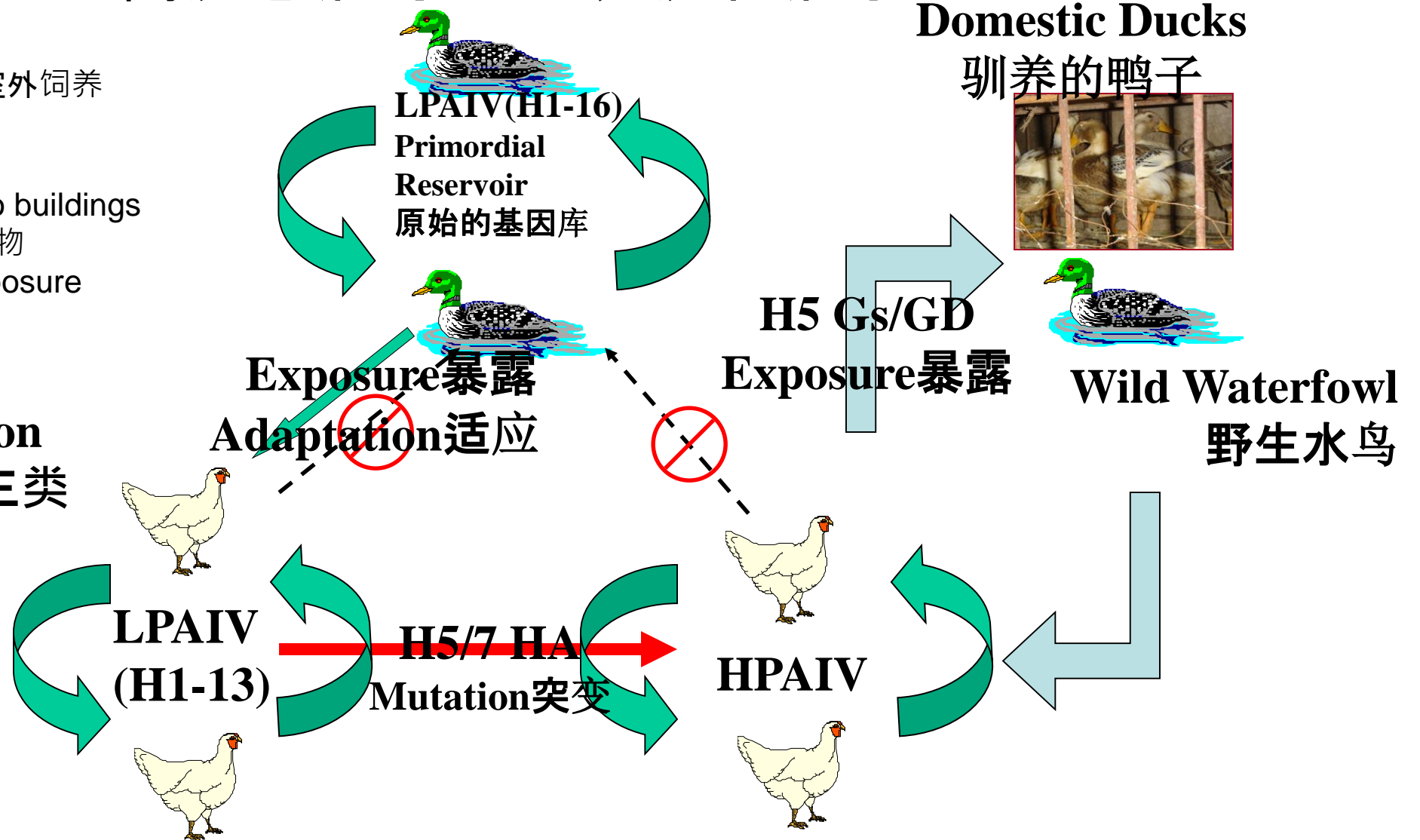
1. Avian Influenza Virus Ecology/Epidemiology

禽流感病毒生态学/流行病学

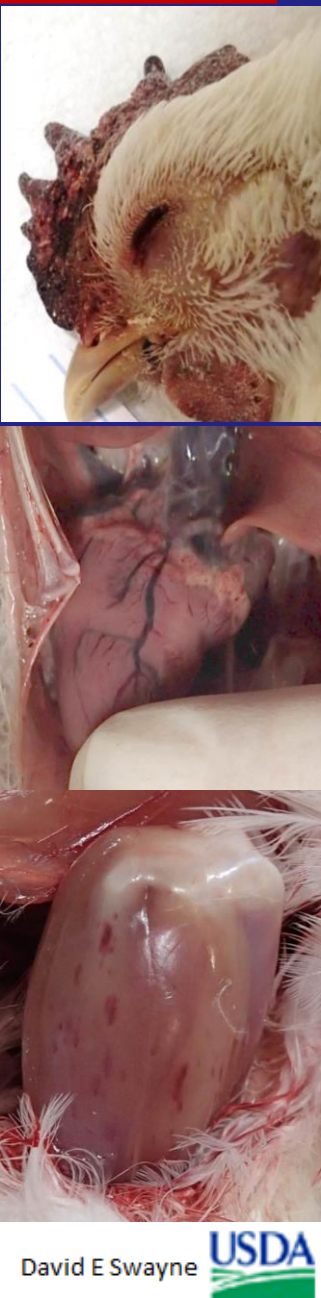
Outdoor rearing 室外饲养
Outdoor access
户外通道
Wild bird access to buildings
野生鸟类进入建筑物
Environmental exposure
环境暴露

3 types of AI based on control strategies: 三类流感病毒

- Non-H5/H7 LPAI (H1-4, H6, H8-16)
- H5/H7 LPAI
- HPAI (H5/H7)

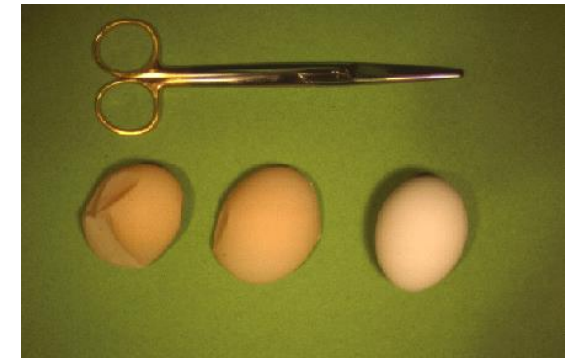


RELATIVE SPREAD RISKS



2. Low Pathogenicity Avian Influenza: Disease 低致病性禽流感：疾病

- **Subclinical and no mortality** 亚临床与无死亡
- Rhinitis & tracheitis 鼻炎/气管炎
- Ocular discharge 眼黏分泌物
- Respiratory signs 呼吸道症状
- **Diarrhea** 腹泻
- Drops in egg production 产蛋下降
- Thinning egg shells 蛋壳质量下降
- Ovary involution & hemorrhage 卵巢退化与出血



2. Low Pathogenicity Avian Influenza: Disease 低致病性禽流感：疾病

- Air sacculitis 气囊炎
- Mild increase in mortality with 2 pathogens
- 2种病原死亡率轻度上升
- Hens: 母鸡
 - Swollen kidneys and urates 肾肿尿酸盐沉积
 - Visceral urate deposits 内脏尿酸盐沉积
 - “Yolk peritonitis” 卵黄性腹膜炎



2. High Pathogenicity Avian Influenza: Disease 高致病性禽流感：疾病

Birds reared on litter: (chickens, turkeys, guinea-fowl) 饲养的（鸡、火鸡、珍珠鸡）

- High mortality 高死亡率
- Rapid spread inside the house 舍内快速扩散
- Listlessness 精神萎靡, severe decrease in feed and water consumption 饮水量和采食量明显下降
- Swollen to dead comb/wattle 肿大、发绀的鸡冠和肉髯



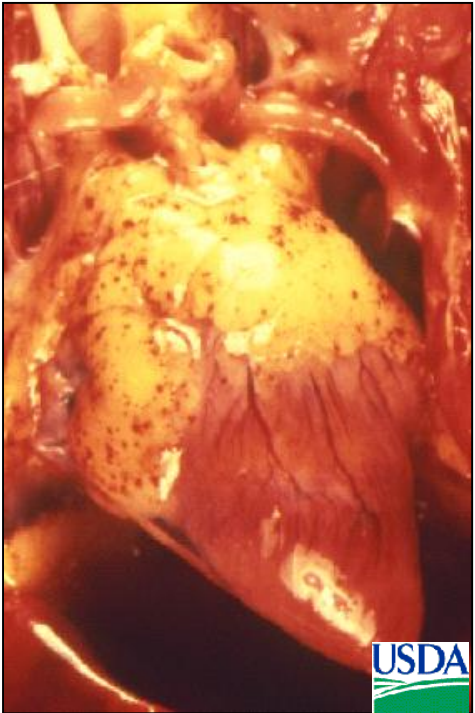
Caged Birds (layers and quail) 笼养的蛋鸡和鹌鹑

- Slow progression inside the house 室内缓慢发展
- 100% mortality in 10-15 days 10-15天死亡率100%
- Severe listlessness 严重倦怠
- +/- nervous signs 神经症状



2. High Pathogenicity Avian Influenza: Disease 高致病性禽流感：疾病

- Swollen legs and feet with subcutaneous hemorrhage 腿和爪的鳞片下出血
- Lungs fill with fluid and blood 心脏出血肿大
- Small hemorrhages on internal organs 内脏多器官有小的出血点



3. Non-H5/H7 LPAI 不是H5和H7的低致病性禽流感

- **Non-H5/H7 LPAI infections are economic issues (Includes H1-H4, H6, H8-H16) 非H5/H7的LPAI感染造成经济损失（包括H1-H4、H6、H8 H16）：**
 - **H9N2 Asia & Middle East – commercial & village poultry H9N2在亚洲和中东地区流行**
 - **Sporadic other subtypes (H6N1, H10N7, etc.): village/comm. Poultry**
 - **其他亚型也零星散发**
- **LPAI augmented severity by secondary pathogens (mycoplasma, NDV, IBV, E. coli, salmonella, etc. → increased losses from mortality/morbidity, respiratory disease and loss of egg production 低致病性禽流感与其他病原（支原体、NDV、IBV、大肠杆菌、沙门氏菌等）混合感染，加重了病情，增加了死亡率/发病率、呼吸道疾病和产蛋损失的损失。**



3. Non-H5/H7 LPAI: Control 低致病性禽流感的控制

- **Control programs are economically based and similar to control of other respiratory diseases 类似于其他呼吸系统疾病的控制程序是有效的**
 - Exposure avoidance 避免暴露(biosecurity生物安全) (**Prevention预防**)
 - Surveillance for detection 检测(**Where is it?**)
 - Controlling environmental factors 控制环境因素(bacteria and other viruses细菌和 temperature/humidity温度和湿度, etc.) (**Reduce severity**)降低严重程度
 - Vaccination may be common 疫苗接种可能是普遍做法 (**Manage the disease**)控制疾病
- **Vaccines for control - field use: 疫苗的使用**
 - **H9N2 most common H9N2比较普遍 (>10 countries 多余10个国家) - China, Pakistan, Middle East and Egypt (billions of doses) 中国、巴基斯坦、中东和埃及**
 - **H1 & H3 swine influenza viruses in breeder turkeys H1 & H3家畜流感在火鸡父母代**
 - **Sporadic with 零星散发 H2, H4 & H6**

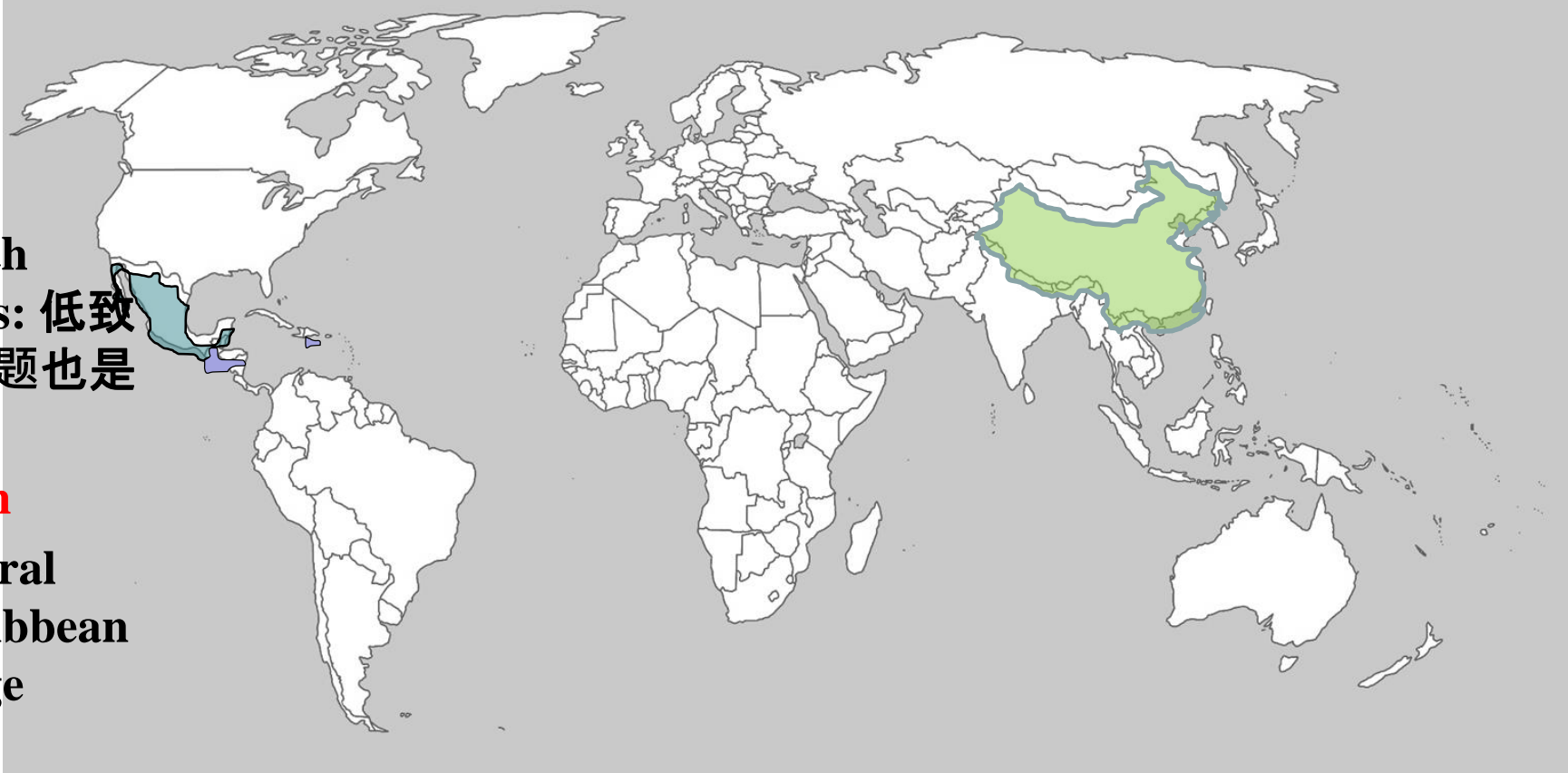


Rev. sci. tech. Off. int. Epiz., 2011, 30 (3), 839-870

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. Swayne^{1,2*}, G. Pavade¹, K. Hamilton¹, B. Vallat¹
& K. Miyagishima¹

3. H5/H7 LPAI



- H5/H7 LPAI infections are both regulatory and economic issues: 低致病性禽流感H5/H7即使监管问题也是经济问题

- H7N9 China – **LPM system**
- H5N2 Mexico墨西哥, Central America 中美洲 & the Caribbean 加勒比海 – comm. & village

- LPAI augmented severity by secondary pathogens (mycoplasma, NDV, IBV, E. coli, salmonella, etc. → increased losses from mortality/morbidity, respiratory disease and loss of egg production 低致病性禽流感与其他病原(支原体、NDV、IBV、大肠杆菌、沙门氏菌等)混合感染, 加重了病情, 增加了死亡率/发病率、呼吸道疾病和产蛋损失的损失。
- Some H5/H7 LPAI → HPAI (Changes at proteolytic cleavage site) 一些H5/H7的低致病性禽流感转变成高致病性禽流感(蛋白酶裂解位点的变化)
 - Increased # basic amino acids 碱性氨基酸的增加
 - Increased extraneous RNA 外源RNA的引入

3. Non-H5/H7 LPAI: Control 低致病性禽流感的控制

- Control programs are economically based and similar to control of other respiratory diseases

类似于其他呼吸系统疾病的控制程序是有效的

- Exposure avoidance 避免暴露(biosecurity生物安全) (**Prevention预防**)
- Surveillance for detection 检测(**Where is it?**)
- Controlling environmental factors 控制环境(bacteria and other viruses temperature/humidity etc. 细菌和病毒, 温度和湿度等因素) (**Reduce severity降低严重程度**)
- Infected poultry elimination: stamping-out or controlled marketing (Eliminate the source) 消灭家禽: 消灭或控制市场(消除来源)**
- ± vaccination (Manage the disease) 疫苗接种, 控制疾病**



Vaccines for control - field use: 控制用疫苗-现场使用:

H7N9 – China, began 2nd half 2017 H7N9 -中国, 第二开始2017

H5N2 second most common – Mexico, Central America and some Caribbean Islands

H5N2第二常见——墨西哥、美国中部和加勒比一些岛屿

H7N1 – Italy 2003-2005 (bivalent Vaccines used) H7N1——意大利2003-2005(二价疫苗)

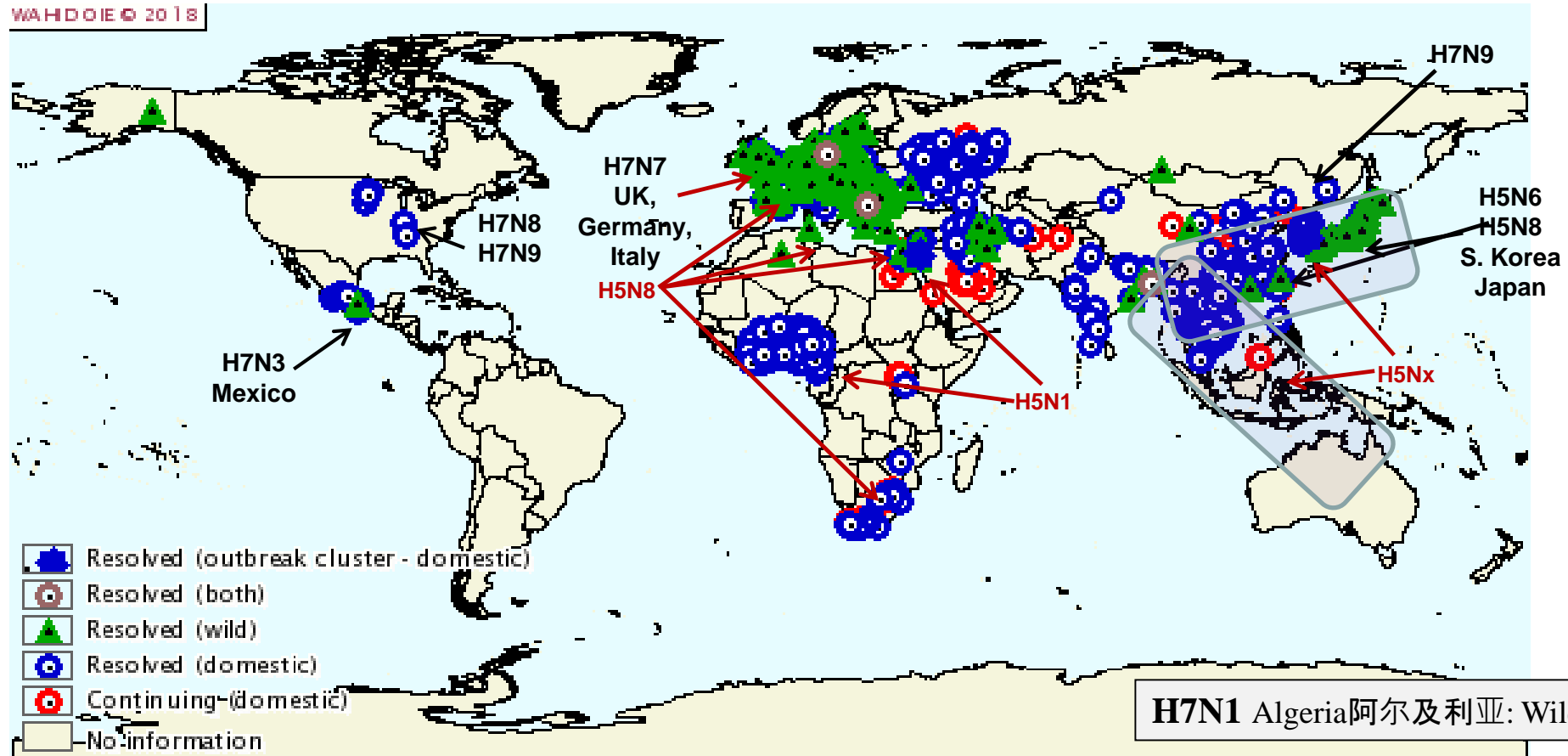
H7N3 – Connecticut USA 2003-2005 (limited use) H7N3-美国康涅狄格2003-2005(有限用途)

H5/H7 – recently, no vaccines used in EU & USA H5/H7-近日来, 欧盟和美国没有疫苗

Rev. sci. tech. Off. int. Epiz., 2011, 30 (3), 839-870

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

3. HPAI高致病性禽流感 (11/2015-10/2018): 68 countries 国家



H5 Gs/GD-lineage 谱系 (N1/N2/N3/N5/N6/N8)

68 countries 国家 – poultry 家禽, wild birds 野鸟, humans 人类 (1996 – present)

H7N3 Mexico 墨西哥: layers 产蛋鸡 (2012–present 现在)

H7N7 UK 英国, Germany 德国, Italy 意大利: Poultry 家禽 (2015)

H5N1/N2/N9 France 法国: poultry 家禽 (2015-17)

H7N1 Algeria 阿尔及利亚: Wild Bird (2017)

H7N8 USA 美国: turkey flock (2016)

H7N9 China 中国: LPM (2016-present)

H7N9 USA 美国: Broiler Breeders 肉种 (2017)

3. 36 of 42 HPAI Events : Stamping-out only

42个高致病性禽流感事件中仅有36个扑杀

1. 1959: Scotland 苏格兰, H5N1
2. 1961: S. Africa 非洲, H5N3
3. 1963: England 英格兰, H7N3
4. 1966: Canada 加拿大, H5N9
5. 1975: Australia 澳大利亚, H7N7
6. 1979: Germany 德国, H7N7
7. 1979: England 英格兰, H7N7
8. 1983-84: USA 美国, H5N2
9. 1983: Ireland 爱尔兰, H5N8
10. 1985: Australia 澳大利亚, H7N7
11. 1991: England 英格兰, H5N1
12. 1992: Australia 澳大利亚, H7N3
13. 1994: Australia 澳大利亚, H7N3

§ 14. 1994-95: Mexico 墨西哥, H5N2

§ 15. 1995 & 2004: Pakistan 巴基斯坦, H7N3

16. 1997: Australia 澳大利亚, H7N4

17. 1997: Italy 意大利, H5N2

§ 18. 1996-present: Eurasia 欧亚/Afr 非洲./N. America 北美洲, H5Nx (including N1, N2, N3, N5, N6, N8 reassortants)

19. 1999-2000: Italy 意大利, H7N1

20. 2002: Chile 智利, H7N3

21. 2003: Netherlands 荷兰 (BLGM, GRM), H7N7

31. 2012: Chinese Taipei, H5N2 2004: USA 美国, H5N2

23. 2004: Canada 加拿大, H7N3

24. 2004: S. Africa 非洲, H5N2 (ostriches)

25. 2006: S. Africa 非洲, H5N2 (ostriches)

§ 26. 2005: N. Korea 朝鲜, H7N7

27. 2007: Canada 加拿大, H7N3

28. 2008: England 英格兰, H7N7

29. 2009: Spain 西班牙, H7N7

30. 2011-3: S. Africa 非洲南部, H5N2 (Ostriches)

§ 32. 2012-present: Mexico 墨西哥, H7N3

33. 2012: Australia 澳大利亚, H7N7

34. 2013: Italy 意大利, H7N7

35. 2013: Australia 澳大利亚, H7N2

36. 2015: England 英格兰, H7N7

37. 2015: Germany 德国, H7N7

38. 2015: France 法国, H5Nx

39. 2016: USA (Indiana) 美国印第安纳州, H7N8

40. 2016: Italy 意大利, H7N7

41. 2017: China 中国, H7N9

42. 2017: USA (Tennessee) 美国田纳西州, H7N9

§ Vaccine used in the control strategy 疫苗被用来控制

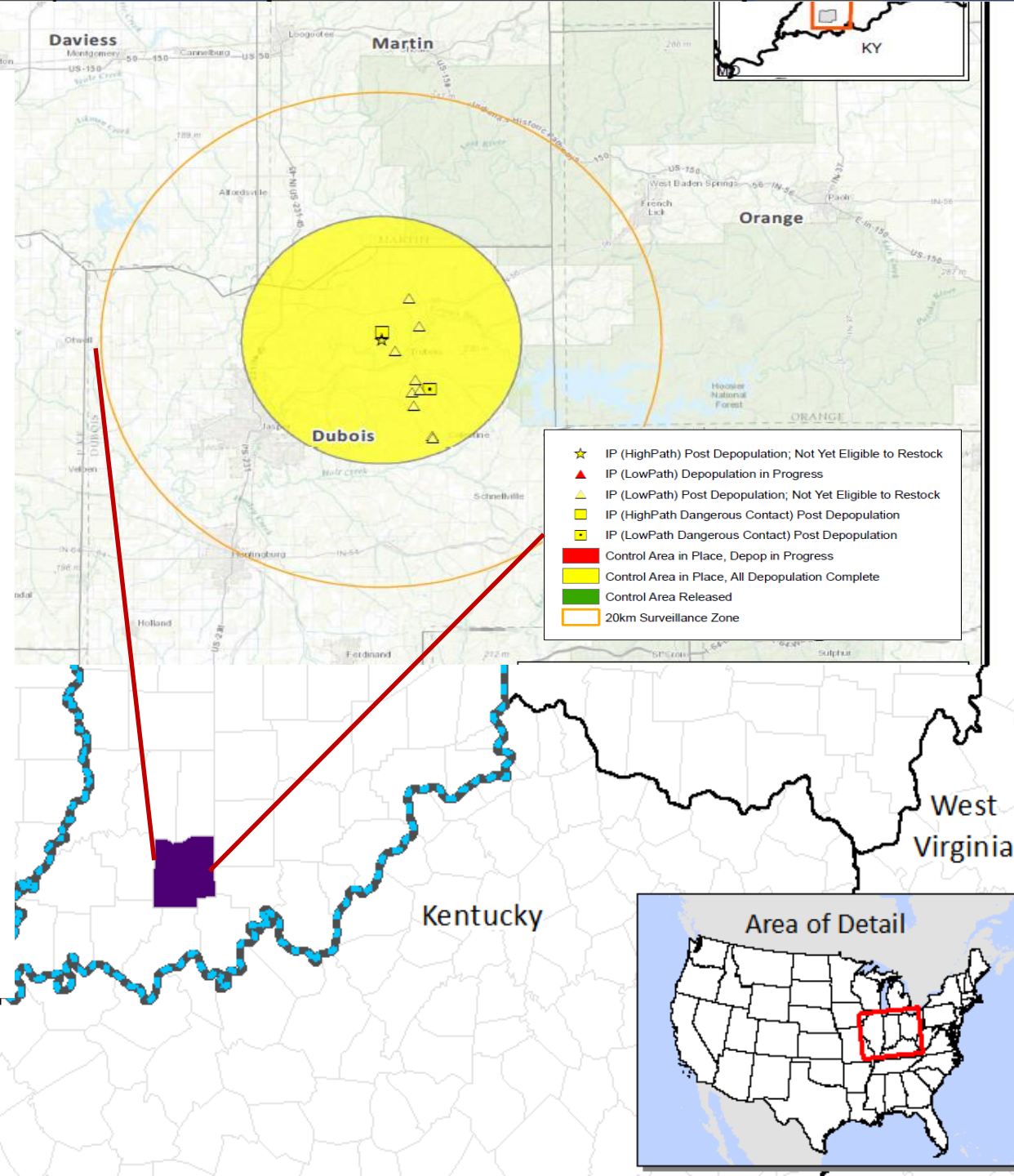
Historical “Stamping-out”

Program: 历史上的扑杀计划

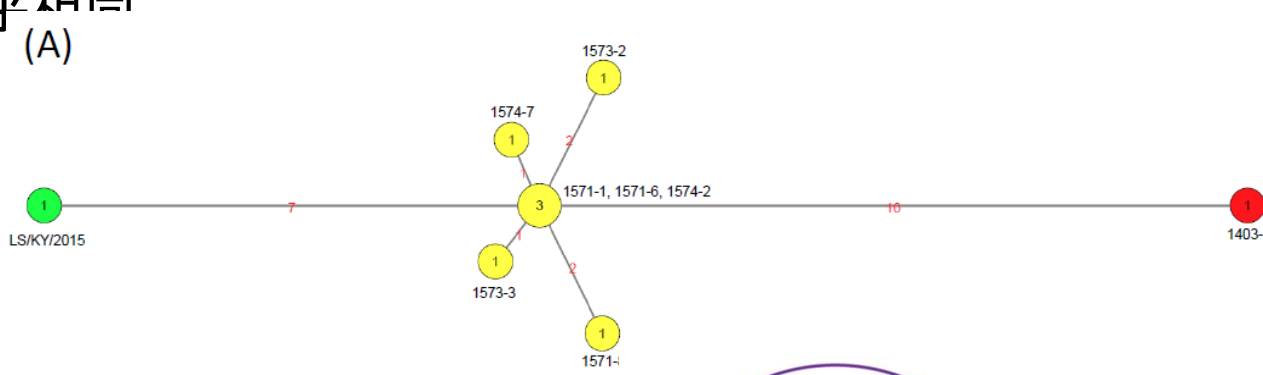
- Enhanced biosecurity 增强生物安全性 → **prevent HPAI introduction onto naïve farms or from leaving affected farms; movement control essential** 防止 HPAI 传入幼群或离开受影响农场, 运输控制是必不可少的。
- **Diagnostics and surveillance** 诊断与监测 → **quickly find** 快速发现 **HPAI**
- **Elimination of infected poultry (culling)** 剔除感染的鸡群 → **stamp-out HPAI action plan** 扑杀高致病性禽流感行动计划
- **Education** 教育 → **your individual responsibility and high compliance rate** 你的个人责任和高的服从

HPAI Deter

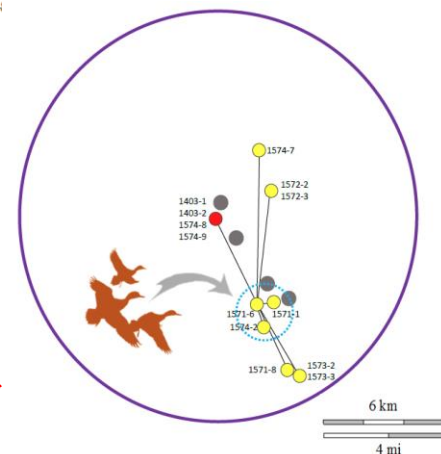
- **10 Jan 16:** ↓ water consumption & pulmonary edema, meat turkeys 饮水量下降, 肺水肿, 火鸡
- **13 Jan 16:** 100 dead birds (1.3%) 100只死亡
- **14 Jan 16:**
 - 800 dead birds (10.5%) 800只死亡, 10.5%的死亡率
 - +ACIA and preliminary +H7 rRT-PCR
- **15 Jan 16:**
 - +H7N8 North American HPAIV 北美洲高致病性禽流感
 - Depopulation initiated 快速扑杀
- **16 Jan 16:**
 - Depopulation complete HPAI turkeys 全部扑杀高致病性禽流感感染的火鸡
 - 10km zone 65 comm 10公里的区域. premises surveillance identified H7N8 LPAIV on 9 premises; 2 dangerous contacts 监控的鸡场中有9个鸡场为H7N8低致病性禽流感, 2个危险的接触
- **20 Jan 16:** all depopulation completed 扑杀完成 (414,000; 12 premises 鸡场)



- LPAIV, IVPI = 0.00, PENPKTR/GLF
- HPAIV, IVPI = 2.84, PENPKKRKTR/GLF – 9 nucleotide insert 9核苷酸插入物
- Closest related H7 AIV 与H7禽流感病毒密切相关的, A/Lesser scaup/Kentucky/AH0012935/2015 (28 Nov 2015), 7 weeks prior & 200km from outbreak farm 7周前和爆发场200公里
- Full genome analysis suggests all LPAIV & HPAIV nearly identical 全基因组分析表明所有的LPAIV和HPAIV几乎相同



H7N8 LPAIV highly similar and support a single introduction followed by lateral spread
 H7N8 LPAIV高度相似，支持单一传入侧向传播
 /secondary spread and single HP mutation without spread to epidemiologically linked farms
 二次扩散和单HP突变不扩散到流行病学扩散的农场



3. 6 HPAI Events事件: Tenacious Outbreaks严重爆发

1. 1959: Scotland 苏格兰, 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 墨西哥, H5N2 (HP & LP)

§ 15. 1995 & 2004: Pakistan 巴基斯坦, H7N3

16. 1997: Australia, H7N4

17. 1997: Italy, H5N2

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21. 2003: Netherlands (BLGM, GRM), H7N7

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28. 2008: England, H7N7

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31. 2012: Chinese Taipei, H5N2

§ 32. 2012-present: Mexico 墨西哥, H7N3

33. 2012: Australia, H7N7

34. 2013: Italy, H7N7

35. 2013: Australia, H7N2

36. 2015: England, H7N7

37. 2015: Germany, H7N7

38. 2015: France, H5Nx

39. 2016: USA (Indiana), H7N8

40. 2016: Italy, H7N7

41. 2017: China 中国, H7N9 (HP & LP)

42. 2017: USA (Tennessee), H7N9

§ Vaccine used in the control strategy

Historical “Stamping-out” Program: 历史上的扑杀计划

- **Enhanced biosecurity** 增强生物安全性 → **prevent HPAI introduction onto naïve farms or from leaving affected farms; movement control essential** 防止HPAI传入幼群或离开受影响农场, 运输控制是必不可少的。

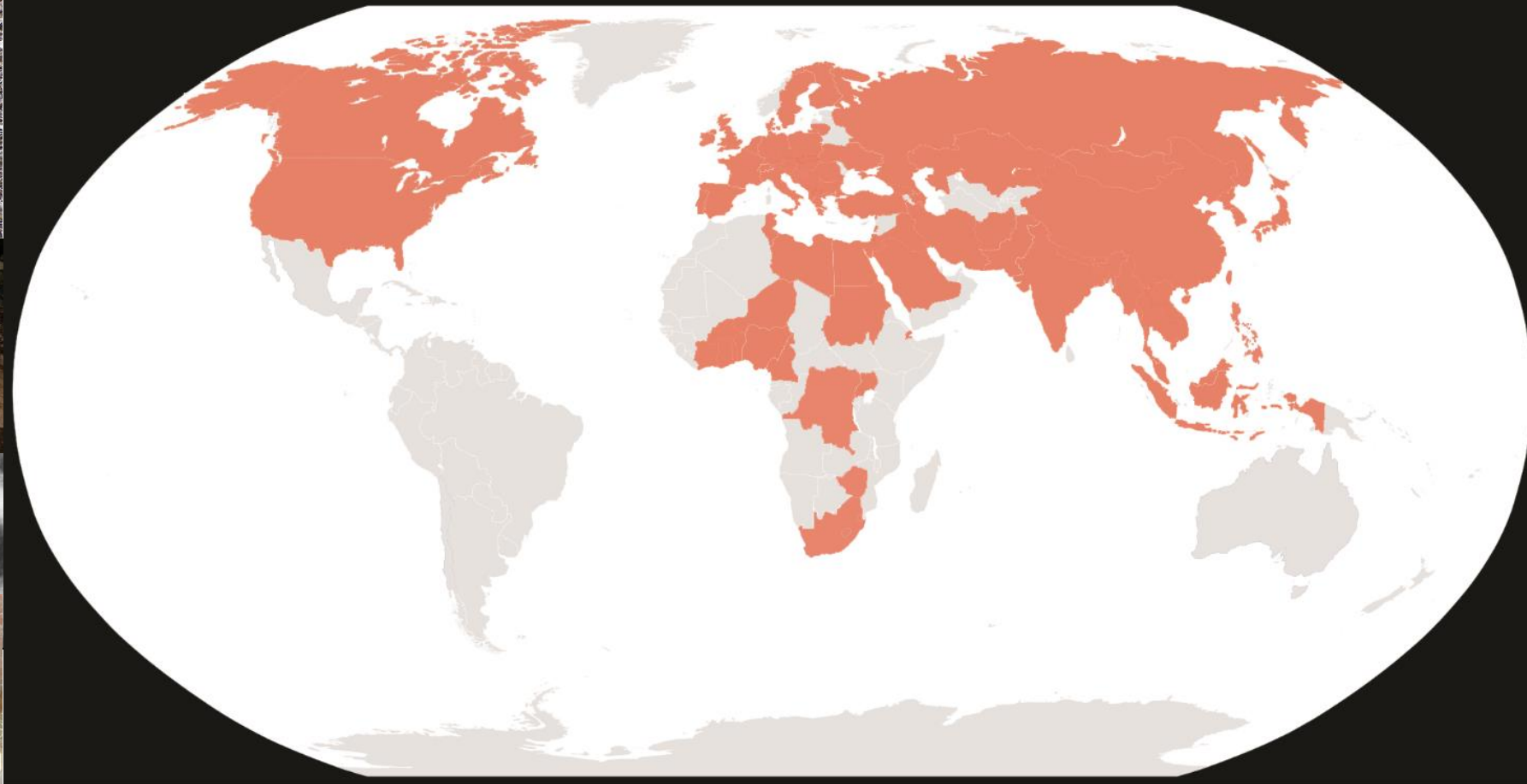
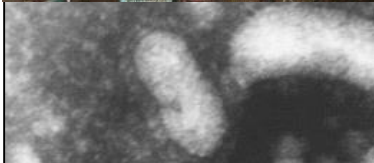
- **Diagnostics and surveillance** 诊断与监测

→ **quickly find** 快速发现 **HPAI**

- **Elimination of infected poultry (culling)** 剔除感染的鸡群 → **stamp-out HPAI action plan** 扑杀高致病性禽流感行动计划

- **Education** 教育 → **your individual responsibility and high compliance rate** 你的个人责任和高的服从

- **Decreasing host susceptibility (vaccines/vaccination)** 降低宿主易感性 (疫苗/疫苗接种) → **temporary solution (6 of 42 epizootics)** : 临时解决方案 (42种流行病疫苗中的6种)



- **H5N1 Gs/GD largest最大 & longest最强 since 1920-30, >500 million poultry died/culled死亡/扑杀**
- **Began in China in domestic geese during 1996 1996年在中国中的家鹅中发现**
- **83 countries in poultry, wild birds or humans (Endemic in 6 & recurring in 10-12 countries)**
83个国家的家禽、野生鸟类或人类（6国家流行，10~12个国家复发）
- **Focused in Northern Hemisphere across Asia, Europe, Africa and North America**
集中在北半球横跨亚洲、欧洲、非洲和北美洲
- **Affected more poultry than the other 41 HPAI Disease Events combined**
感染的家禽比其他的41中高致病性禽流感的总和都要多

3. One Predictable Issue About Avian Influenza Viruses – They Change 关于禽流感病毒的一个可预测的问题——它们改变了

Drift 突变

H5N1 HPAI hemagglutinin clades 血凝素序列
2.1.3.2 2.2.1 2.3.2.1 2.3.4.4

Gene segment reassortment: 基因片段重组

- Neuraminidase 神经氨酸酶
- Other 6 gene segments such as PA, PB2, PB1, etc. 像 PA, PB 2, PB 1 等等的其他 6 个基因片段

Spread: 传播

- Five episodes of transboundary H5Nx Gs/GD lineage HPAIV introduction by wild aquatic birds 跨界 H5Nx Gs/Gd 高致病性禽流感通过水禽传入
- Major farm-to-farm spread by human/agricultural activities 农场到农场的传播主要通过人 / 农业活动



Reassortment of Genes 基因重组

Other Avian Influenza Viruses from Wild Birds and Live Poultry Markets 来自野生鸟类和活禽市场的其他禽流感病毒

H5N1 (2.3.4.4)

H5N2 (2.3.4.4)

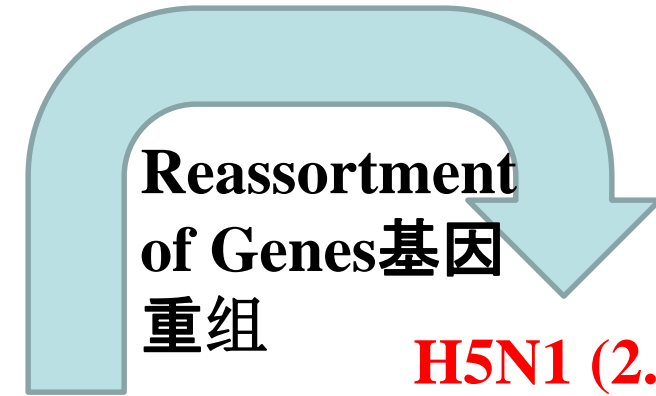
H5N3 (2.3.4.4)

H5N5 (2.3.4)

H5N6 (2.3.4.4)

H5N8 (2.3.4.4)

Shift 替换



4. How Avian Influenza is Globally Controlled? Economic Impact?

禽流感如何在全球受到控制？经济影响？



World Organization for Animal Health 世界动物卫生组织
(Office International des Epizooties) (国际动物流行病学办公室)

Oie

- **181 Member countries: 181个成员国**
- **“Notifiable” avian influenza: non-tariff trade barriers (\$\$\$)**
“可呈报的” 禽流感：非关税贸易壁垒
 - **HPAI (Fowl Plague – since 1924) – High Risk in Trade (commodity specific)**
禽流感（1924以来）——高风险的贸易（特定商品）
 - **H5/H7 LPAI (since 2005) – Low Risk in Trade (commodity specific)**
H5/H7 LPAI（自2005以来）-低风险贸易（特定商品）
- **Non-H5/H7 LPAI not notifiable (H1-4, H6, H8-16): economic diseases (ex. H9N2)** 非H5/H7LPAI不呈报（H1-4, H6, H8-16）：经济疾病（Ex.H9N2）
- **Standards (science-based):标准（科学基础）**
 - **Terrestrial Animal Health Code** 陆生动物卫生法典
 - **Manual of Diagnostic Tests and Vaccines for Terrestrial Animals**
陆生动物诊断试验和疫苗手册



Conclusions:

- **LPAI viruses can be any of 16 hemagglutinin subtypes, but HPAI have been only H5 or H7** LPAI病毒可以是16种血凝素亚型中的任何一种，但HPAI仅为H5或H7。
- **Rapid detection and elimination of H5/H7 LPAIV is preventative measure to avert mutation to HPAIV & trigger a newly emergent HPAI disease event**

快速检测和消除H5/H7 LPAIV是预防HPAIV突变和触发新的HPAI疾病事件的措施

- **42 HPAI disease events have occurred since 1959:**

自1959年以来，发生了42起HPAI疾病事件

36 events were eradicated through stamping-out programs & 6 used vaccine, in addition to stamping-out, as a management strategy

其中36个通过扑杀根除，6个通过疫苗免疫，而不是扑杀，作为一个管理策略

- **Current major outbreaks Gs/GD (H5N6, H5N8 and H5N1) HPAIV (Europe, Africa and Asia) and H7N3 Mexican HPAIV**

目前主要爆发（H5N6、H5N8和H5N1）HPAIV（欧洲、非洲和亚洲）和H7N3墨西哥HPAIV

- **HPAI and H5/H7 LPAI have negatively impacted trade but risk varies with virus pathotype (LP vs HP) and mitigation strategies**

HPAI和H5/H7 LPAI对贸易产生负面影响，但风险与病毒的致病性和缓解策略有关。

Merci Beaucoup!

