INFLUENZA VIRUS

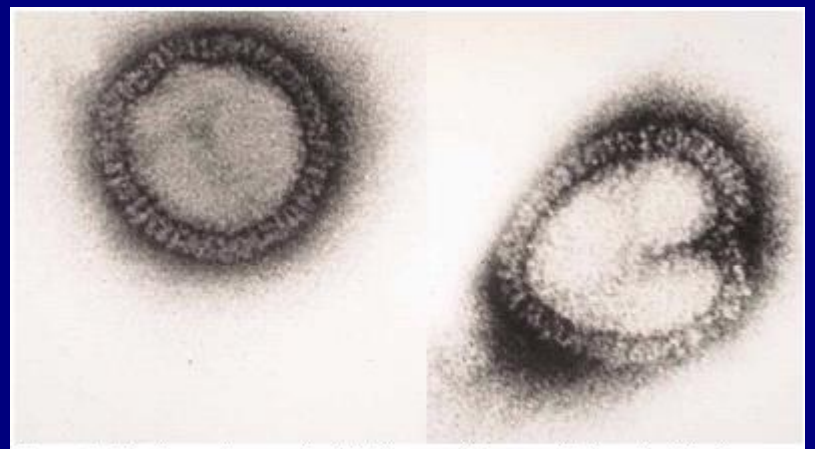


Figure 1 Electron micrograph of influenza A virus particles. Provided by M-T. Hsu and P. Palese.

INSTITUTO BUTANTAN

Dra. Viviane Fongaro Botosso

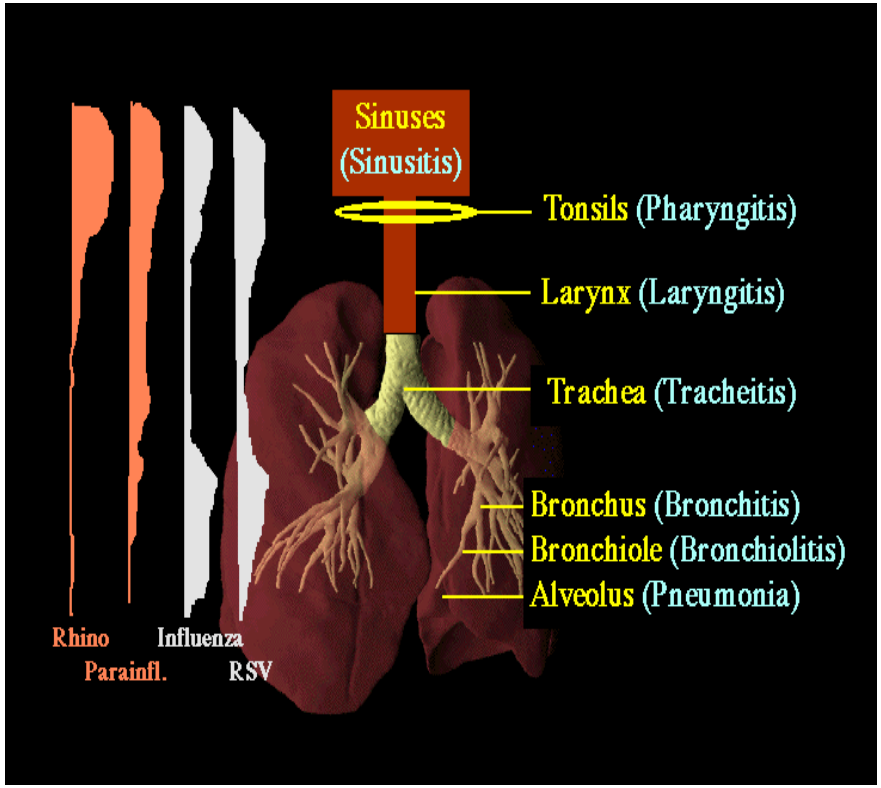
Outubro 2016

Influenza ou Gripe

- Doença viral aguda do trato respiratório causado pelo **Vírus Influenza**
- Distribuição global
  - 600 milhões de infectados no mundo
  - 3 a 5 milhões de casos
  - 250 a 500 mil mortes
- Sintomas
- Transmissão
- Agente – vírus Influenza
- Tratamento
- Controle e prevenção

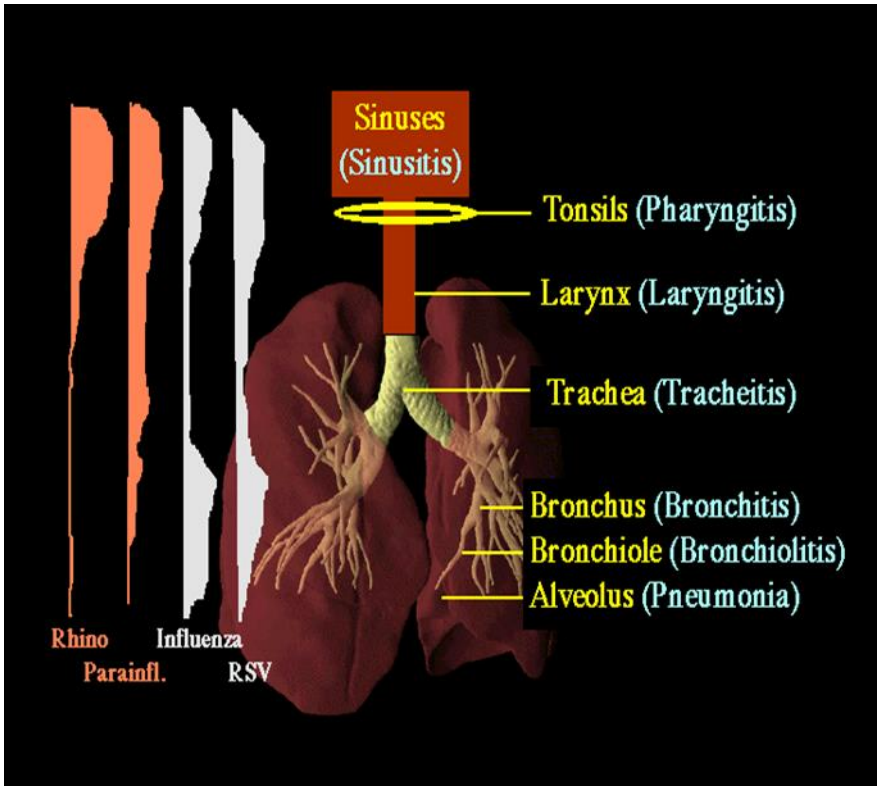
Resfriado

- Mais de 200 virus envolvidos: Rhinovírus, Coronavírus, Parainfluenza, Vírus Respiratório Sincicial, Adenovírus...
- Sintomas aparecem geralmente de maneira gradual e mais brandos: Coriza, dor de garganta, obstrução nasal, espirros, tosse irritativa, febre (rara)



Gripe

- ✓ Início súbito de febre, associada a calafrios, dor de garganta, cefaléia, anorexia, mialgia, mal estar, fadiga. Com menor frequencia – náusea, dor abdominal, diarréia.
- ✓ Complicações: pneumonias, infarto e AVcs pos infecção, otites...
- ✓ Mortalidade: em crianças (<10 anos), idosos (>60 anos), imunodeprimidos



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Transmissão

- Principalmente por gotículas geradas pela fala, tosse, espirro.
  - Um bom espirro chega a 6m !!
- Contato com mãos e superfícies contaminadas.
- Incubação – Tipicamente 2 dias (1-4)
- Eliminação do vírus
  - Pode começar 1 dia ANTES dos sintomas
  - É máxima nos 3 dias iniciais de doença
  - Correlaciona-se com a febre
  - Diminui depois de 5-7 dias
    - Pode durar mais de 10 dias em crianças

Influenza ou Gripe

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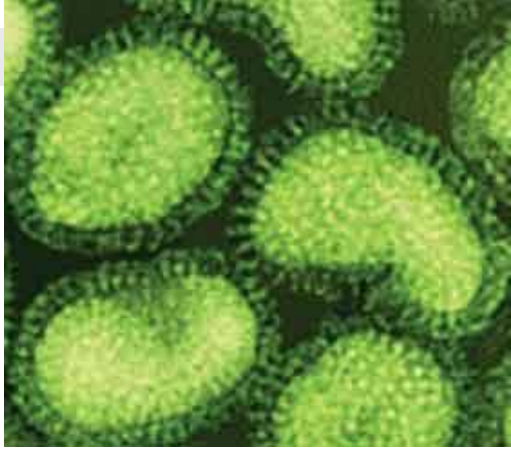
  - 3 a 5 milhões de casos
  - 250 a 500 mil mortes
- Sintomas
- Transmissão
- Agente – vírus Influenza
- Tratamento: paliativo, antivirais
- Controle e prevenção: **Vacinação Anual**

VIRUS DA INFLUENZA



✓ Família – *Orthomyxoviridae* (6 gêneros - ***Influenzavirus A, Influenzavirus B, Influenzavirus C***, *Thogotovirus, Quaranjavirus e Isavirus)*

- **Influenza A:**
  Dividido em subtipos baseado na variedade das glicoproteínas de superfície: Hemaglutinina (HA) e Neuraminidase (NA)

- **Influenza B:** infecta o homem, com surtos localizados

- **Influenza C:** doenças respiratórias leves

INFLUENZA - Características

- ✓ Pleomórficos – 80 a 120 nm diâmetro
- ✓ Envelopados
- ✓ Capsídeo de Simetria helicoidal

RNAss-, segmentado

- IA e IB - 8 segmentos – 15 proteínas

PB1, PB2, PA, HA, NA, NP, M1, M2,

NS1,NS2, 5 proteínas complementares:

PB1-F2, PB1N40,PA-X,PAN155, PAN182

- IC – 7 segmentos

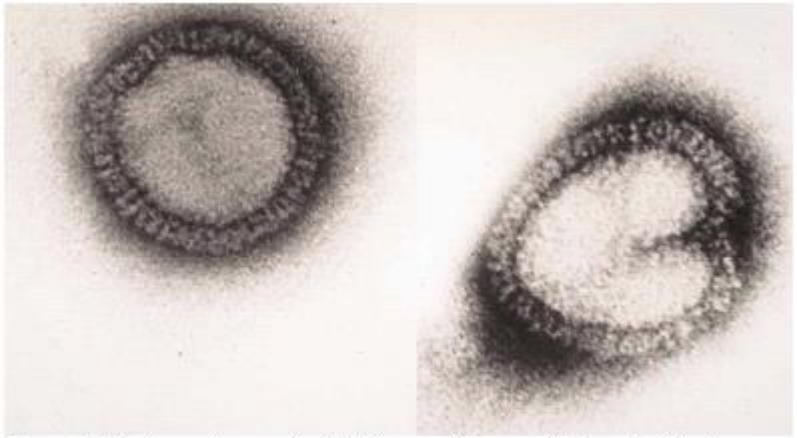
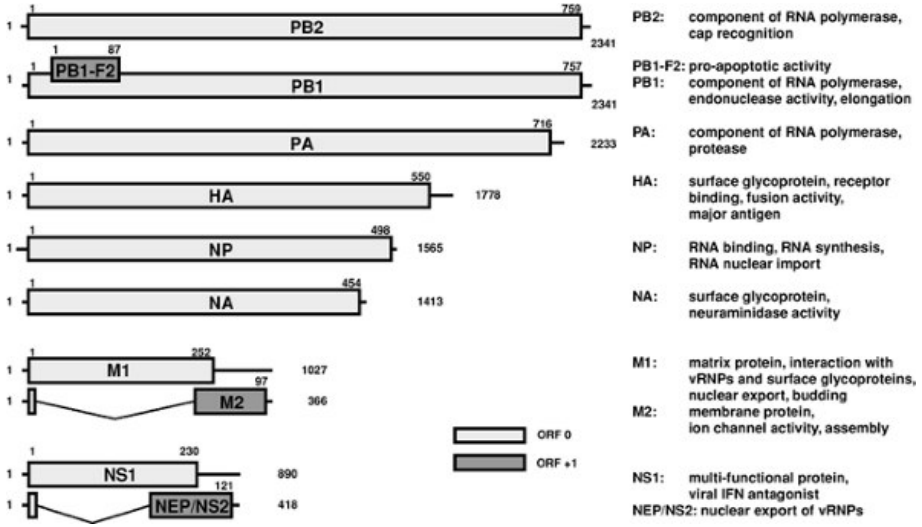
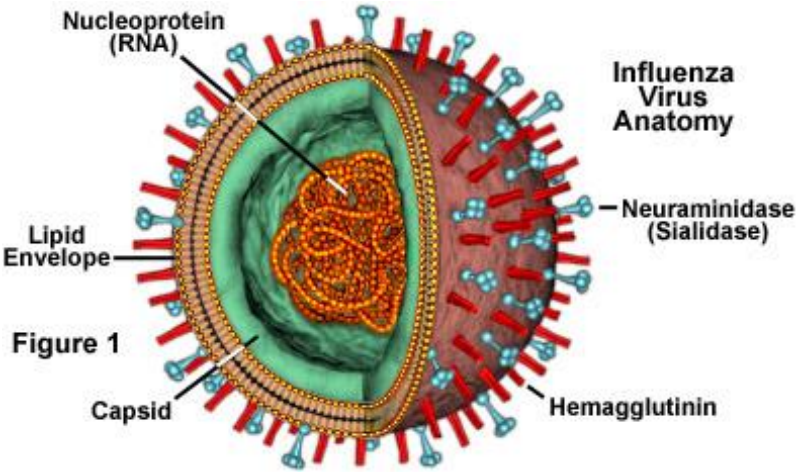


Figure 1 Electron micrograph of influenza A virus particles. Provided by M-T. Hsu and P. Palese.

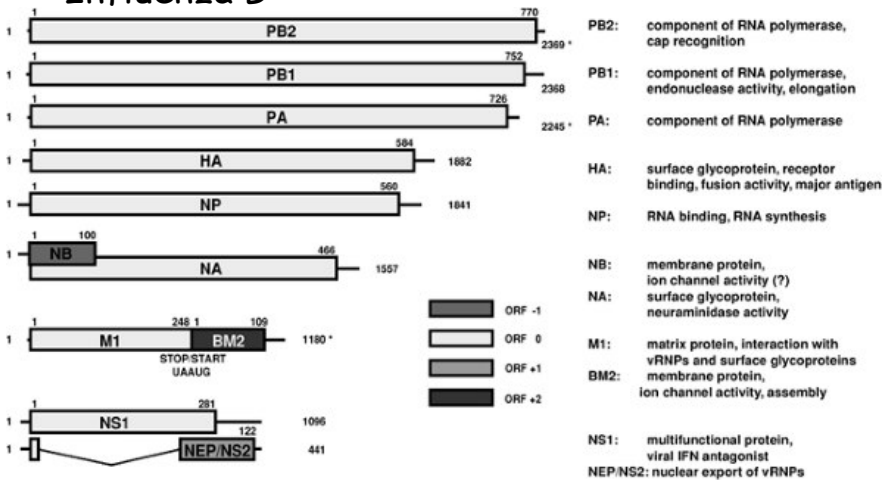
INFLUENZA - Características

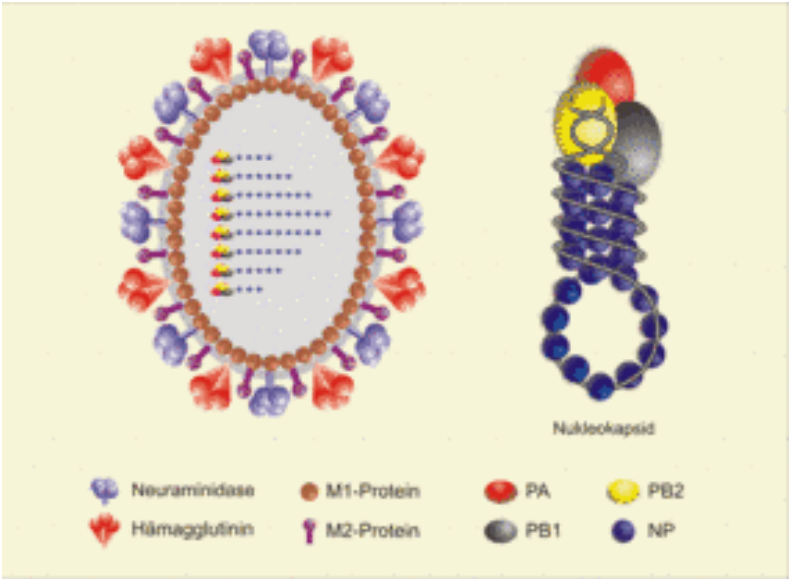
Influenza A





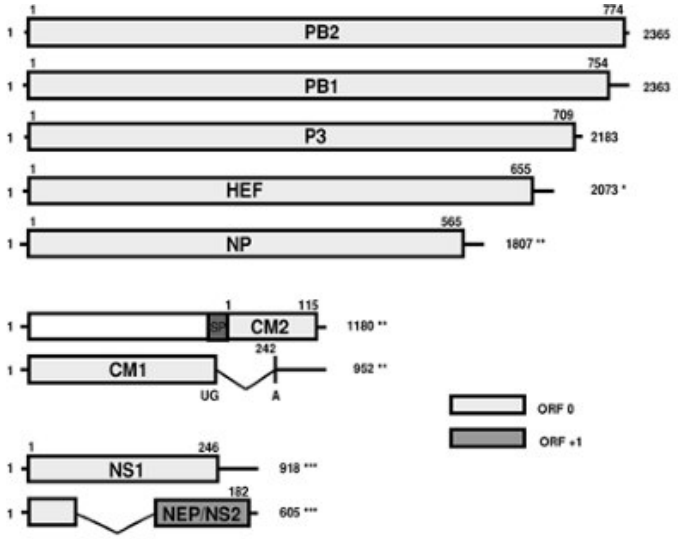
Influenza B





INFLUENZA - Características

Influenza C



PB2: component of RNA polymerase

PB1: component of RNA polymerase

P3: component of RNA polymerase

HEF: surface glycoprotein, receptor binding, esterase and fusion activity, major antigenic determinant

NP: RNA binding, RNA synthesis

CM2: surface glycoprotein, ion channel activity (?)

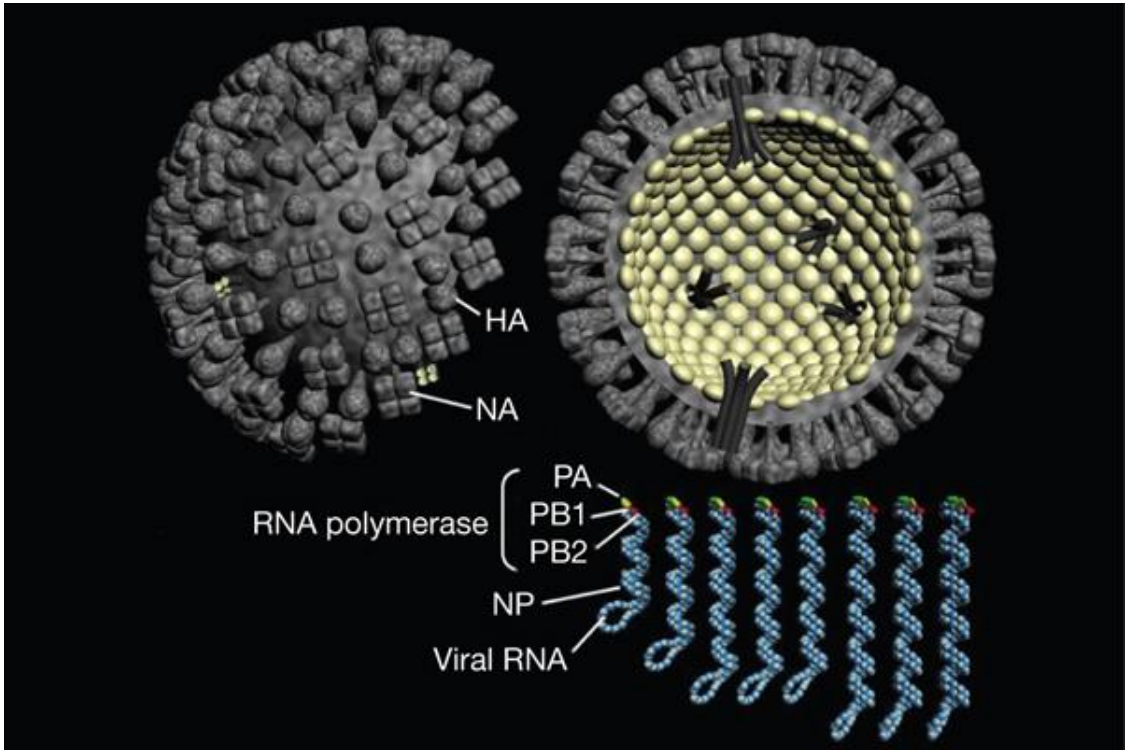
CM1: matrix protein, interaction with vRNPs and surface glycoproteins, generation of cord-like structures

NS1: multi-functional protein, viral IFN antagonist

NEP/NS2: nuclear export of vRNPs

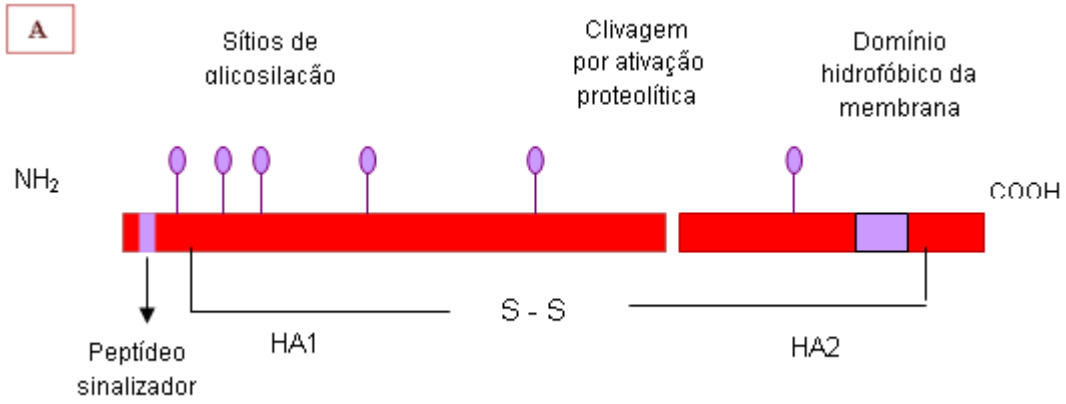
Schematic diagram of influenza A viruses.

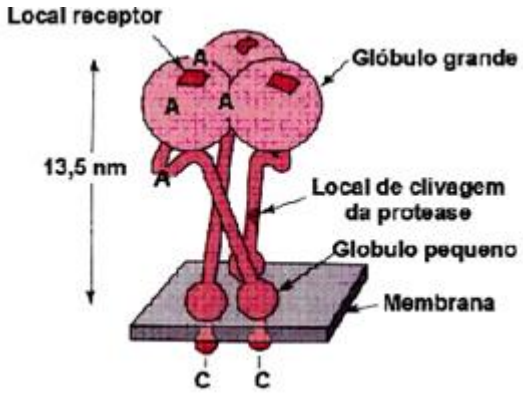
- HA: adsorção e penetração do vírus
- NA: liberação viral e disseminação trato respiratório
- M2 – canais transporte protons

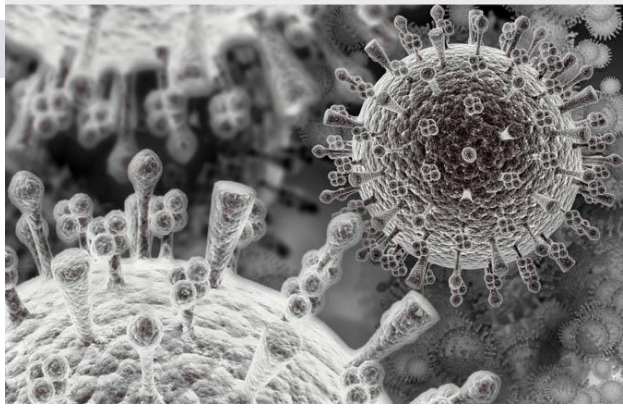


G Neumann *et al. Nature* **000**, 1-9 (2009) doi:10.1038/nature08157

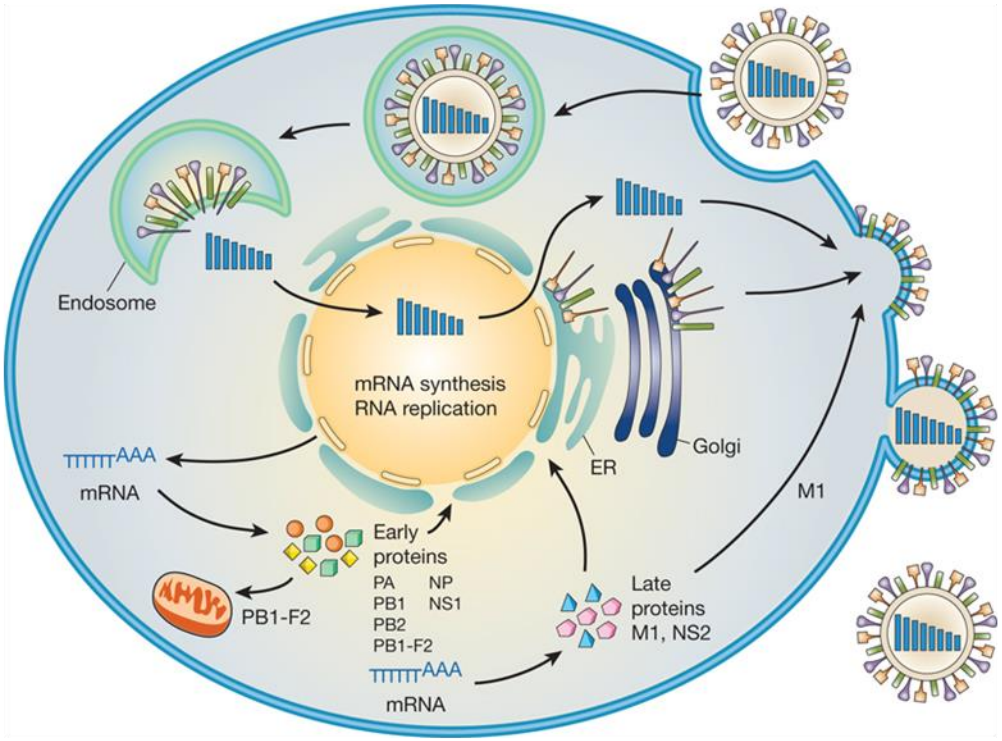
nature


A
Sítios de glicosilacão
Clivagem por ativação proteolítica
Domínio hidrofóbico da membrana
NH2
COOH
Peptídeo sinalizador
HA1
S - S
HA2

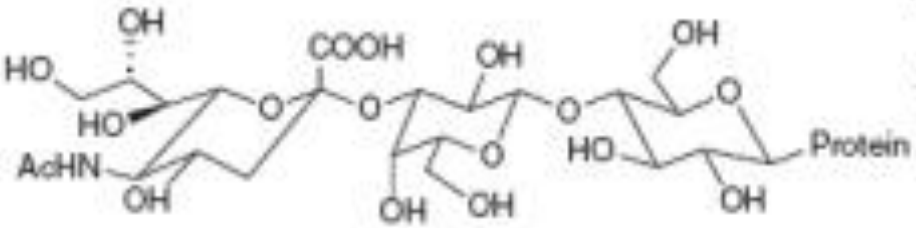

Local receptor
Glóbulo grande
13,5 nm
Local de clivagem da protease
Globulo pequeno
Membrana
A
C



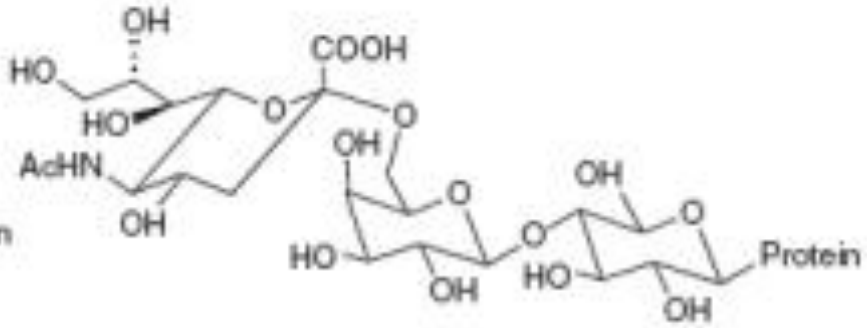
Schematic diagram of the influenza viral life cycle.



G Neumann *et al. Nature* **459**, 931-939 (2009) doi:10.1038/nature08157

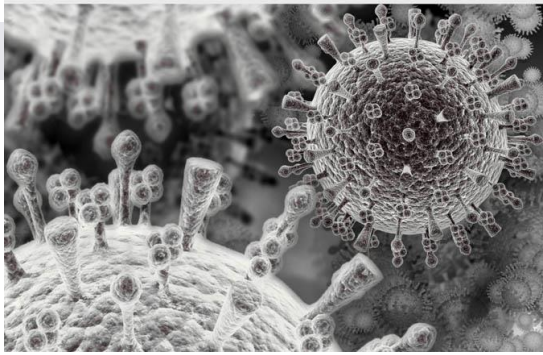


Sialic acid-(α-2,3)-galactose



Sialic acid-(α-2,6)-galactose

Os vírus da gripe humana utilizam receptores de ácido siálico alfa-2,6, encontrada em células epiteliais da parte superior do sistema respiratório (nariz, faringe, traquéia). Gripe aviária utilizam receptores de ácido siálico alfa -2,3, encontrada em células de intestino de aves.



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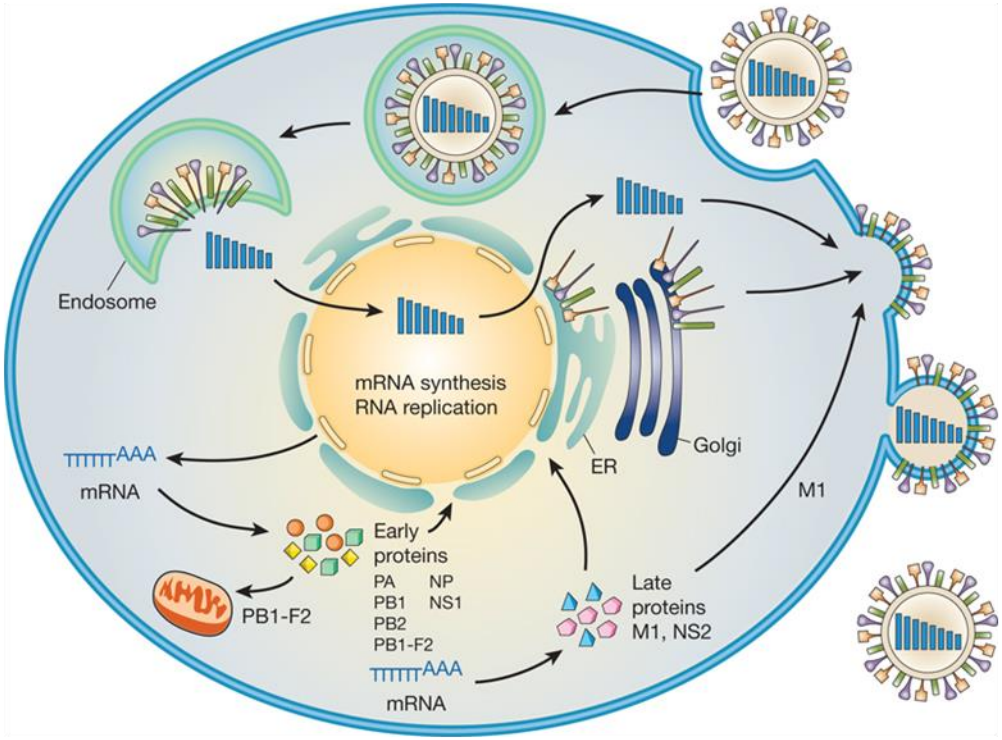


G Neumann *et al. Nature* **459**, 931-939 (2009) doi:10.1038/nature08157

HEMAGLUTININAS E O SÍTIO DE CLIVAGEM

	Cleavage site ↓	
Avian isolates		
Avirulent strain (H5)	P Q – – – – R E T R	G
Avirulent strain (H7)	P E X P – – – K X R	G
Virulent strain (H5)	P Q – – R K R K K R	G
Virulent strain (H7)	P E P S K K R K K R	G
Human isolates: pandemic strains		
1918 Spanish flu (H1N1)	P S – – – – I Q S R	G
1957 Asian flu (H2N2)	P Q – – – – I E S R	G
1968 Hong Kong flu (H3N2)	P E – – – – K Q T R	G
1977 Russian flu (H1N1)	P S – – – – I Q S R	G
Human isolates: avian strains from humans		
1997 Hong Kong (H5N1)	P Q R E R R R K K R	G
1999 Hong Kong (H9N2)	P Q – – – – R S S R	G
2003 the Netherlands (H7N7)	P E I P – K R R R R	G
2004 Asian (H5N1)	P Q R E (R) R R K K R	G

Figure 3 | **HA cleavage site sequence of influenza A viruses.** Basic amino acids are shown in blue boxes. Dashes are for the purpose of alignment only.

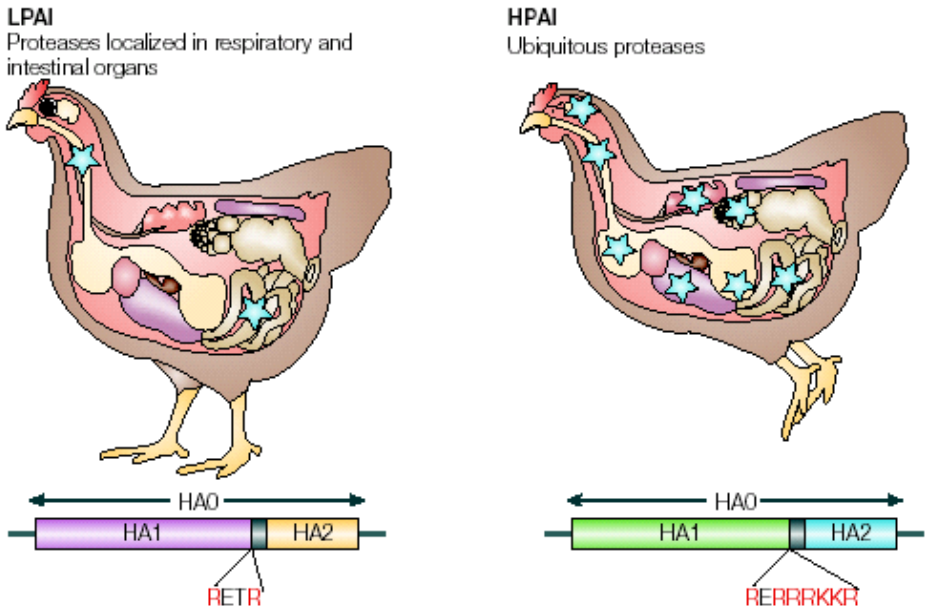
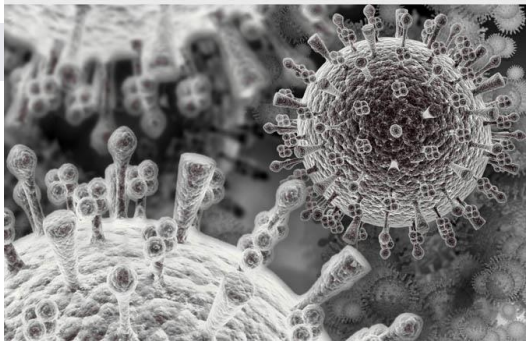


Figure 4 | **Haemagglutinin (HA) as a major determinant of the pathogenicity of avian influenza viruses in poultry.** Post-translational proteolytic cleavage of the HA precursor molecule (HA0) into HA1 and HA2 subunits by host proteases generates a fusogenic domain at the amino terminus of HA2 (shown in grey), which mediates fusion between the viral envelope and the endosomal membrane. Therefore, proteolytic activation of the HA molecule is essential for viral infectivity. The HAs of low-pathogenicity avian influenza (LPAI) viruses do not contain a series of basic amino acid (RETR) at the protease cleavage site and are cleaved by proteases that are localized in respiratory and intestinal organs, resulting in mild localized infections. By contrast, the HAs of high-pathogenicity avian influenza (HPAI) viruses possess multiple basic amino acids at the cleavage site (RERRRKKR), which are cleaved by ubiquitous proteases in a wide range of organs, resulting in lethal systemic infection.



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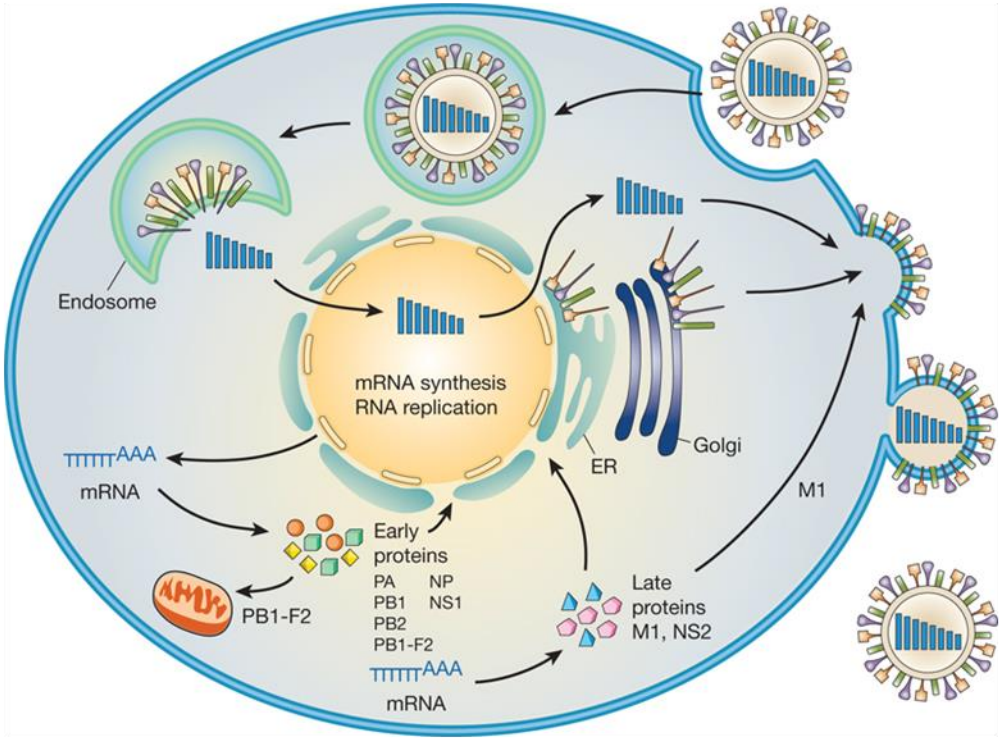
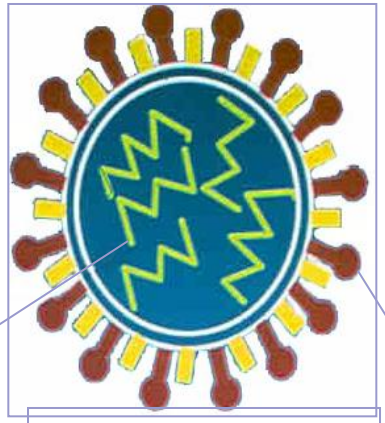


G Neumann *et al. Nature* **459**, 931-939 (2009) doi:10.1038/nature08157

nature

INFLUENZA VIRUS NOMENCLATURA



Hemaglutinina

Neuraminidase

A/Beijing/32/92 (H3N2)

Tipo

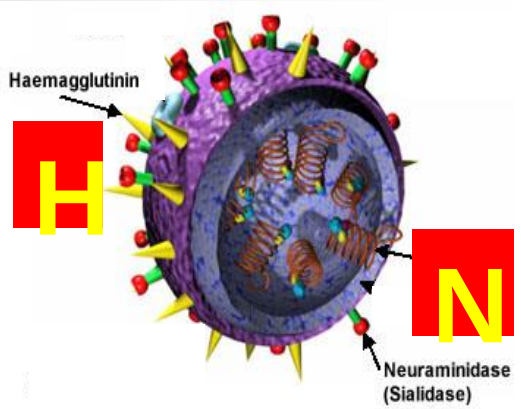
Origem geográfica

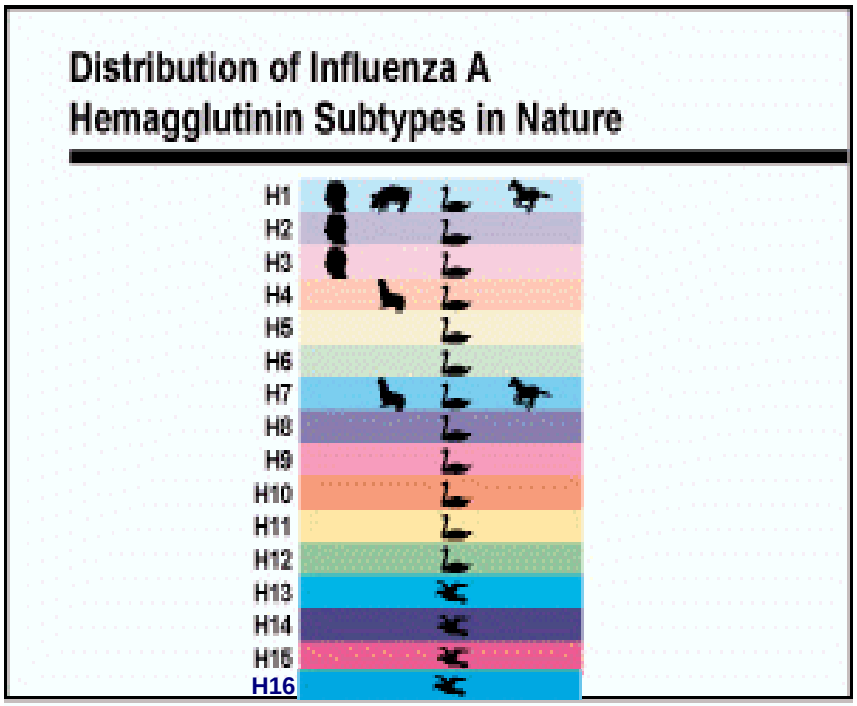
Número da amostra

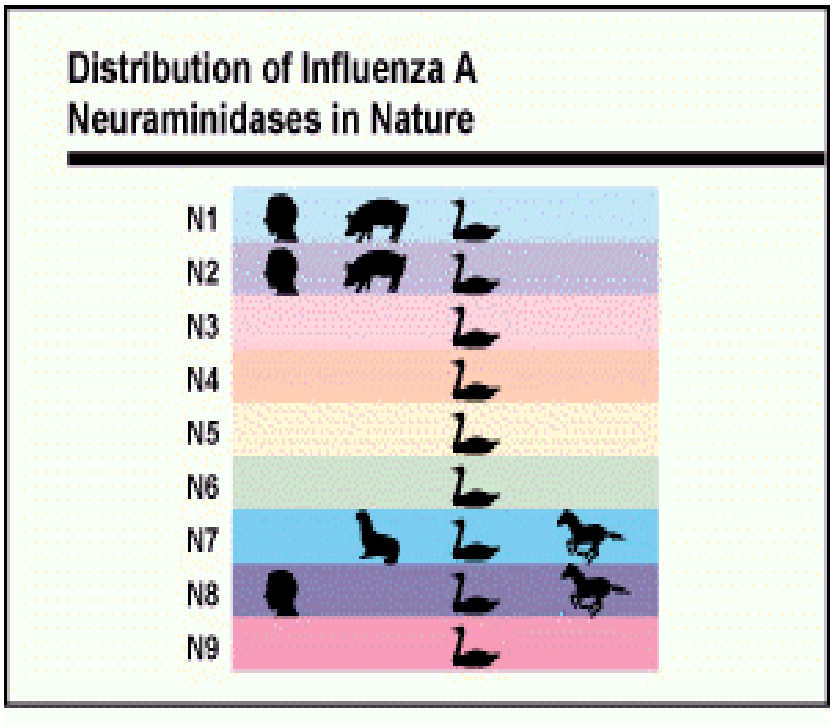
Ano de isolamento

Subtipo

Influenza A







Reservatórios – H1- H16 e N1 – N9 aves aquáticas. Transmissão demonstrada entre homens e porcos. Evidências de transmissão das aves para outras espécies

H17 e H18 e N10 e N11 - morcegos

Acesso - http://www.vetscite.org/

HOSPEDEIROS RECONHECIDOS DE INFLUENZA A

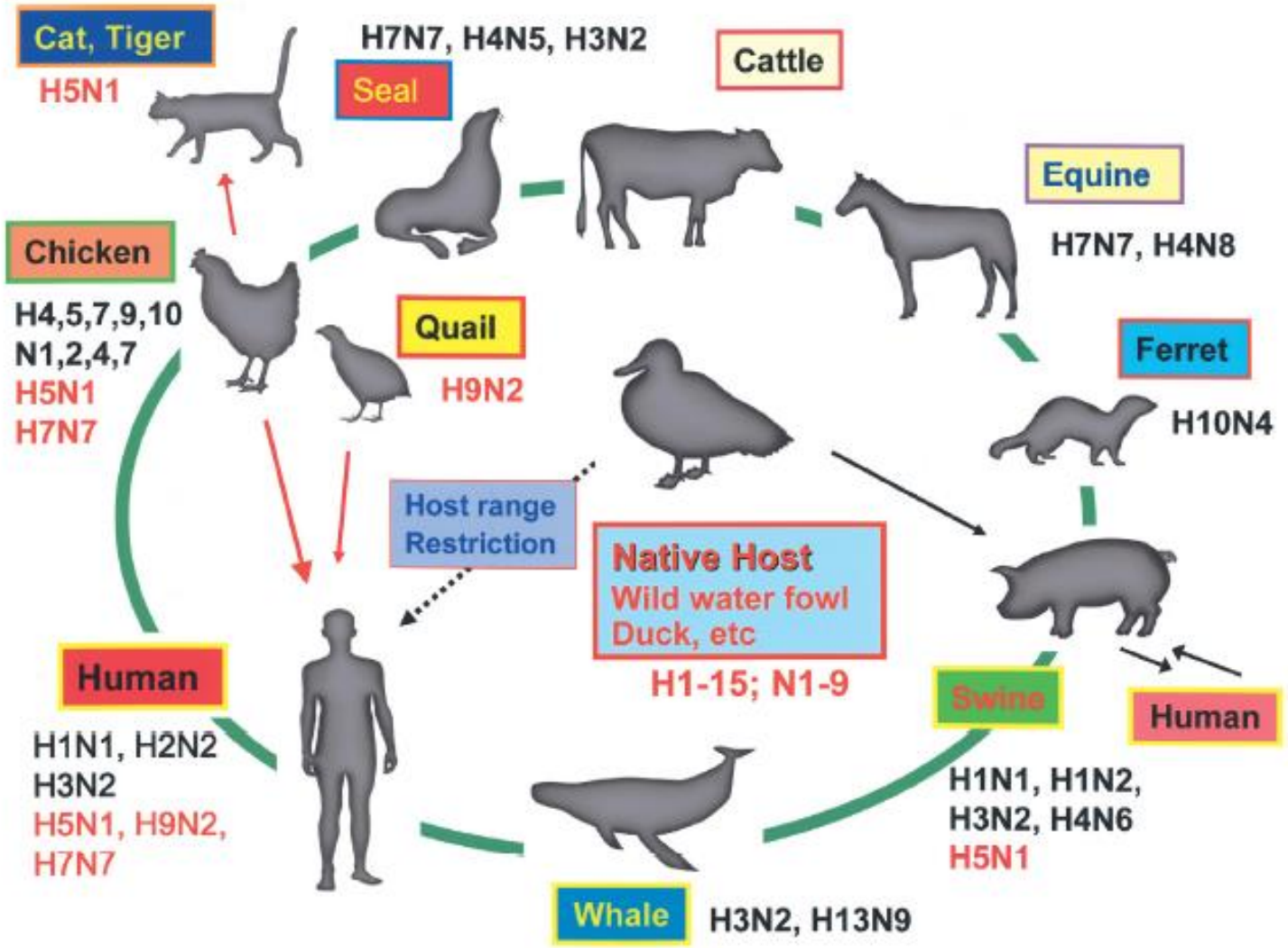
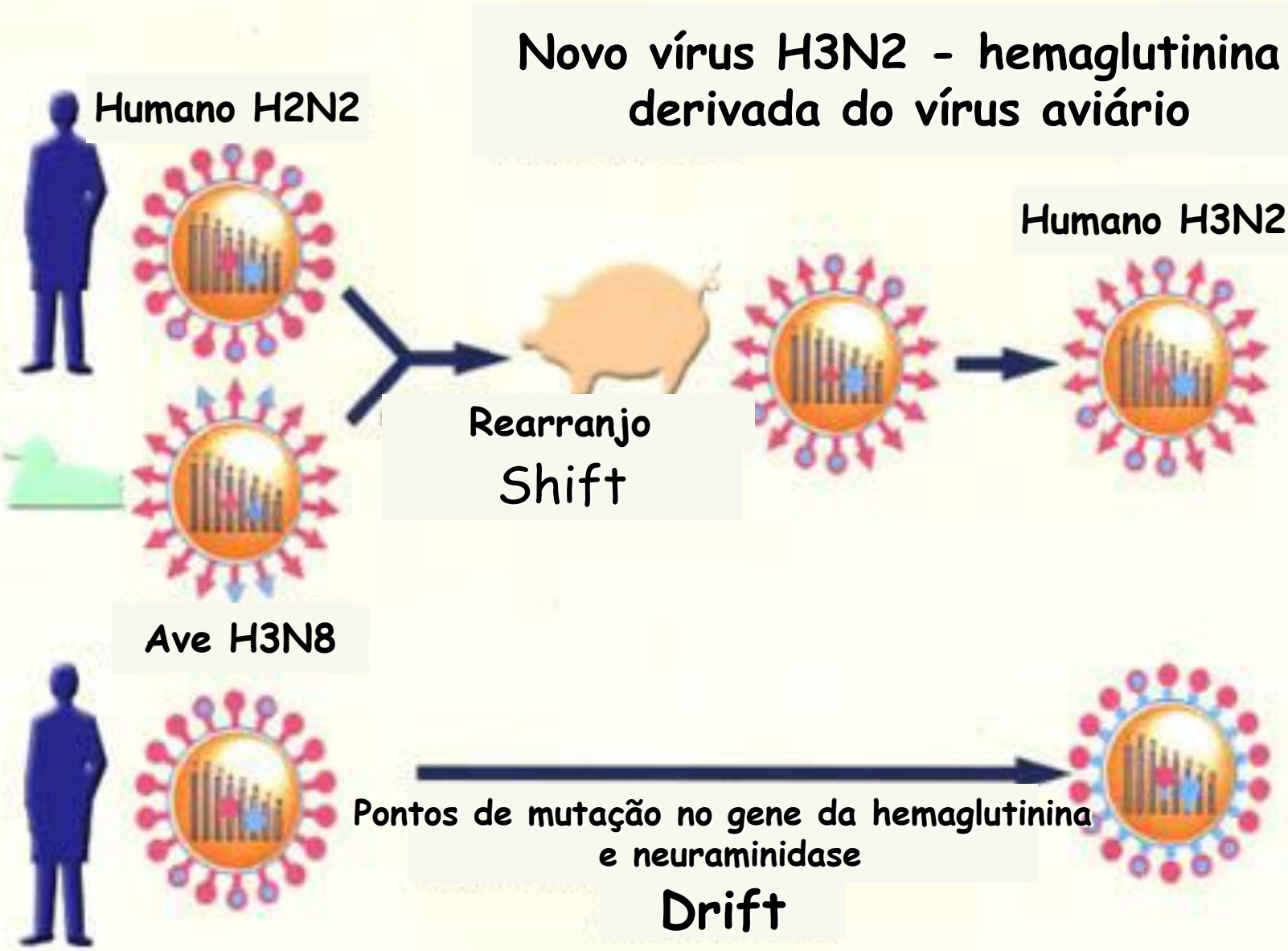


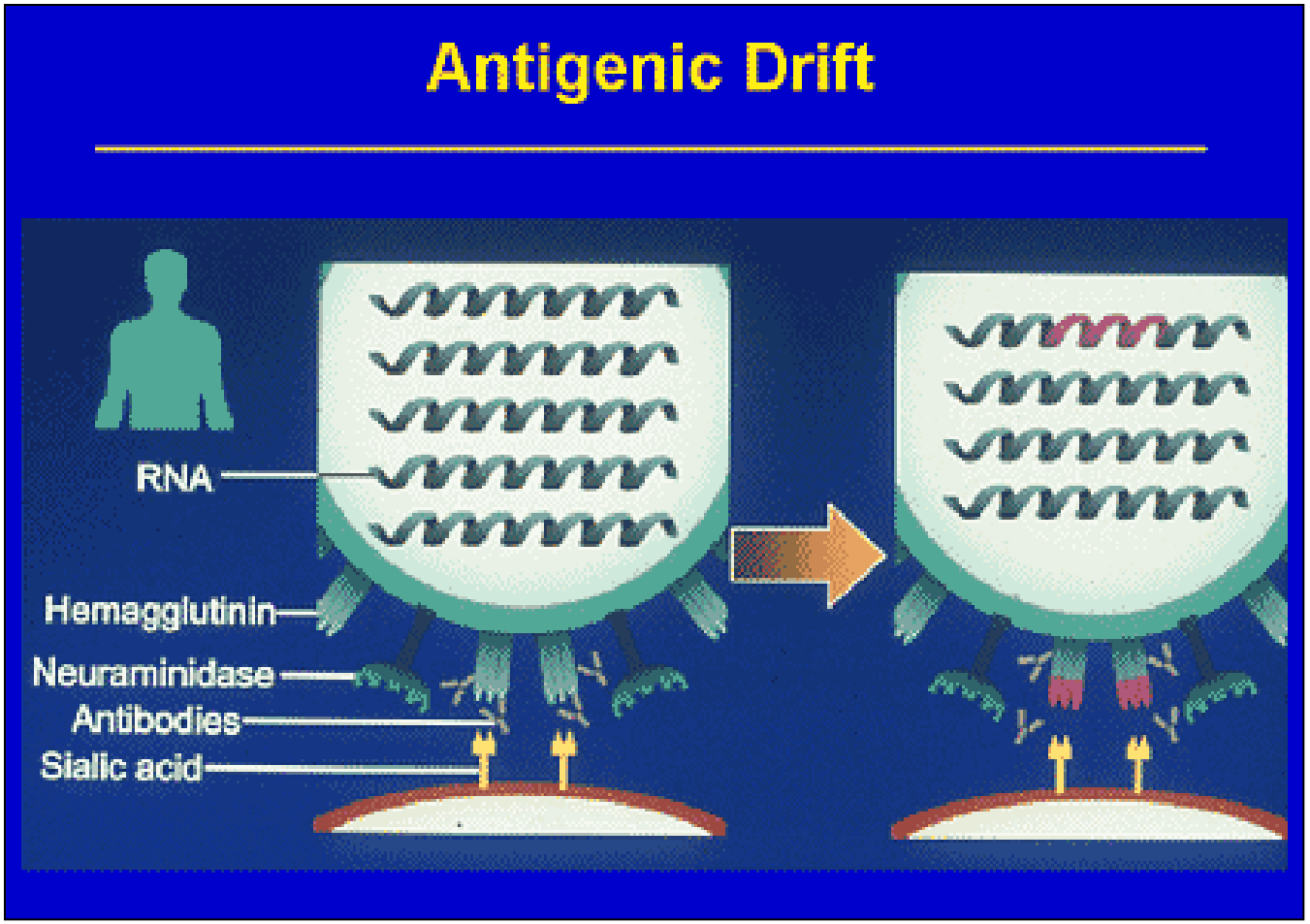
Fig. 1. Host Range of Influenza Viruses

Variações do vírus de Influenza A

GlycoWord



Variações Antigênicas Menores

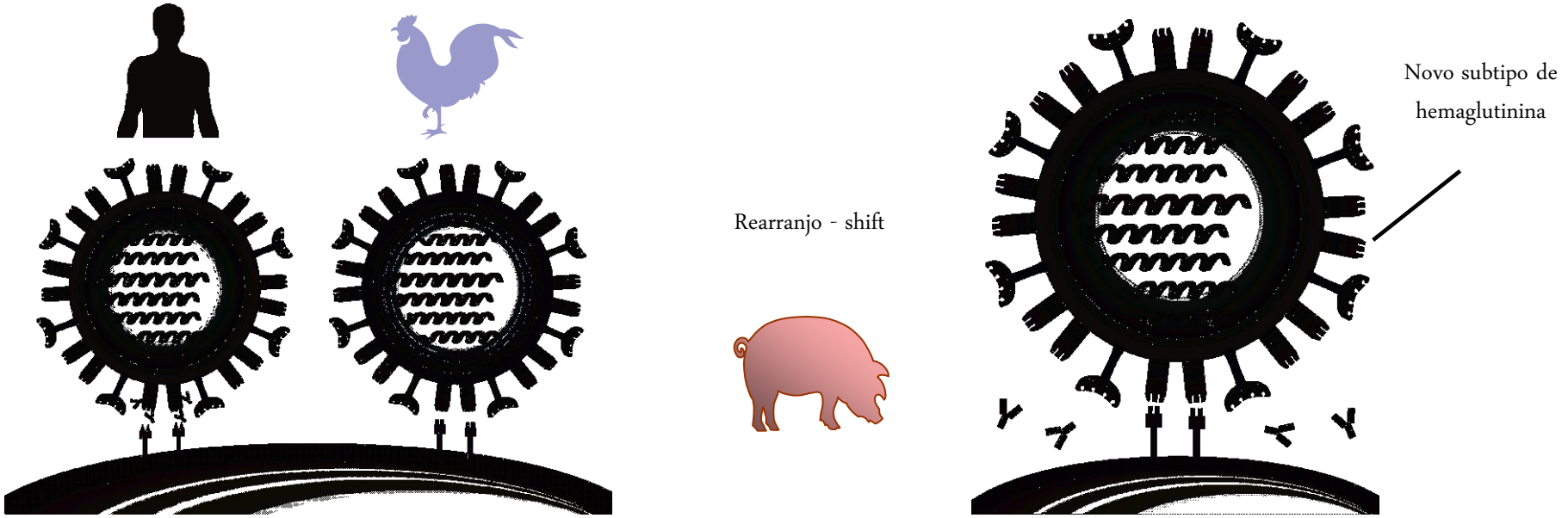


Drift : mutações pontuais nos segmentos de RNA ⟶ mudanças nos aa que compõem as glicoproteínas de superfície ⟶ novas variantes de vírus ⟶ escape da imunidade ⟶ **Epidemias**

Cox and Fukuda. Infect Dis Clin North Am 1998;12:27–38. Laver et al. Sci Am 1999;280:78–87.

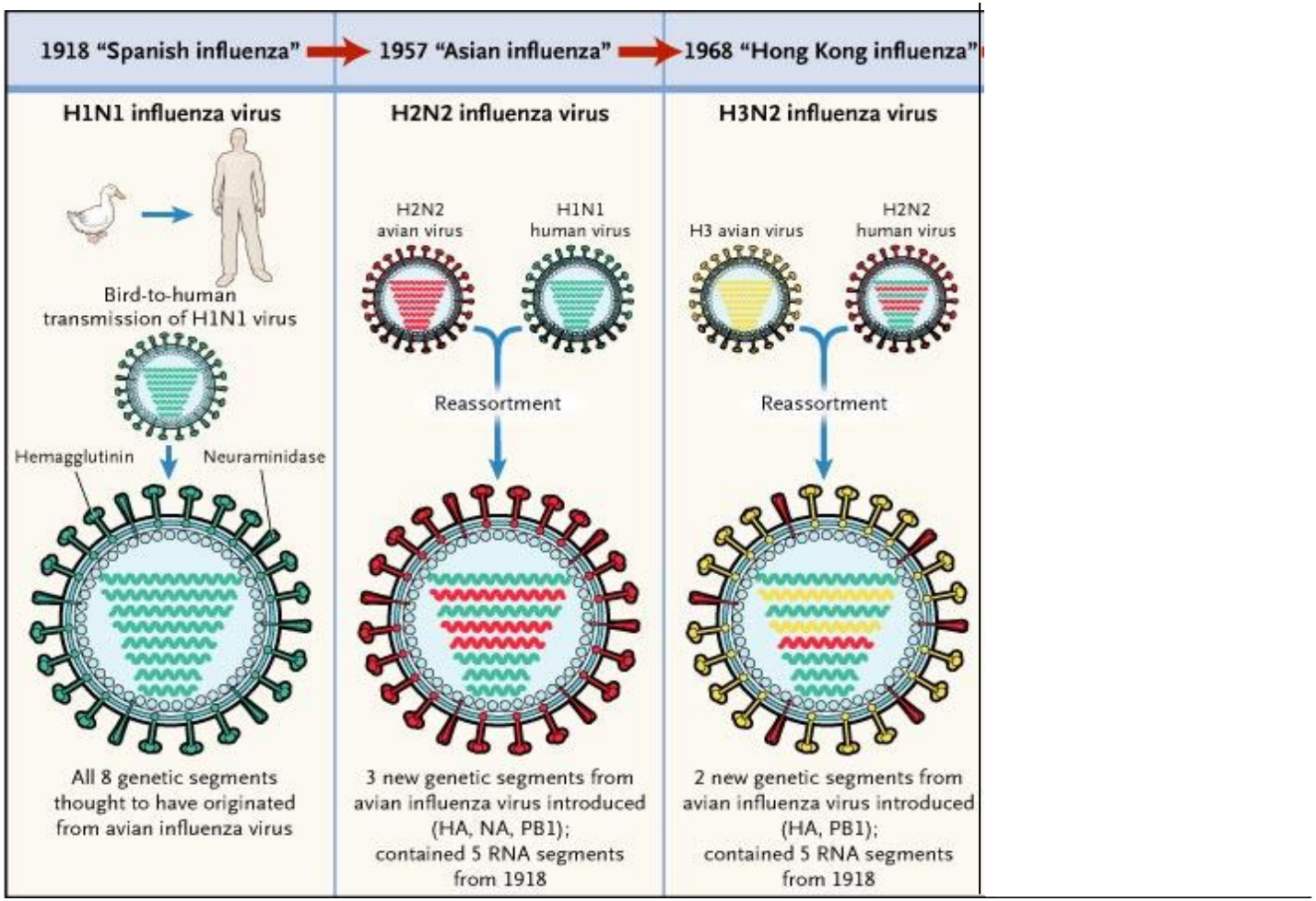
Variações Antigênicas Maiores

Shifts



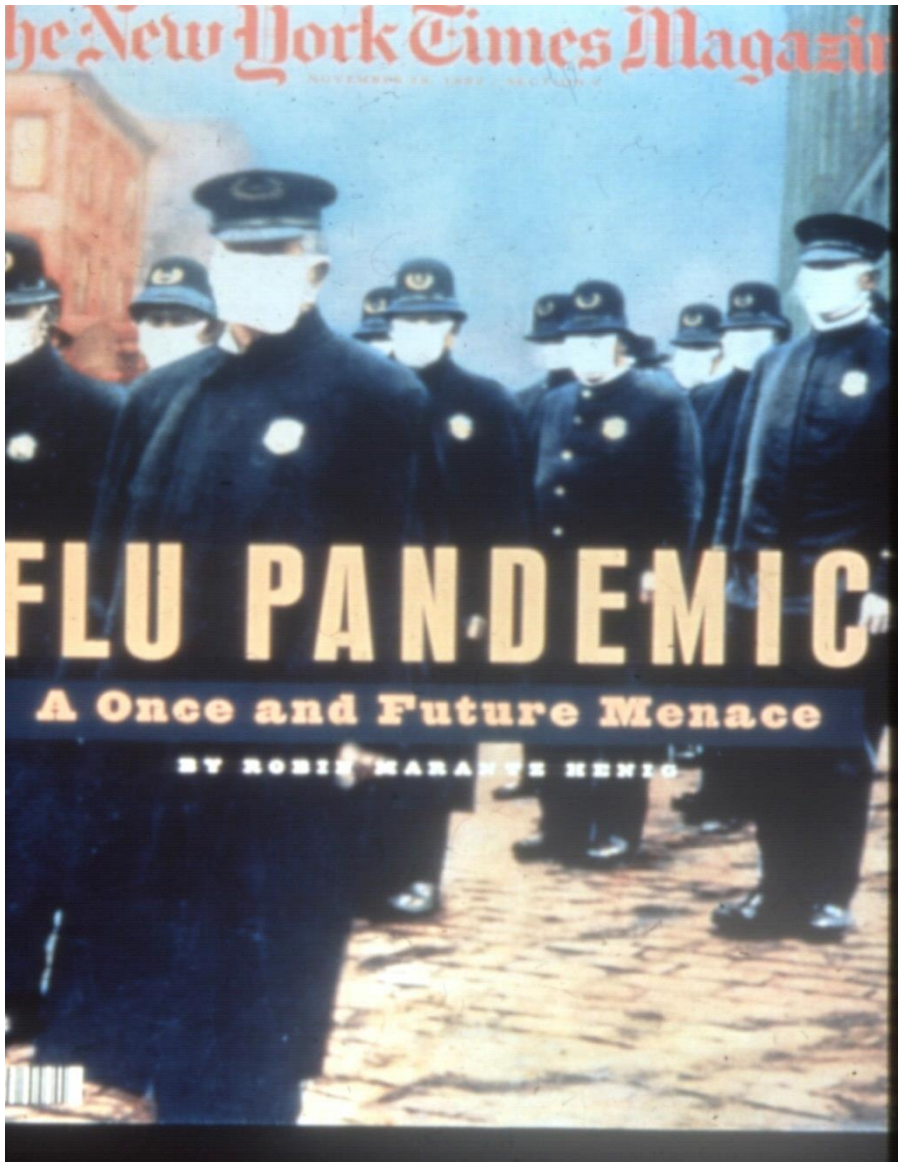
Shift: rearranjo entre os vírus de Influenza A ⟶ completa substituição de segmentos do genoma ⟶ novos vírus ⟶ população sem imunidade ⟶ disseminação da doença ⟶ **Pandemias**

PANDEMIAS- século XX

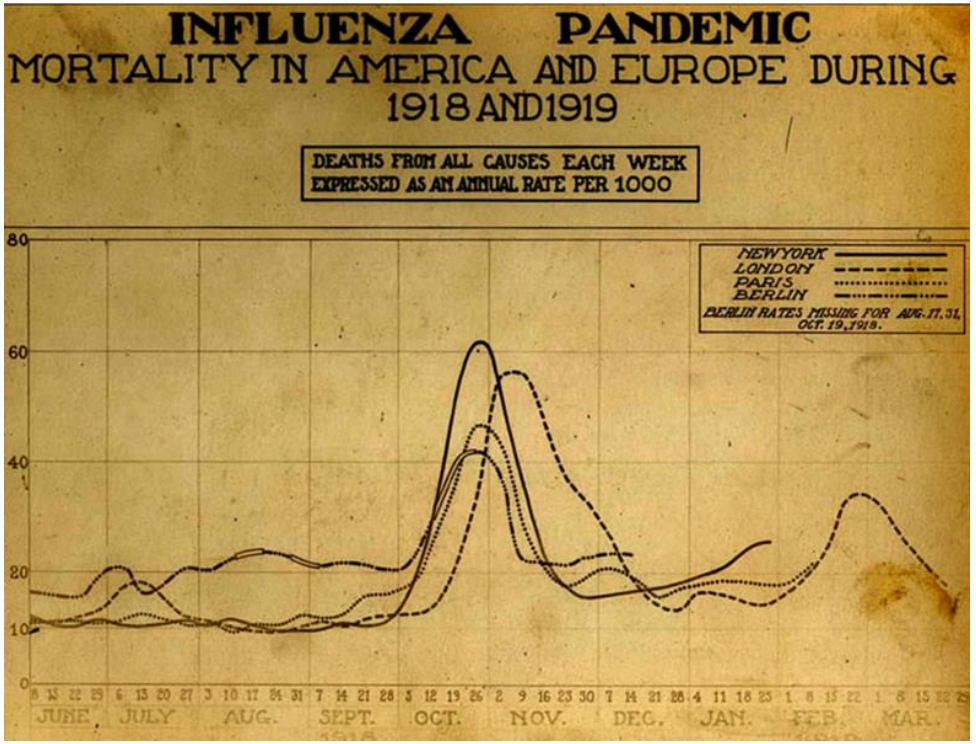


Shift: rearranjo entre os vírus de Influenza *A* ⟶ completa substituição de segmentos do genoma ⟶ novos vírus ⟶ população sem imunidade ⟶ disseminação da doença ⟶ **Pandemias**

Influenza Pandêmica 1918



20-40 milhões pessoas



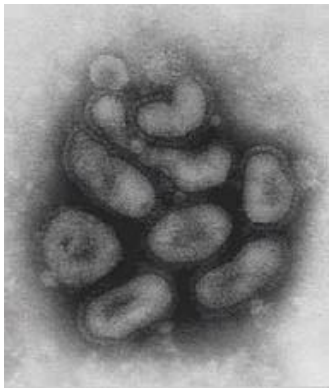
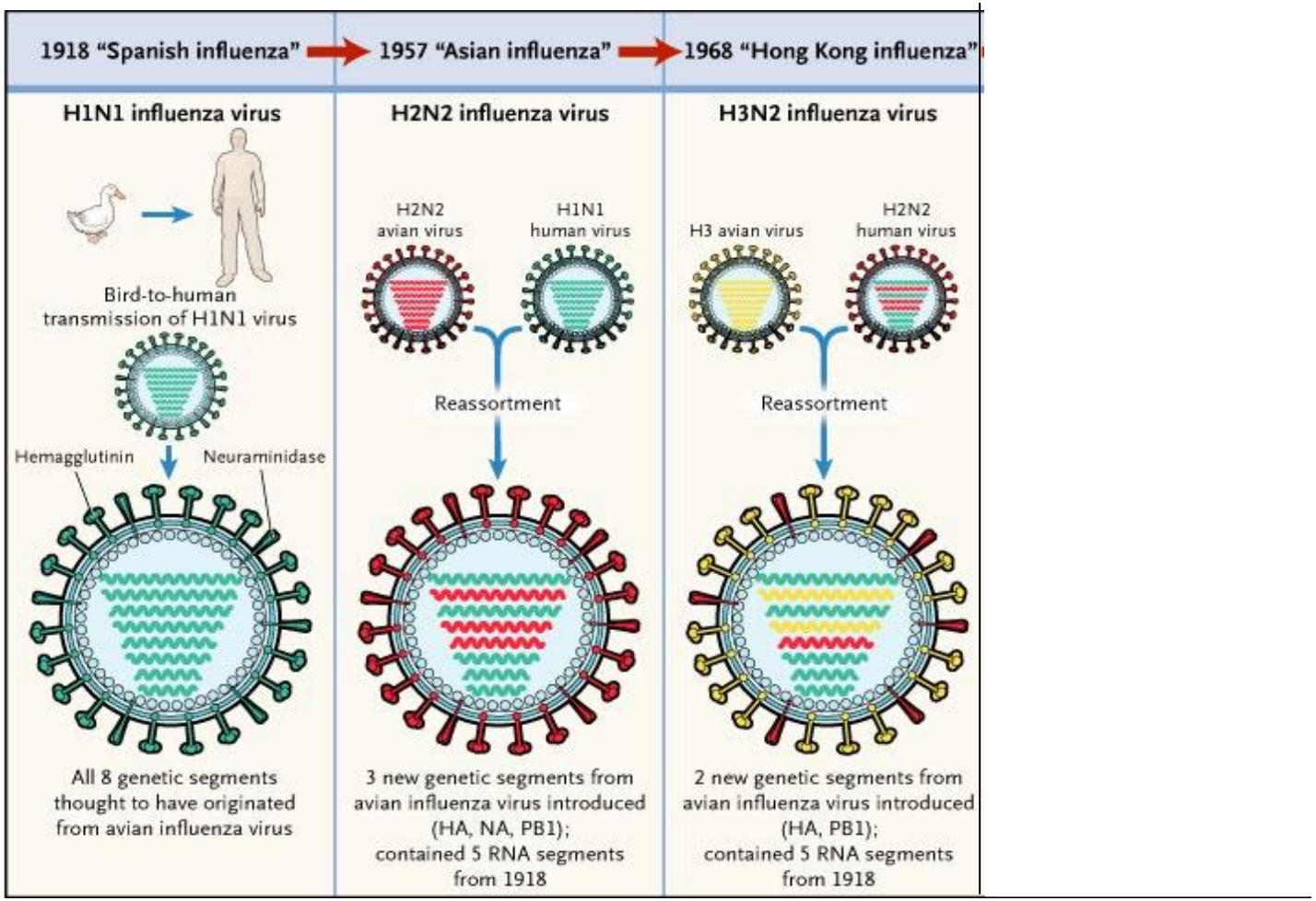


Image: courtesy of the National Museum of Health and Medicine)
Pandemic Influenza: The Inside Story.
Nicholls H, PLoS Biology Vol. 4/2/2006, e50

www.ncbi.nlm.nih.gov/ICTVdb/Ictv/index.htm

PANDEMIAS- século XX



Shift: rearranjo entre os vírus de Influenza *A* ⟶ completa substituição de segmentos do genoma ⟶ novos vírus ⟶ população sem imunidade ⟶ disseminação da doença ⟶ **Pandemias**

A(H2N2) – gripe asiática

Fevereiro de 1957

Maio – OMS divulgou epidemia

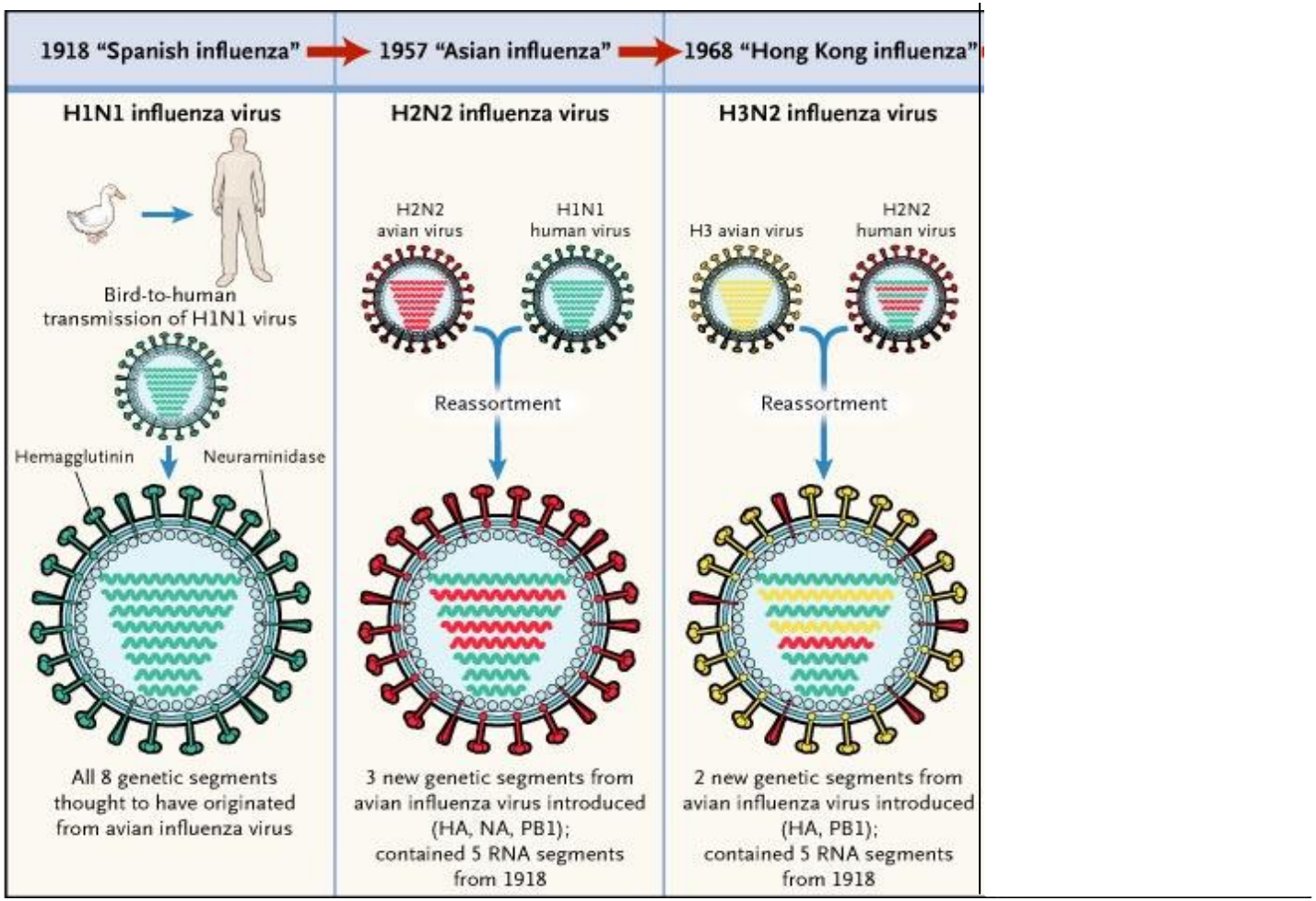
Pico – outubro

Brasil – julho primeiros casos,

1-4 milhões mortes

70,000 US mortes

PANDEMIAS- século XX



Shift: rearranjo entre os vírus de Influenza *A* ⟶ completa substituição de segmentos do genoma ⟶ novos vírus ⟶ população sem imunidade ⟶ disseminação da doença ⟶ **Pandemias**

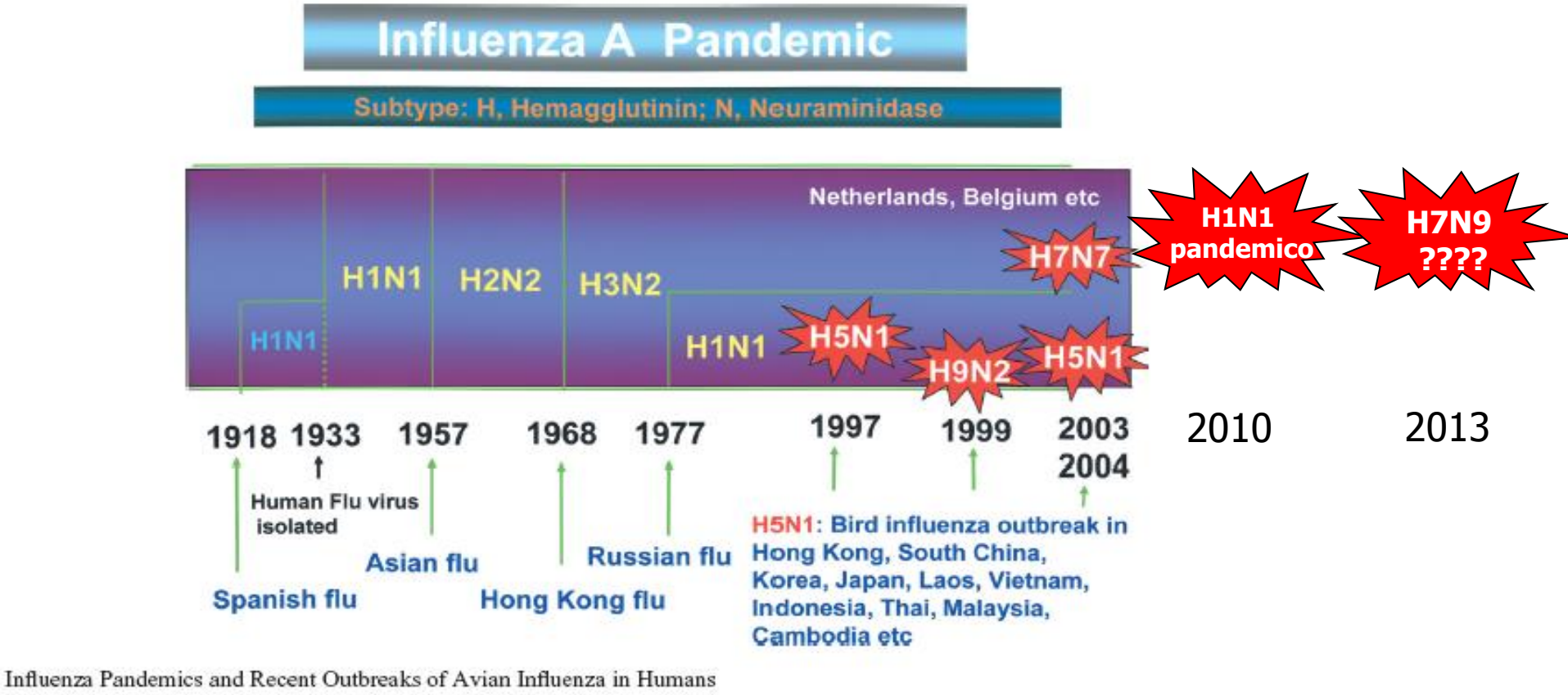
1968: Gripe – Hong Kong – H3N2

Isolado em julho de 1968 – incidência 40% 10-14 anos, alta hospitalização e mortalidade em idosos, crianças e indivíduos com risco definido

1 milhões mortes

34,000 US mortes

HISTÓRICO DAS PANDEMIAS:



Influenza Pandemics and Recent Outbreaks of Avian Influenza in Humans

Recentemente subtipos puramente aviários H5N1, H9N2, H7N7 e H7N9 foram distribuídos diretamente em humanos.

Influenza Aviária – H5N1

INFLUENZA AVIÁRIA

- Identificada na Itália há mais de 100 anos *(1878)*. Vírus isolado da década de 1950.
- Reservatório
- Raramente infecta pessoas!!!!! Contágio em humanos raros (até 1997 - desde 1959 apenas 11 casos notificados)
- Risco de transmissão direta maior para pessoas que têm contato com aves domésticas infectadas.
- Atualmente - evidências da sua circulação entre aves domésticas - 9 países asiáticos

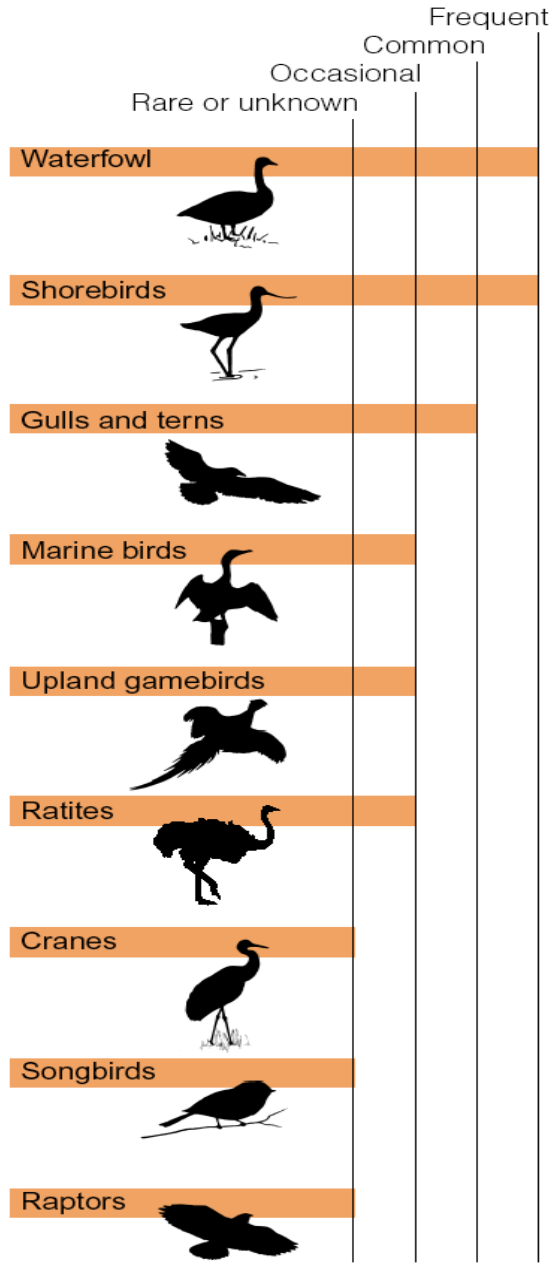


Figure 22.1 *Relative occurrence of avian influenza virus in various bird groups.*

- Aves selvagens são o reservatório natural do vírus (+ de 90 espécies), nos quais é assintomático e está em estágio evolucionário "estático", demonstrando adapatção do vírus ao hospedeiro.
- Todos os subtipos de HA e NA podem estar envolvidos.
- Aves aquáticas - Patos, gaivotas, saracura (grandes distâncias)
- Podem infectar aves domésticas causando infecções brandas, incluindo redução da produção de ovos e sintomas respiratórios ou infecções graves, altamente contagiosa, invade múltiplos órgãos e tecidos, com 100% mortalidade *(chicken ebola).*

Field Manual of Wildlife Diseases: Birds

INFLUENZA AVIÁRIA

- Identificada na Itália há mais de 100 anos. Vírus isolado da década de 1950
- Reservatório
- H5 e H7 - patogenicidade
- Raramente infecta pessoas!!!!! Contágio em humanos raros (de 1959 até 1997 apenas 11 casos notificados)
- Casos em humanos -
  - H5N1 - 1997 - 18 casos, 6 óbitos
  - H9N2 - 1999 - 2 casos crianças em Hong Kong.
  - H7N71 - dezembro 2003 - 1 caso criança em Hong Kong
  - H7N7 - março 2003 - 89 casos (conjuntivite) e 1 óbito na Holanda (pneumonia viral)
  - H5N1 - 2003 até dias atuais

HEMAGLUTININAS E O SÍTIO DE CLIVAGEM

	Cleavage site ↓	
Avian isolates		
Avirulent strain (H5)	P Q – – – – R E T R	G
Avirulent strain (H7)	P E X P – – – K X R	G
Virulent strain (H5)	P Q – – R K R K K R	G
Virulent strain (H7)	P E P S K K R K K R	G
Human isolates: pandemic strains		
1918 Spanish flu (H1N1)	P S – – – – I Q S R	G
1957 Asian flu (H2N2)	P Q – – – – I E S R	G
1968 Hong Kong flu (H3N2)	P E – – – – K Q T R	G
1977 Russian flu (H1N1)	P S – – – – I Q S R	G
Human isolates: avian strains from humans		
1997 Hong Kong (H5N1)	P Q R E R R R K K R	G
1999 Hong Kong (H9N2)	P Q – – – – R S S R	G
2003 the Netherlands (H7N7)	P E I P – K R R R R	G
2004 Asian (H5N1)	P Q R E (R) R R K K R	G

Figure 3 | **HA cleavage site sequence of influenza A viruses.** Basic amino acids are shown in blue boxes. Dashes are for the purpose of alignment only.

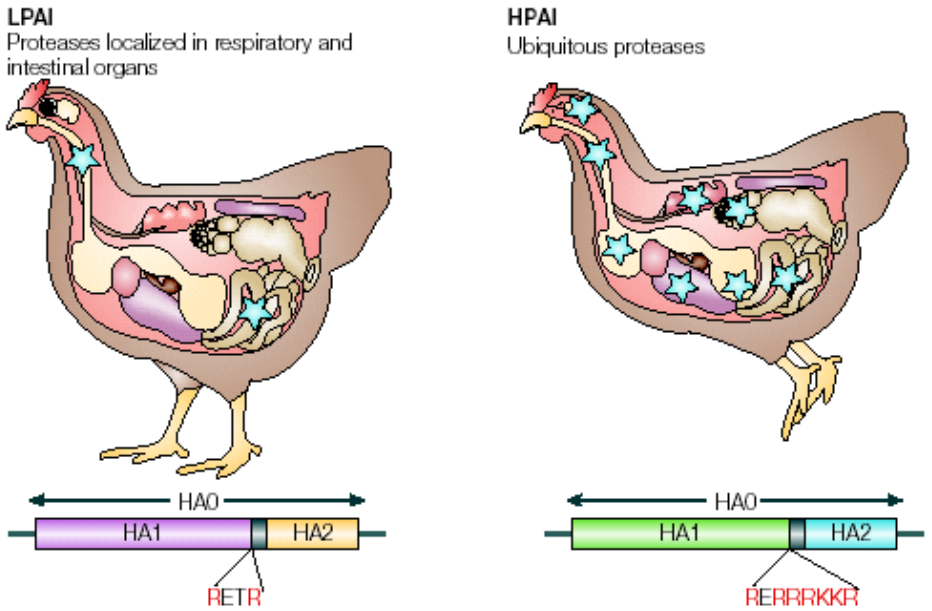


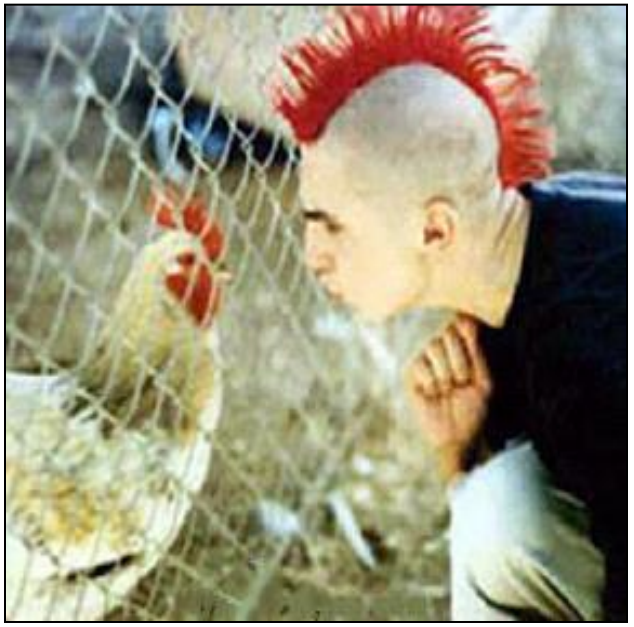
Figure 4 | **Haemagglutinin (HA) as a major determinant of the pathogenicity of avian influenza viruses in poultry.** Post-translational proteolytic cleavage of the HA precursor molecule (HA0) into HA1 and HA2 subunits by host proteases generates a fusogenic domain at the amino terminus of HA2 (shown in grey), which mediates fusion between the viral envelope and the endosomal membrane. Therefore, proteolytic activation of the HA molecule is essential for viral infectivity. The HAs of low-pathogenicity avian influenza (LPAI) viruses do not contain a series of basic amino acid (RETR) at the protease cleavage site and are cleaved by proteases that are localized in respiratory and intestinal organs, resulting in mild localized infections. By contrast, the HAs of high-pathogenicity avian influenza (HPAI) viruses possess multiple basic amino acids at the cleavage site (RERRRKKR), which are cleaved by ubiquitous proteases in a wide range of organs, resulting in lethal systemic infection.

INFLUENZA AVIÁRIA

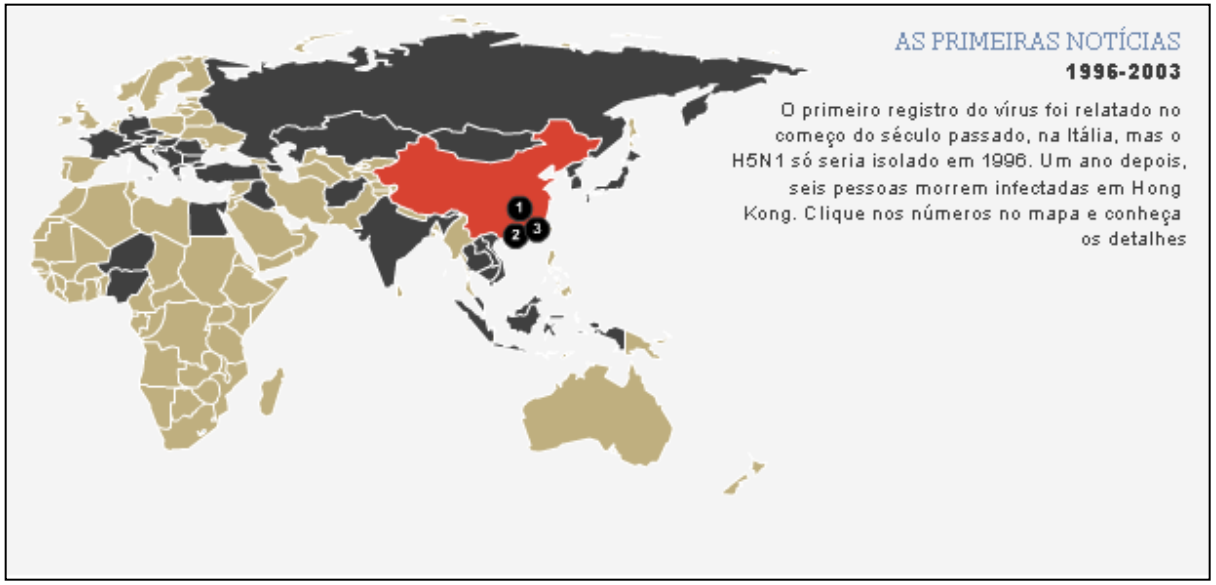
- Identificada na Itália há mais de 100 anos. Vírus isolado da década de 1950
- Reservatório
- H5 e H7 - patogenicidade
- Raramente infecta pessoas!!!!! Contágio em humanos raros (de 1959 até 1997 apenas 11 casos notificados)
- Casos em humanos -
  - H5N1 - 1997 - 18 casos, 6 óbitos
  - H9N2 - 1999 - 2 hospitalizações (crianças em Hong Kong)
  - H5N1 - dezembro 2003 - 2 casos 1 óbito (China)
  - H7N7 - março 2003 - 89 casos (conjuntivite) e 1 óbito na Holanda (pneumonia viral)
  - H7N3 – 2 casos de conjutivite e sintomas respiratórios leves, Canadá
  - H5N1 - 2003 até dias atuais, com emergência de novas linhagens originárias de drifts antigênicos

Influenza Aviária - H5N1

- Transmissão
  direta – aves infectadas, suas secreções (saliva, secreção nasal e ocular e fezes), vísceras ou solo contaminado
  indireta – equipamentos, roupas calçados, insetos, alimentos, água ...
  aerossóis

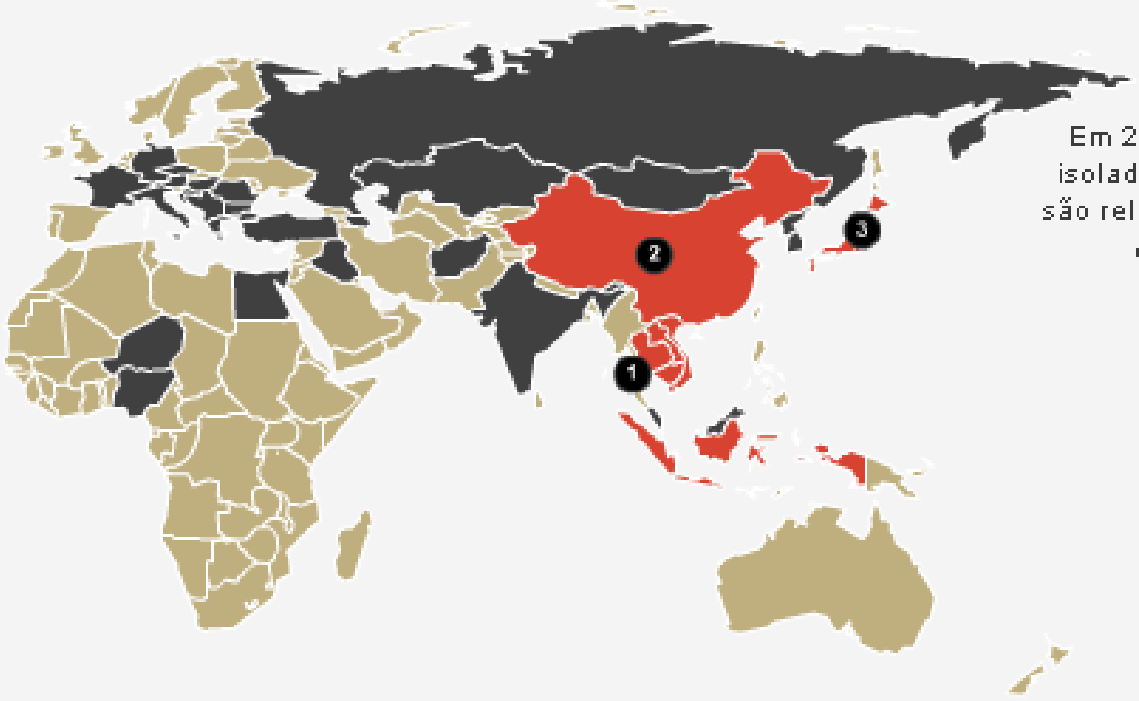


- Inativado em 24 h a 25°C, estável nas fezes por 4 dias, excretados por +10 dias
- Doença grave em humanos
- Alta letalidade (~ 50%)



- **Década de 1990** - evidências da circulação entre aves domésticas em países asiáticos , Co-circulação de H5N1 em gansos (não patogênico) e H9N2 em galinhas e patos na China
- **1997 – H5N1** epidemia em aves domésticas, com transmissão para humanos com alta taxa de mortalidade em ambos: 100% em galinhas (48 horas), 30% em humanos (18 casos notificados com 6 óbitos devido à pneumonia viral fatal e falência múltipla de órgãos)
- **2003 - H5N1 China, 2 hospitalizações, 1 morte**

INFLUENZA AVIÁRIA H5N1



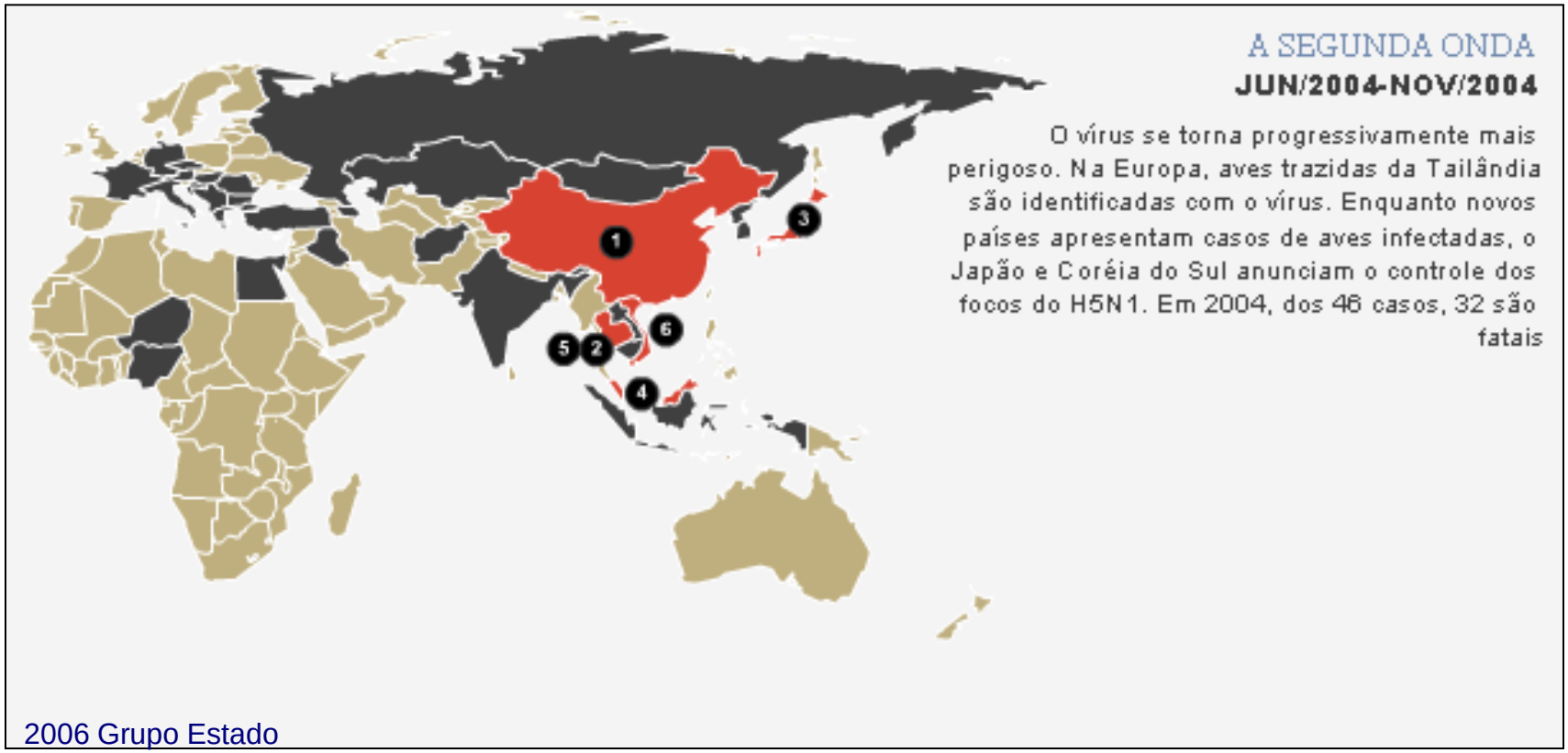
A PRIMEIRA ONDA

DEZ/2003-MAR/2004

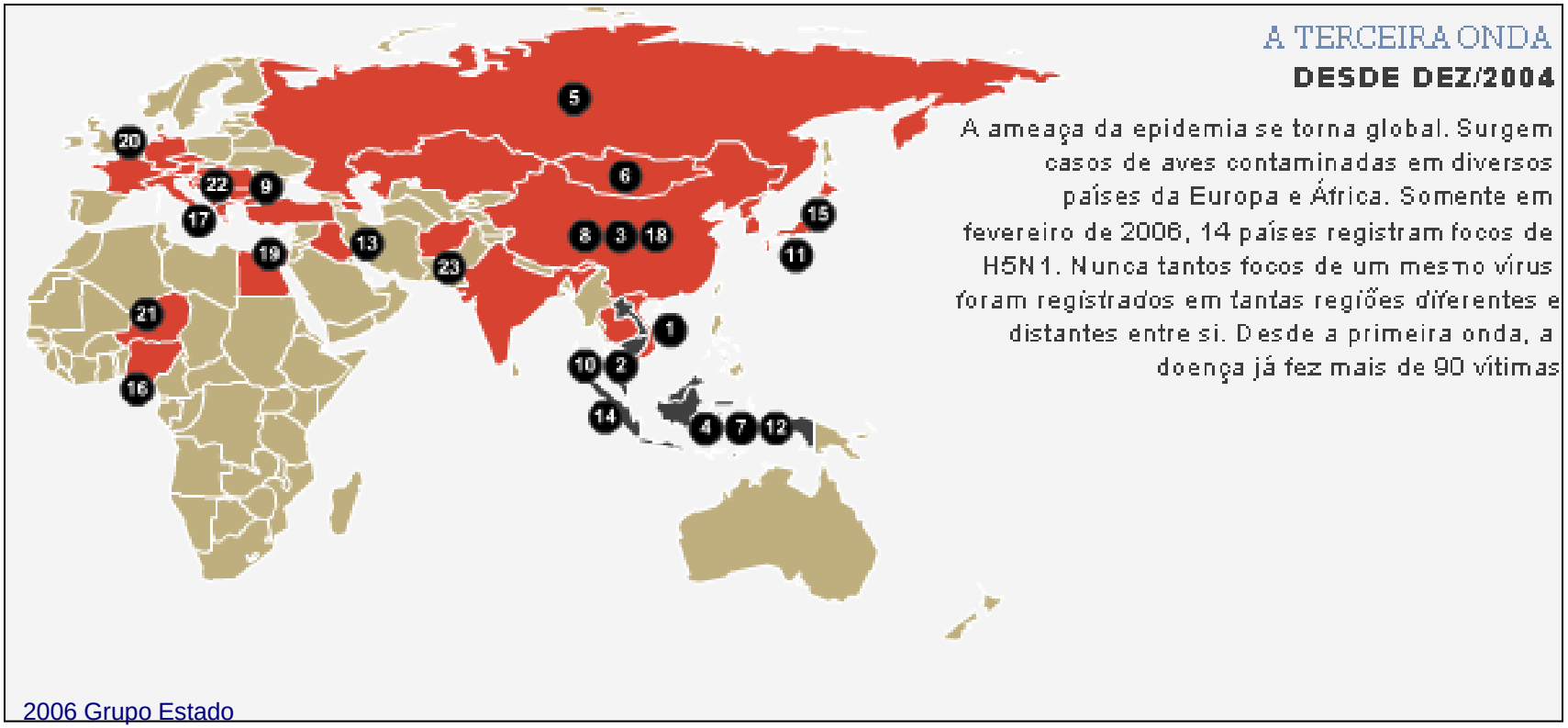
Em 2003 o vírus se espalha pela Ásia. Antes isolado na China, casos de aves com o H5N1 são relatados em mais sete países. Em menos de um ano são registrados 35 casos em humanos, dos quais 24 morrem.

2006 Grupo Estado

INFLUENZA AVIÁRIA H5N1



INFLUENZA AVIÁRIA H5N1

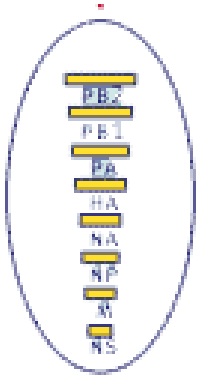


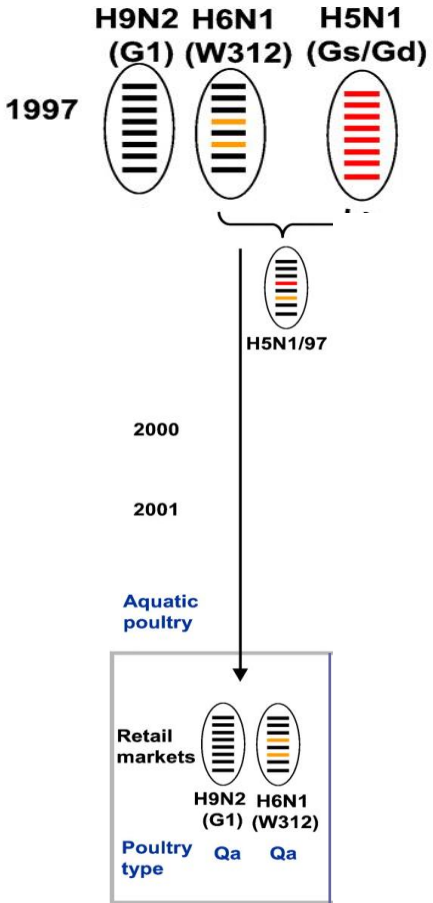
Verificação da forma patogênica do vírus em aves aquáticas (selvagens), bem como a verificação da excreção do vírus por patos domésticos assintomáticos

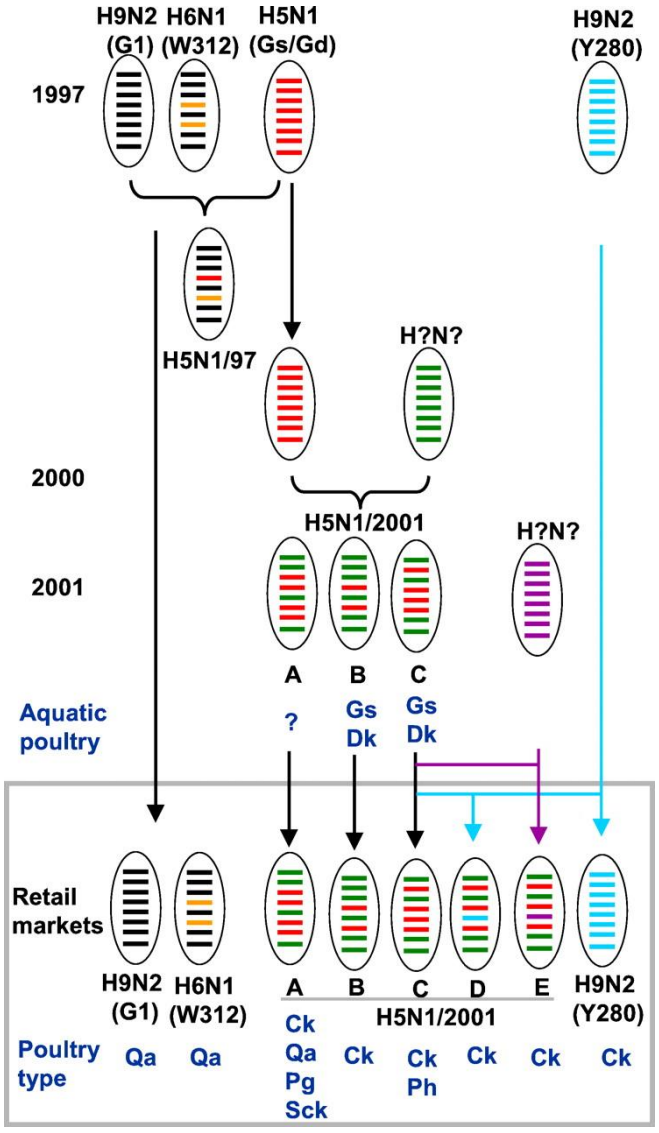
INFLUENZA AVIÁRIA H5N1

origens múltiplos reagrranjos entre vírus aviários

- **H5N1-1997** (A/Hong Kong/156/97) - Hipótese de surgimento - um rearranjo entre diferentes vírus aviários sendo a **HA** de H5N1 Gs/Gd (**ganso**) e os genes das proteínas internas **(PB2, PB1, PA, NP, M, NS)** originários de Quail/HK/G1/97 (codorna) [**H9N2** (~98% de homologia ou Teal/HK/W312/97 (marrecos) [**H6N1** (W312)]-like. A neuraminidase (NA) do H5N1/97 é similar à W312-like H6N1 viruses.







Circulação
Genotipo C - 1º isolado galinhas
Genotipo D - gen. C adquiriu gene NP (Y280)
Genotipo E - gen. C adquiriu gene NP vírus aviário
Genotipo A - apenas em terrestres >disseminação

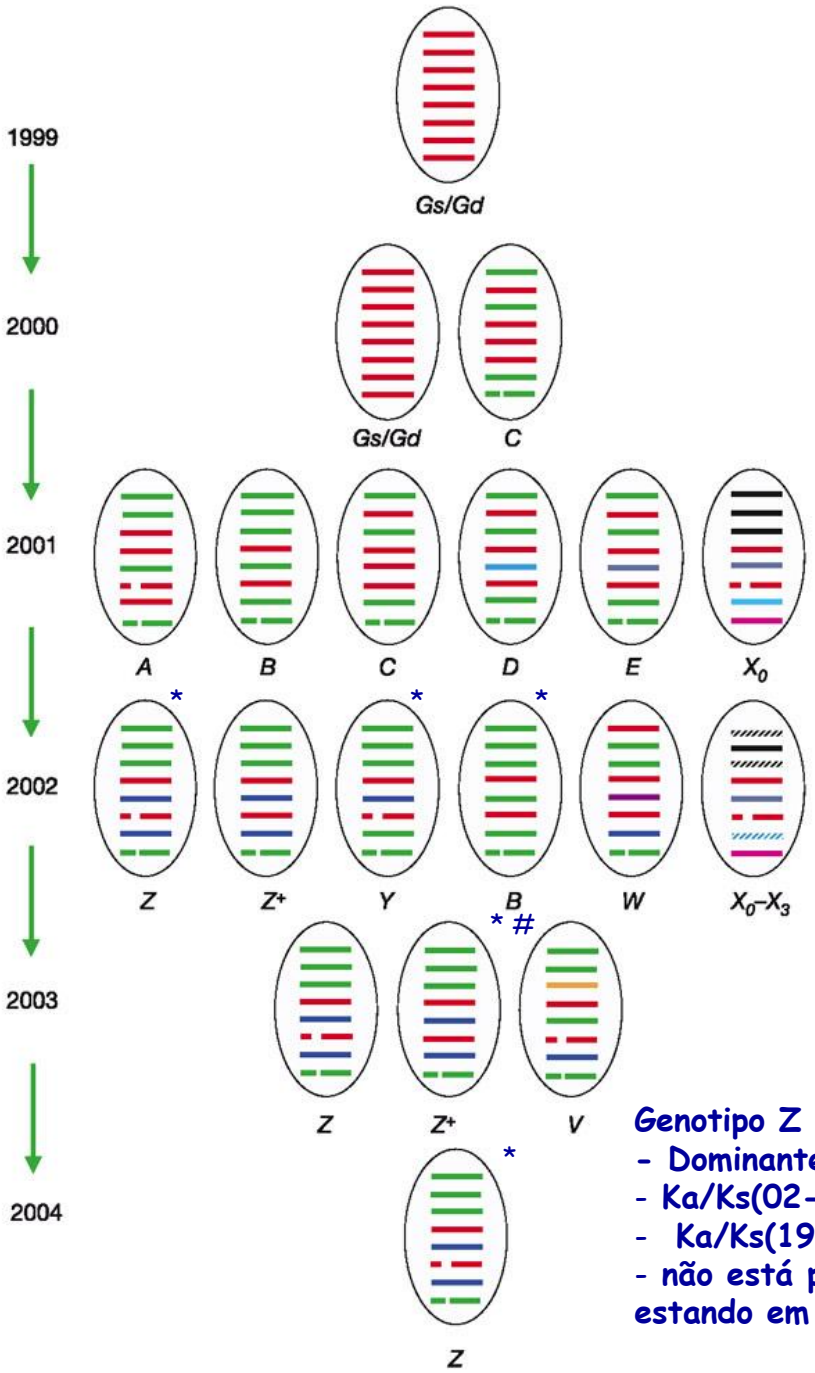
Patogenicidade
A,B,E - > patogenicidade para galinhas
A,E - > codornas
A,B e C particularmente letais em camundongos - replicação no pulmão, disseminação vários órgãos.
Neurotropismo ausente no precursor

Genotipo A - deleção de 20 aa (~H5N1/97)
Transmissão interespécies?

8 segmentos genômicos: *PB2*, *PB1*, *PA*, *HA*, *NP*, *NA*, *M* and *NS*. Cada cor representa uma linhagem viral (vermelho indica origem Gs/Gd/1/96). Genotipos (indicado por letras) foram definidos por análise filogenética

Guan, Y. et al. (2002) Proc. Natl. Acad. Sci. USA 99, 8950-8955

PNAS



Deleção de 20 aa NA (posição 49-68)

Deleção de 5 aa - NS1 (posição 80-84)

Genotipo *X0–X3* - rearranjo do genotipo E com outro gene de outro vírus aviário aquático sendo distinto pela fonte dos genes *PB2*, *PA* and *NS* genes.

Genotipo *W* - difere do *B* somente pelo *PB2*, *NP* and *M* genes.

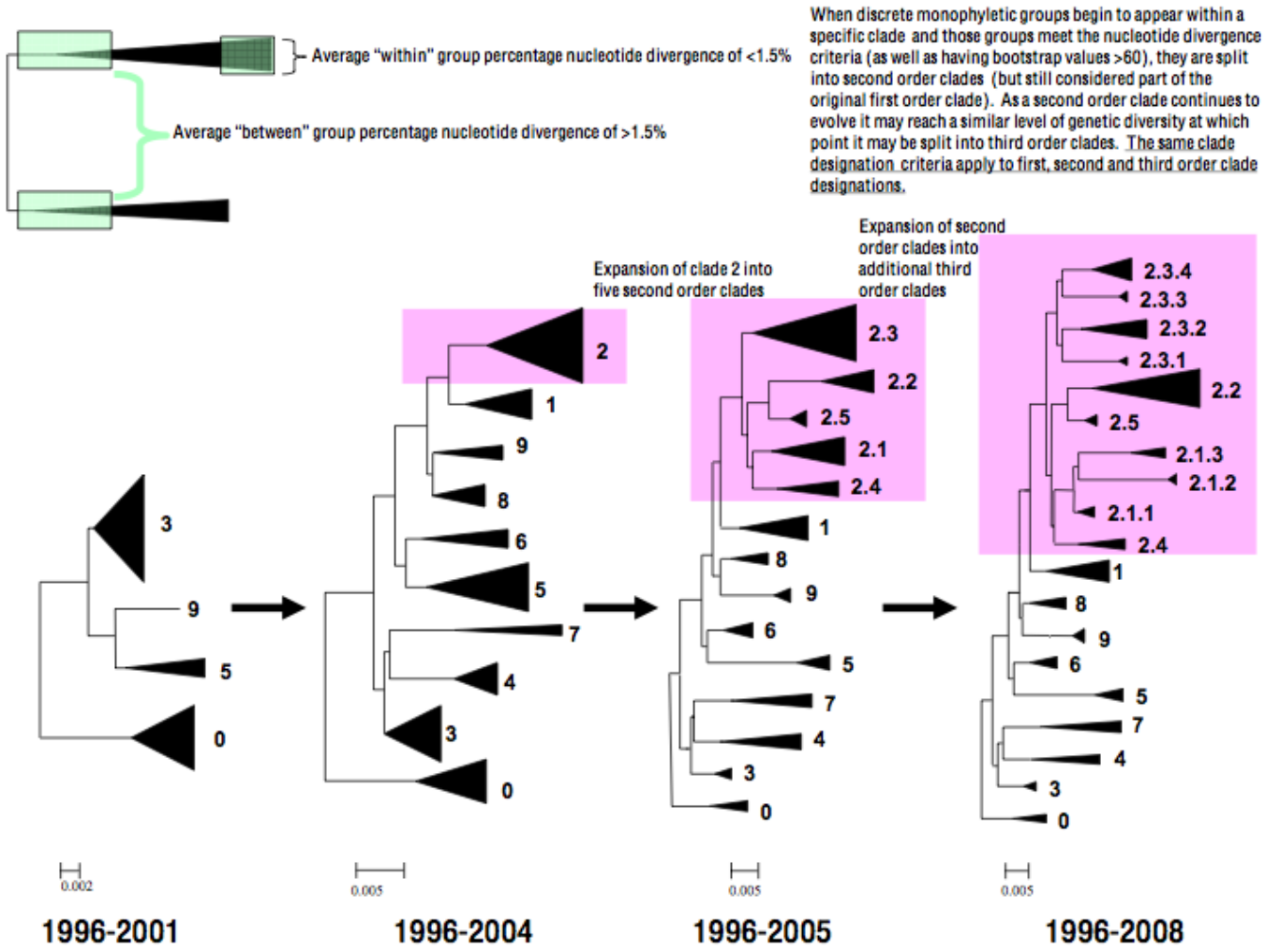
Rearranjo do genotipo *A* ou *B* com outro vírus deu origem aos genotipos *V*, *Y*, *Z* and *Z+*.

Alternativamente o genotipo V resultou do rearranjo do genótipo Z com outro vírus.

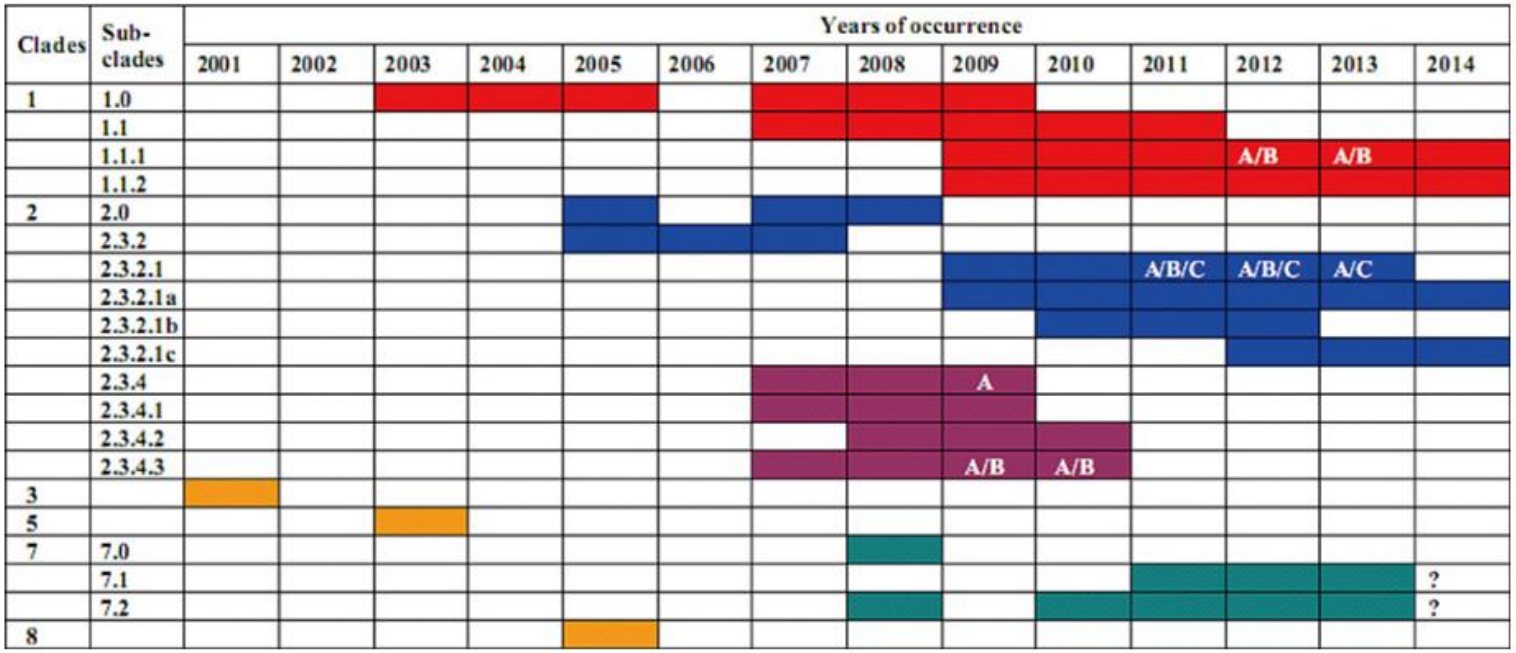
 # caso de H5N1 em humanos

·mutação Ser31Asn gene M2- resistência a amantadina

Genotipo Z
- Dominante em aves aquáticas e terrestres 2004
- Ka/Ks(02-04 nos genes internos) >1 pressão positiva
- Ka/Ks(1997-2004) >1 pressão positiva HA (↑ anos)
- não está perfeitamente adaptados em aves domésticas estando em evolução


Average "within" group percentage nucleotide divergence of <1.5%
Average "between" group percentage nucleotide divergence of >1.5%
When discrete monophyletic groups begin to appear within a specific clade and those groups meet the nucleotide divergence criteria (as well as having bootstrap values >60), they are split into second order clades (but still considered part of the original first order clade). As a second order clade continues to evolve it may reach a similar level of genetic diversity at which point it may be split into third order clades. The same clade designation criteria apply to first, second and third order clade designations.
Expansion of clade 2 into five second order clades
Expansion of second order clades into additional third order clades
2
1
9
8
6
5
7
4
3
0
2.3
2.2
2.5
2.1
2.4
2.3.4
2.3.3
2.3.2
2.3.1
2.1.3
2.1.2
2.1.1
0.002
0.005
0.005
0.005
1996-2001
1996-2004
1996-2005
1996-2008

VACCINE RESEARCH
ISSN(Print): 2287-3651
ISSN(Online): 2287-366x
www.ecevr.org



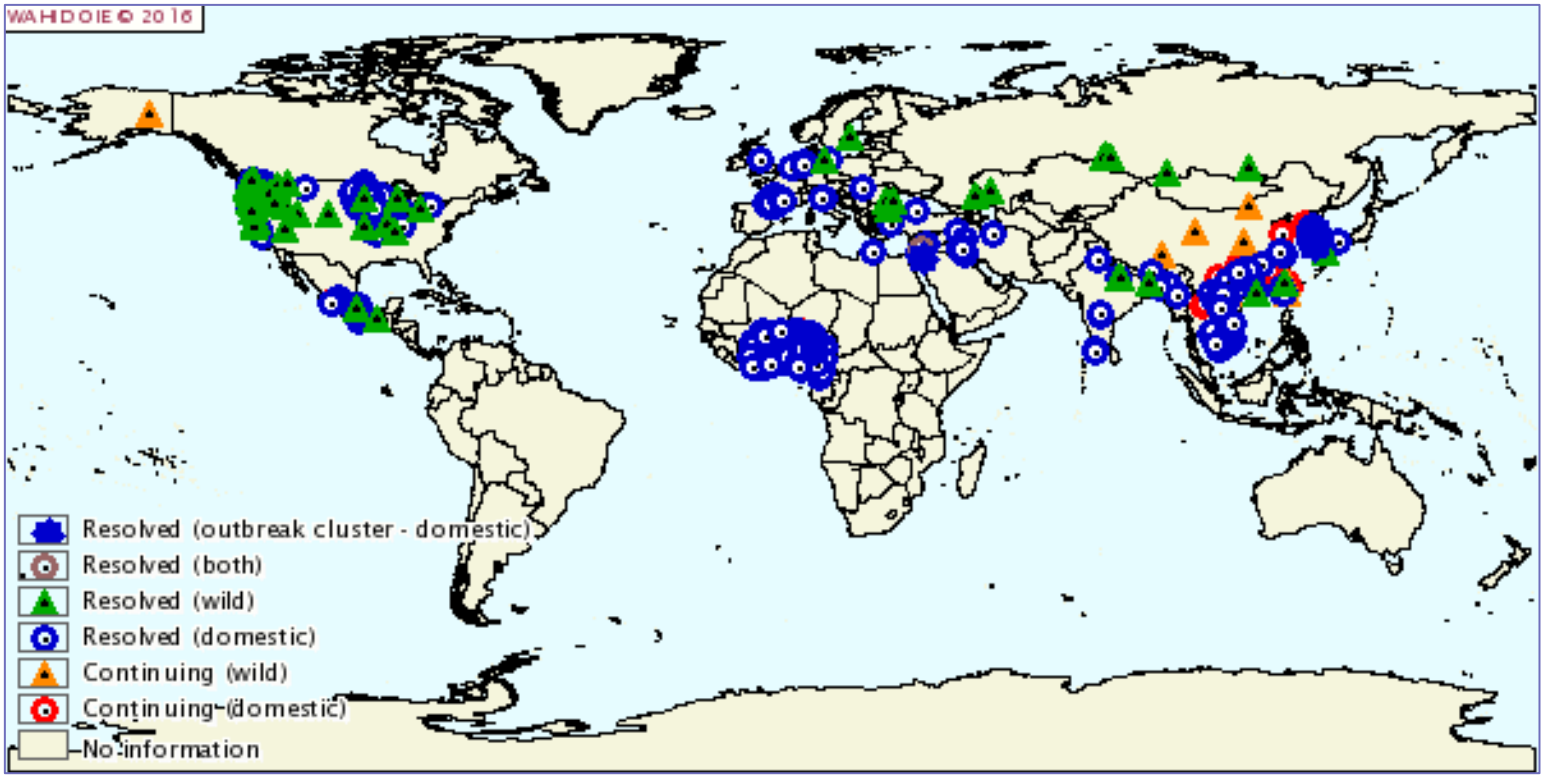
Clades	Sub-clades	Years of occurrence													
		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
1	1.0														
	1.1														
	1.1.1												A/B	A/B	
	1.1.2														
2	2.0														
	2.3.2														
	2.3.2.1											A/B/C	A/B/C	A/C	
	2.3.2.1a														
	2.3.2.1b														
	2.3.2.1c														
	2.3.4									A					
	2.3.4.1														
	2.3.4.2														
	2.3.4.3									A/B	A/B				
3															
5															
7	7.0														
	7.1														?
	7.2														?
8															

Fig. 1.

Emergence timelines of hemagglutinin-based clades of A/H5N1 in Vietnam (only those clades that emerged and identified in Vietnam are presented). Data used for making timelines of H5N1 occurence were collected from the following published sources: Nguyen et al. [41,42], Creanga et al. [43], World Health Organization/World Organisation for Animal Health/Food and Agriculture Organization (WHO/OIE/FAO) H5N1 Evolution Working Group [44], Inui [45]; A/B/C marks for clades were taken from the above listed publications; question mark (?) indicates upcoming confirmation of clades in 2014.

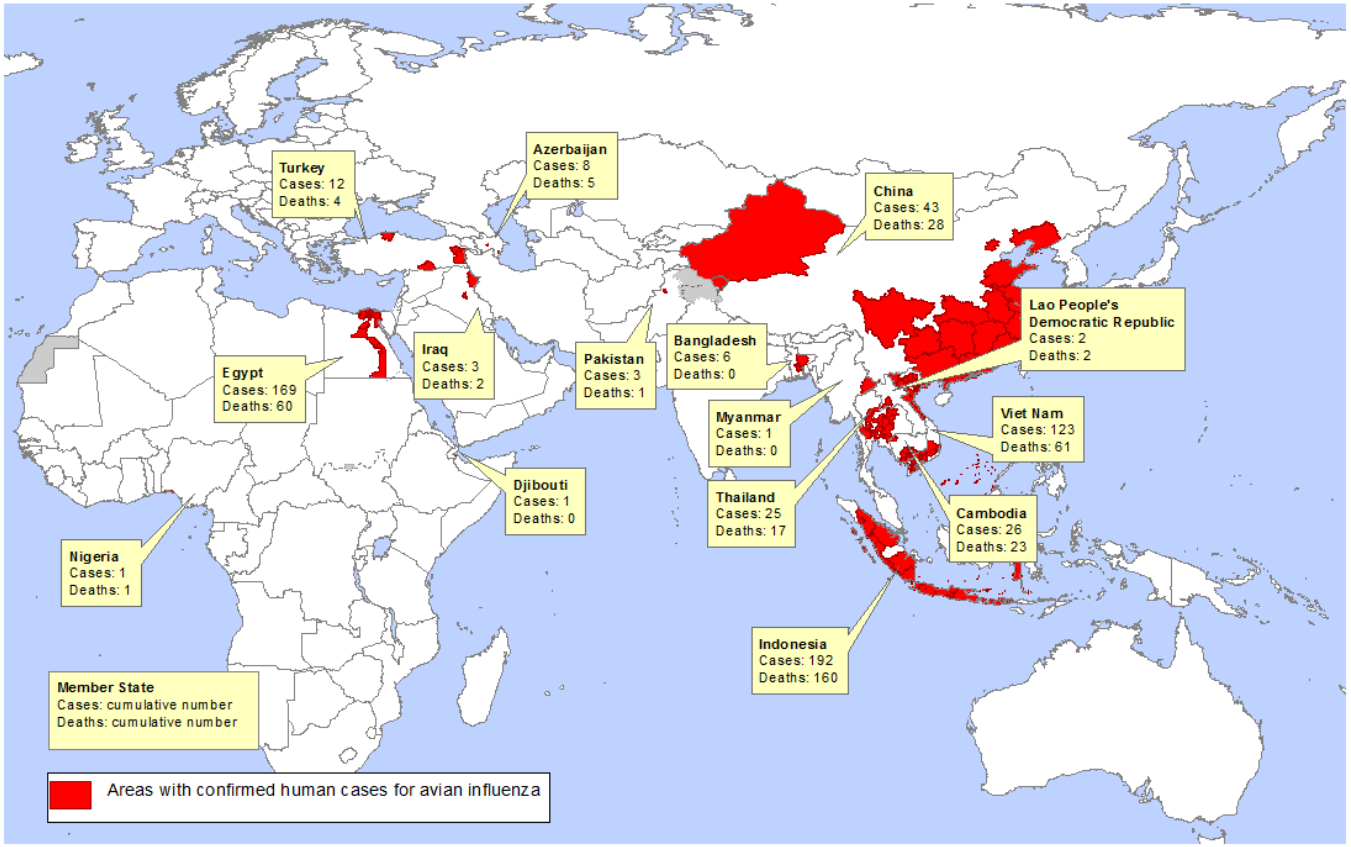
Clin Exp Vaccine Res. 2014 Jul;3(2):117-127.
https://doi.org/10.7774/cevr.2014.3.2.117

Influenza Aviária - H5N1



Influenza Aviária H5N1

Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013*



*All dates refer to onset of illness
Data as of 01 February 2013
Source: WHO/HIP

16 países, 856 casos notificados/452 óbitos (Out./16)

To date there has been no evidence of sustained human-to-human transmission.

Morbidity and Mortality Weekly Report (*MMWR*)

Outbreaks of Avian Influenza A (H5N2), (H5N8), and (H5N1) Among Birds — United States, December 2014–January 2015

Weekly
February 6, 2015 / 64(04);111

On February 3, 2015, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Michael A. Jhung, MD[1], Deborah I. Nelson, PhD[2] (Author affiliations at end of text)

During December 15, 2014–January 16, 2015, the U.S. Department of Agriculture received 14 reports of birds infected with Asian-origin, highly pathogenic* avian influenza A (HPAI) (H5N2), (H5N8), and (H5N1)† viruses. These reports§ represent the first reported infections with these viruses in U.S. wild or domestic birds. Although these viruses are not known to have caused disease in humans, their appearance in North America might increase the likelihood of human infection in the United States. Human infection with other avian influenza viruses, such as HPAI (H5N1) and (H5N6) viruses and (H7N9) virus, has been associated with severe, sometimes fatal, disease (*1–3*), usually following contact with poultry.

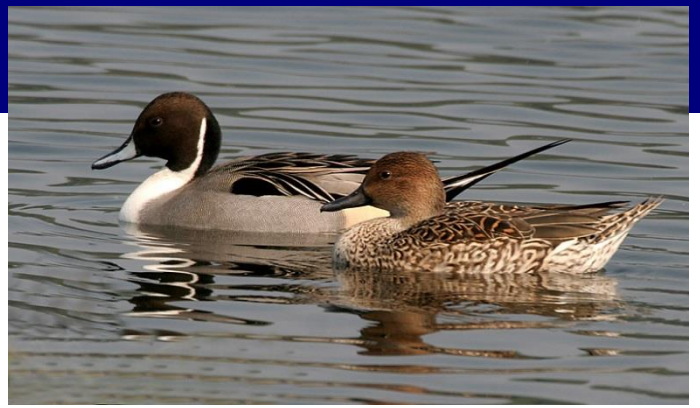
The 14 HPAI H5 detections, seven (H5N2), six (H5N8), and one (H5N1), occurred in five northwestern states (California, Idaho, Oregon, Utah, and Washington). Outbreaks occurred in five domestic, backyard flocks, two captive wild birds, and seven wild aquatic birds. All backyard flocks were destroyed after identification of HPAI H5 virus. Of 24 persons reporting exposure to infected birds, one person developed influenza-like illness (ILI) after exposure but subsequently tested negative for influenza.

CDC has developed testing (http://www.cdc.gov/flu/avianflu/severe-potential.htm) and influenza antiviral prophylaxis (http://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm) guidance for persons exposed to birds possibly infected with HPAI H5 viruses. Until more is known about these viruses, CDC is taking a cautious approach, and recommendations are largely consistent with guidance for influenza viruses associated with severe disease in humans. Clinicians and public health workers should consider the possibility of infection with HPAI H5 viruses in patients with ILI who have had recent contact with sick or dead birds, especially in areas where these viruses have been identified. Persons exposed to birds infected with HPAI H5 should be monitored for ILI for 10 days after their last exposure, and influenza antiviral prophylaxis may be considered to prevent infection. Persons who develop ILI after exposure to HPAI H5-infected birds should be tested immediately for influenza by the state health department. State health departments are encouraged to investigate all possible human infections with HPAI H5 virus and should notify CDC promptly when testing for influenza in persons with ILI who have been exposed to birds possibly infected with these viruses.

Time Line Of Outbreaks in United Estates

Highly pathogenic avian influenza, United States of America

Date of start of the event	10/12/2014
Date of confirmation of the event	14/12/2014
Report date	13/02/2015
Date submitted to OIE	13/02/2015
Reason for notification	Reoccurrence of a listed disease
Date of previous occurrence	2004
Manifestation of disease	Clinical disease
Causal agent	Highly pathogenic avian influenza
Serotype	H5N8
Nature of diagnosis	Laboratory (advanced)
This event pertains to	a defined zone within the country
Related reports	Immediate notification (16/12/2014) Follow-up report No. 1 (19/12/2014) Follow-up report No. 2 (29/12/2014) Follow-up report No. 3 (07/01/2015) Follow-up report No. 4 (22/01/2015) Follow-up report No. 5 (25/01/2015) Follow-up report No. 6 (03/02/2015) Follow-up report No. 7 (13/02/2015) Follow-up report No. 8 (25/02/2015) Follow-up report No. 9 (05/03/2015) Follow-up report No. 10 (20/03/2015) Follow-up report No. 11 (31/03/2015) Follow-up report No. 12 (22/04/2015)



These H5N8 and H5N2 detections involve only wild birds

Captive Wild Bird Findings Confirmed by USDA's National Veterinary Services Laboratories:

State	County	Species	Avian influenza subtype*	*Confirmation date*
MT	Flathead	Captive gyrfalcon	EA/AM-H5N2	March 27, 2015
MO	St. Louis	Captive falcon (hybrid)	EA/AM-H5N2	March 27, 2015
ID	Kootenai	Captive gyrfalcon (2)	EA-H5N8	January 29, 2015 February 6, 2015
ID	Canyon	Captive falcons, Great horned owl	EA/AM-H5N2	January 16, 2015 February 2, 2015
WA	Whatcom	Captive gyrfalcon	EA-H5N8	December 14, 2014

** References to EA and AM under avian influenza subtype indicate Eurasian and American strains of the virus.*

United States Department of Agriculture

USGS science for a changing world

NATIONAL FLYWAY COUNCIL
Pacific est. 1952 - Central est. 1948 - Mississippi est. 1952 - Atlantic est.1952

Last Updated: 05/14/2015

WILD BIRD HIGHLY PATHOGENIC AVIAN INFLUENZA CASES IN THE UNITED STATES [a]

Case #	COLLECTION DATE	SPECIES	COUNTY	STATE	SUBTYPE*	CONFIRMATION DATE	COLLECTING AGENCY
1	12-08-2014	Northern Pintail	Whatcom	WA	EA/AM H5N2	12-15-2014	Washington State DFW
2	12-08-2014	Mallard	Whatcom	WA	EA/AM H5N2	12-24-2014	Washington State DFW
3	12-16-2014	American Wigeon	Whatcom	WA	EA H5N8	12-24-2014	Washington State DFW
4	12-20-2014	Mallard	Lane	OR	EA/AM H5N2	01-12-2015	USDA-APHIS
5	12-22-2014	Mallard	Bingham	ID	EA H5N8	03-18-2015	USDA-APHIS
6	12-22-2014	Mallard	Bingham	ID	EA H5N8	03-18-2015	USDA-APHIS
7	12-23-2014	Northern Pintail	Clark	WA	EA/AM H5N2	01-16-2015	USGS-NWHC
8	12-23-2014	Mallard	Whatcom	WA	EA/AM H5N2	02-02-2015	Washington State DFW
9	12-24-2014	Mallard	Columbia	OR	EA/AM H5N2	01-16-2015	USGS-NWHC
10	12-24-2014	Mallard	Columbia	OR	EA H5N8	02-23-2015	USGS-NWHC
11	12-28-2014	Gadwall	Butte	CA	EA H5N8	01-01-2015	USDA-APHIS
12	12-29-2014	American Green-winged Teal	Whatcom	WA	EA/AM H5N1	01-16-2015	USGS-NWHC
13	12-29-2014	Cooper's Hawk	Whatcom	WA	EA/AM H5N2	01-26-2015	Washington State DFW

WILD BIRD HIGHLY PATHOGENIC AVIAN INFLUENZA CASES IN THE UNITED STATES [a] cont'd

Case #	COLLECTION DATE	SPECIES	COUNTY	STATE	SUBTYPE*	CONFIRMATION DATE	COLLECTING AGENCY
67	03-10-2015	Ring-necked Duck	McCracken	KY	EA/AM H5N2	04-24-2015	Kentucky DFWR
68	03-13-2015	Canada Goose	Lyon	KS	EA/AM H5N2	03-27-2015	Kansas DWP
69	03-16-2015	Lesser Snow Goose	Nodaway	MO	EA H5 [c]	03-24-2015	USDA-APHIS
70	03-16-2015	Canada Goose	Laramie	WY	EA/AM H5N2	03-25-2015	Wyoming GFD
71	04-13-2015	Snowy Owl	Oconto	WI	EA/AM H5N2	05-06-2015	Wisconsin DNR
72	04-14-2015	Cooper's Hawk	Yellow Medicine	MN	EA/AM H5N2	04-29-2015	Minnesota DNR

Update on Avian Influenza Findings
Poultry Findings Confirmed by USDA's National Veterinary Services Laboratories

201
Detections Reported

44,671,073
Birds Affected

19/12/14
First Detection Reported

29/05/15
Last Detection Reported

State	County	Flyway	Flock type	Species	Avian influenza subtype*	Confirmation date	Flock size
Minnesota	Renville	Mississippi	Commercial	Turkey	EA/AM-H5N2	29/05/2015	29.300
Minnesota	Meeker	Mississippi	Commercial	Turkey	EA/AM-H5N2	29/05/2015	4.900
Iowa	Hamilton	Mississippi	Commercial	Turkeys	EA/AM-H5N2	29/05/2015	17.000
Minnesota	Brown	Mississippi	Commercial	Turkey	EA/AM-H5N2	29/05/2015	7.300
Iowa	Wright	Mississippi	Commercial	Chickens	EA/AM-H5N2	28/05/2015	991.500
Minnesota	Renville	Mississippi	Commercial	Turkeys	EA/AM-H5N2	28/05/2015	48.900
Minnesota	Kandiyohi	Mississippi	Commercial	Turkeys	EA/AM-H5N2	28/05/2015	pending

Pilgrim's Pride Corporation (PPC) ★ Watchlist

25.04 **-0.14 (-0.56%)** NASDAQ - As of 4:00PM EDT

After Hours: **25.05** ↑ +0.01 (0.04%) 5:10PM EDT

1d | 5d | 1m | 3m | 6m | YTD | 1y | 2y | 5y | 10y | Max | Custom | Indicator | Comparison | Reset | Go To Symbol

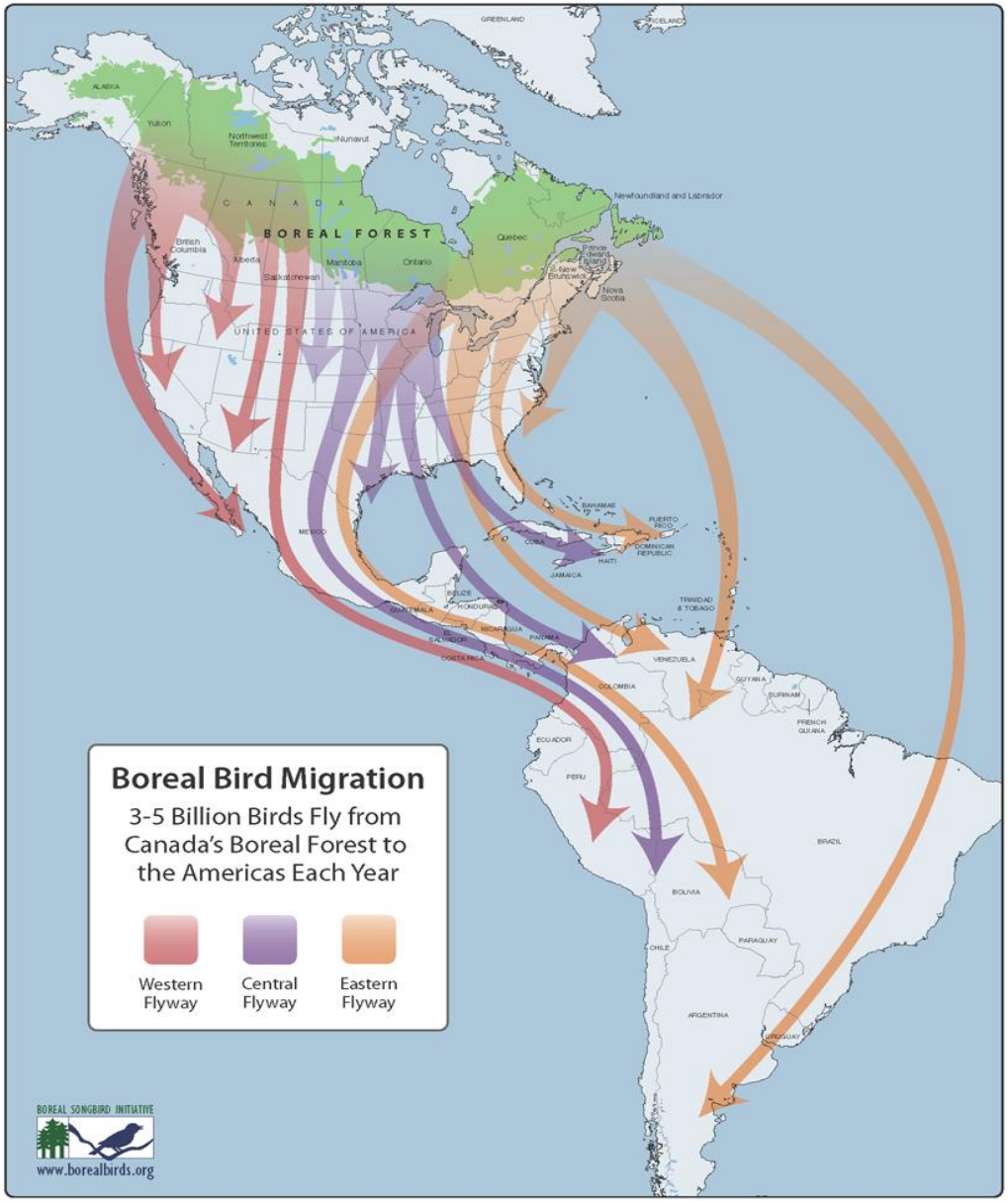
Recent Articles

USDA reports virulent strain of avian flu in Kansas poultry

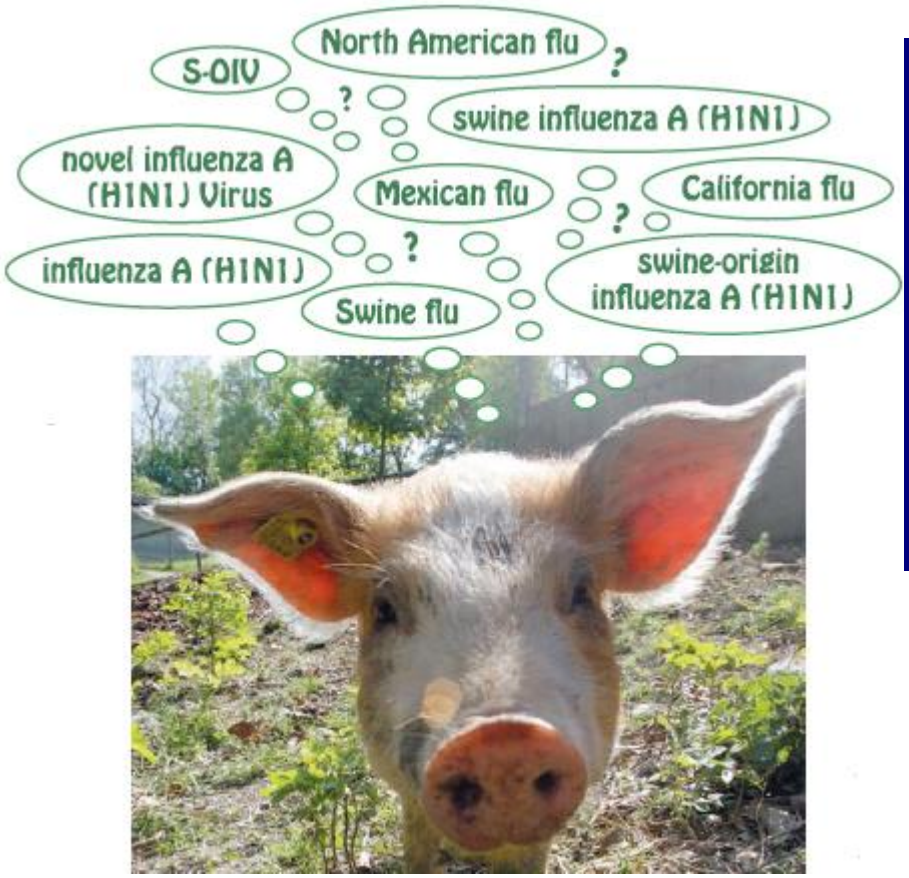
Reuters Sat Mar 14 2015

Prev Close	25.18	High	25.38
Open	25.05	Low	24.68

BIRD MIGATION



INFLUENZA A H1N1



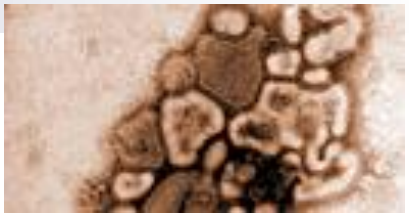
Influenza Suína

- J.S. Cohen – descreveu pela primeira vez durante a pandemia de gripe espanhola em 1918-1919.
- Shope and Lewis, 1930 – primeiro isolamento do vírus a partir de suínos.
- De 1930 a 1998 H1N1. Estável por ~60 anos - década de 80 – drifts importantes
- Desde 1998 surtos de influenza suína H3N2 foram descritos em porcos nos EUA – Vírus humano, duplo rearranjo (humano e suíno) e triplo (humano, suíno e aviário) (Karasin et al. 2000, Olsen et al. 2002)
- Identificação de novos shifts (EUA) – H3N2 e H1N1 circulante em suínos levando ao surgimento de H1N2 e H3N1.
- Transmissão direta Influenza H4N6 aviário
- Atualmente - co-circulação dos subtipos – H1N1, H3N2, H1N2

Influenza Suína em humanos

- 1958 a 2005 (EUA) – total de 37 casos de influenza humana associada a influenza suína, com 4 óbitos.
  - 4 amostras eram H3N2 e o restante H1N1
- Transmissão descrita em outros países da Europa e Nova Zelandia
- 1974 – primeiro isolamento do vírus a partir de pulmão de um menino (Smith *et al.*1976)
- 1976 – surto em recrutas de Fort Dix (New Jersey, EUA) ~200 infectados
- 2005 – caso menino 17 anos com sinais clínicos – isolamento de H1N1 com um rearranjo triplo (circulante em suínos)
  - HA, NA e PB1 - vírus humanos
  - M, NS e NP – vírus suínos
  - PA e PB2 vírus aviários

Influenza Suína



Patient	Reference	Exposure to swine	Nature of exposure	Age, years	Sex	Month	Year	Residence
1	Kluska et al. [9]	Yes	Laboratory worker	40	F	October	1958	Czechoslovakia
2	Kluska et al. [9]	No	None	11	M	November	1958	Czechoslovakia
3	Kluska et al. [9]	No	None	3	F	November	1958	Czechoslovakia
4	Kluska et al. [9]	No	None	7	F	November	1958	Czechoslovakia
5	Kluska et al. [9]	No	None	72	F	December	1958	Czechoslovakia
6	Kluska et al. [9]	No	None	44	M	December	1958	Czechoslovakia
7	Smith [4]	Yes	Lived on swine farm	16	M	July	1974	Minnesota
8	O'Brien et al. [10]	Yes	Lived on swine farm	8	M	October	1975	Wisconsin
9	Thompson et al. [11]	Yes	Feeding pigs	40	F	December	1975	Virginia
10	Thompson et al. [11]	No	No known swine exposure	55	M	December	1975	Virginia/New York
11	Smith [12]	Yes	Meat-packing house worker	17	M	December	1975	Tennessee
12	CDC [13]	No	No known swine exposure	32	M	October	1976	Missouri
13	CDC [14]	Yes	Employed on swine farm	22	M	November	1976	Wisconsin
14	CDC [15]	Yes	Lived on swine farm	13	M	December	1976	Wisconsin
15	Dowdle et al. [16]	Yes	Swine exposure	NA	NA	NA	1976	Minnesota
16	Dacso et al. [17]	Yes	Livestock show swine barn attendant	20	M	February	1979	Texas
17	Dacso [17]	Yes	Livestock show visitor	6	M	February	1980	Texas
18	Patriarca et al. [18]	No	No known swine exposure	4	F	February	1982	Nevada
19	Chuvakova et al. [19]	Yes	Occupational exposure	65	M	November	1983	Russia
20	Chuvakova et al. [19]	No	No known swine exposure	10	F	December	1983	Russia
21	Chuvakova et al. [19]	No	No known swine exposure	27	M	December	1983	Russia
22	de Jong et al. [20]	Yes	Occupational exposure	50	M	January	1986	Switzerland
23	de Jong et al. [20]	No	No known swine exposure	3	NA	January	1986	Switzerland
24	de Jong et al. [20]	Yes	Occupational exposure	29	M	March	1986	Netherlands
25	McKinney et al. [21]	Yes	Pigs (county fair)	32	F	September	1988	Wisconsin
26	Wentworth et al. [22]	Yes	Animal caretaker (swine exposure)	27	M	July	1991	Maryland
27	Claas et al. [23]	No	No known swine exposure	1	F	November	1992	Netherlands
28	Claas et al. [23]	No	No known swine exposure	2	M	January	1993	Netherlands
29	Rimmelzwaan et al. [24]	Yes	Lived on swine farm	5	F	Summer	1993	Netherlands
30	Wentworth et al. [25]	Yes	Laboratory workers exposed to sick pigs	39	M	August	1994	Wisconsin
31	Wentworth et al. [25]	Yes	Laboratory workers exposed to sick pigs	31	F	August	1994	Wisconsin
32	Kimura et al. [26]	Yes	Occupational exposure	37	F	December	1995	Minnesota
33	Cooper et al. [27]	NA	NA	NA	M	NA	1998	United States
34	Gregory et al. [28]	No	No known swine exposure	<1[a]	F	September	1999	Hong Kong
35	Gregory et al. [29]	Yes	Swine farmer	50	M	February	2002	Switzerland
36	Gray et al. [8]	Yes	Swine farmer	50	M	February	2005	Iowa
37	Olsen et al. [30]	Yes	Swine farmer	NA	M	July	2005	Canada

Patient	Reference	Underlying illness	Vital status	Laboratory study	Subtype	Person-to-person transmission
1	Kluska et al. [9]	Healthy	Recovered	Serology	H1N1	Probable
2	Kluska et al. [9]	Healthy	Recovered	Serology	H1N1	Probable
3	Kluska et al. [9]	Healthy	Recovered	Serology	H1N1	Probable
4	Kluska et al. [9]	Thrombocytopenia	Recovered	Serology	H1N1	Probable
5	Kluska et al. [9]	Healthy	Recovered	Serology	H1N1	Probable
6	Kluska et al. [9]	Healthy	Recovered	Serology	H1N1	Probable
7	Smith [4]	Hodgkin disease	Died	Isolate	H1N1	No evidence
8	O'Brien et al. [10]	Healthy	Recovered	Serology	H1N1	Possible
9	Thompson et al. [11]	Healthy	Recovered	Serology	H1N1	No evidence
10	Thompson et al. [11]	Splenectomy	Recovered	Serology	H1N1	No evidence
11	Smith [12]	Hodgkin disease	Recovered	Serology	H1N1	No evidence
12	CDC [13]	NA	Recovered	Serology	H1N1	No evidence
13	CDC [14]	NA	Recovered	Isolate	H1N1	NA
14	CDC [15]	NA	Recovered	Isolate	H1N1	No evidence
15	Dowdle et al. [16]	NA	NA	NA	H1N1	NA
16	Dacso et al. [17]	Healthy	Recovered	Isolate	H1N1	Possible
17	Dacso et al. [17]	Healthy	Recovered	Isolate	H1N1	No evidence
18	Patriarca et al. [18]	ALL in remission	Died	Isolate	H1N1	Possible
19	Chuvakova et al. [19]	NA	Died	Isolate	H1N1	No evidence
20	Chuvakova et al. [19]	NA	Recovered	Isolate	H1N1	No evidence
21	Chuvakova et al. [19]	NA	Recovered	Isolate	H1N1	No evidence
22	de Jong et al. [20]	Asthma	Recovered	Isolate	H1N1	NA
23	de Jong et al. [20]	Healthy	Recovered	Isolate	H1N1	NA
24	de Jong et al. [20]	Healthy	Recovered	Isolate	H1N1	NA
25	McKinney et al. [21]	Pregnancy	Died	Isolate	H1N1	Probable
26	Wentworth et al. [22]	Healthy	Died	Isolate	H1N1	No evidence
27	Claas et al. [23]	Healthy	Recovered	Isolate	H3N2	Possible
28	Claas et al. [23]	Healthy	Recovered	Isolate	H3N2	Possible
29	Rimmelzwaan et al. [24]	Healthy	Recovered	Isolate	H1N1	NA
30	Wentworth et al. [25]	Healthy	Recovered	Isolate	H1N1	No evidence
31	Wentworth et al. [25]	Healthy	Recovered	Isolate	H1N1	No evidence
32	Kimura et al. [26]	Healthy	Died	Isolate	H1N1	NA
33	Cooper et al. [27]	NA	NA	Isolate	H1N1	NA
34	Gregory et al. [28]	NA	Recovered	Isolate	H3N2	No evidence
35	Gregory et al. [29]	NA	Recovered	Isolate	H1N1	No evidence
36	Gray et al. [8]	Healthy	Recovered	Isolate	H1N1	No evidence
37	Olsen et al. [30]	Healthy	Recovered	Isolate	H3N2	NA

CID 2007:44 (15 April) • Myers et al.

Influenza Suína em humanos

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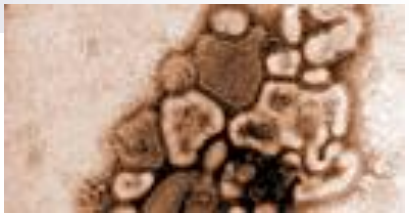
  - HA, NA e PB1 - vírus humanos
  - M, NS e NP – vírus suínos
  - PA e PB2 vírus aviários

Influenza Suína



Influenza A/H1N1 2009

- Casos iniciais México : Março ???
- EUA: 17 Abril - 2 casos confirmados em crianças na Califórnia.
- NY – surto em escola (total de 2700 estudantes 200 apresentaram sintomas)
- H1N1 suína com recombinações humana e aviária.

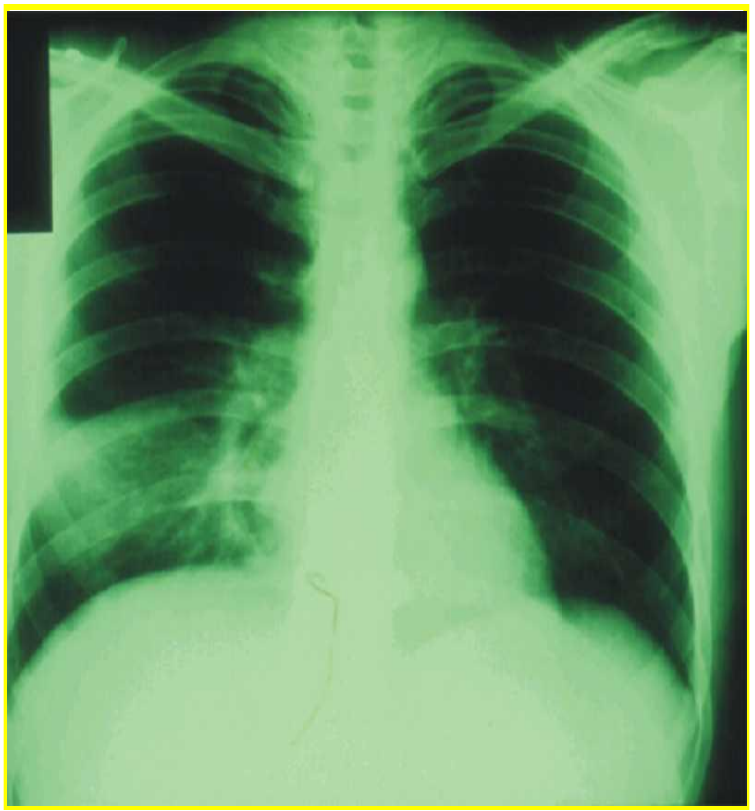
CDC MMWR April 2009

Influenza A/H1N1/2009

- Período de incubação provável: 24 a 72h (variando de 1 a 7 dias)
- Período de excreção viral: média 7 dias, com períodos mais longos em lactentes jovens e imunodeprimido
- Forma de transmissão – gotículas de saliva, secreções respiratórias, aerossól
- Período infeccioso: 1 dia antes do início dos sintomas e até 7 dias após.

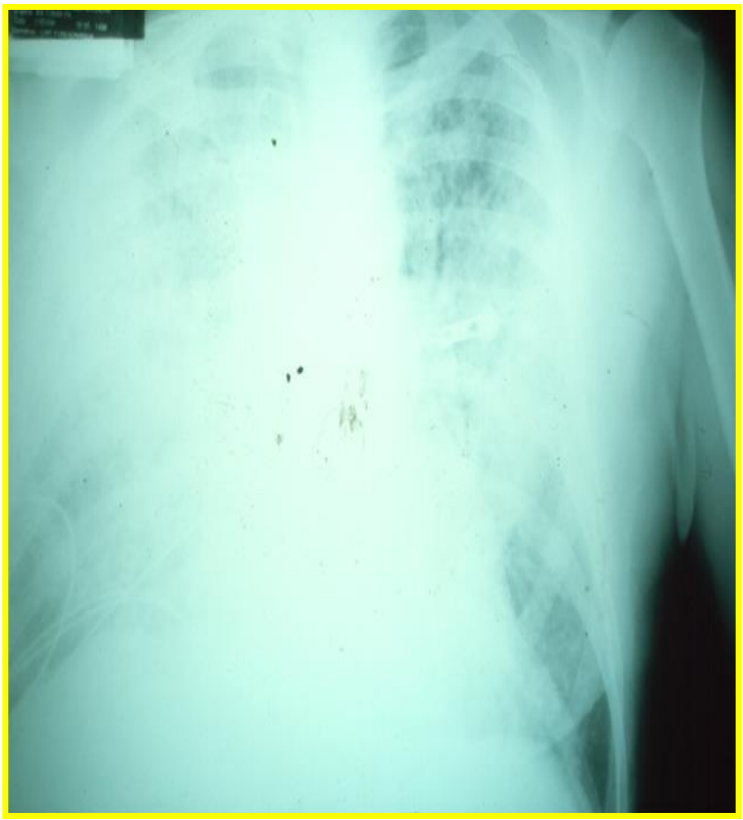
www.cdc.gov/swineflu

PNEUMONIA SECUNDÁRIA



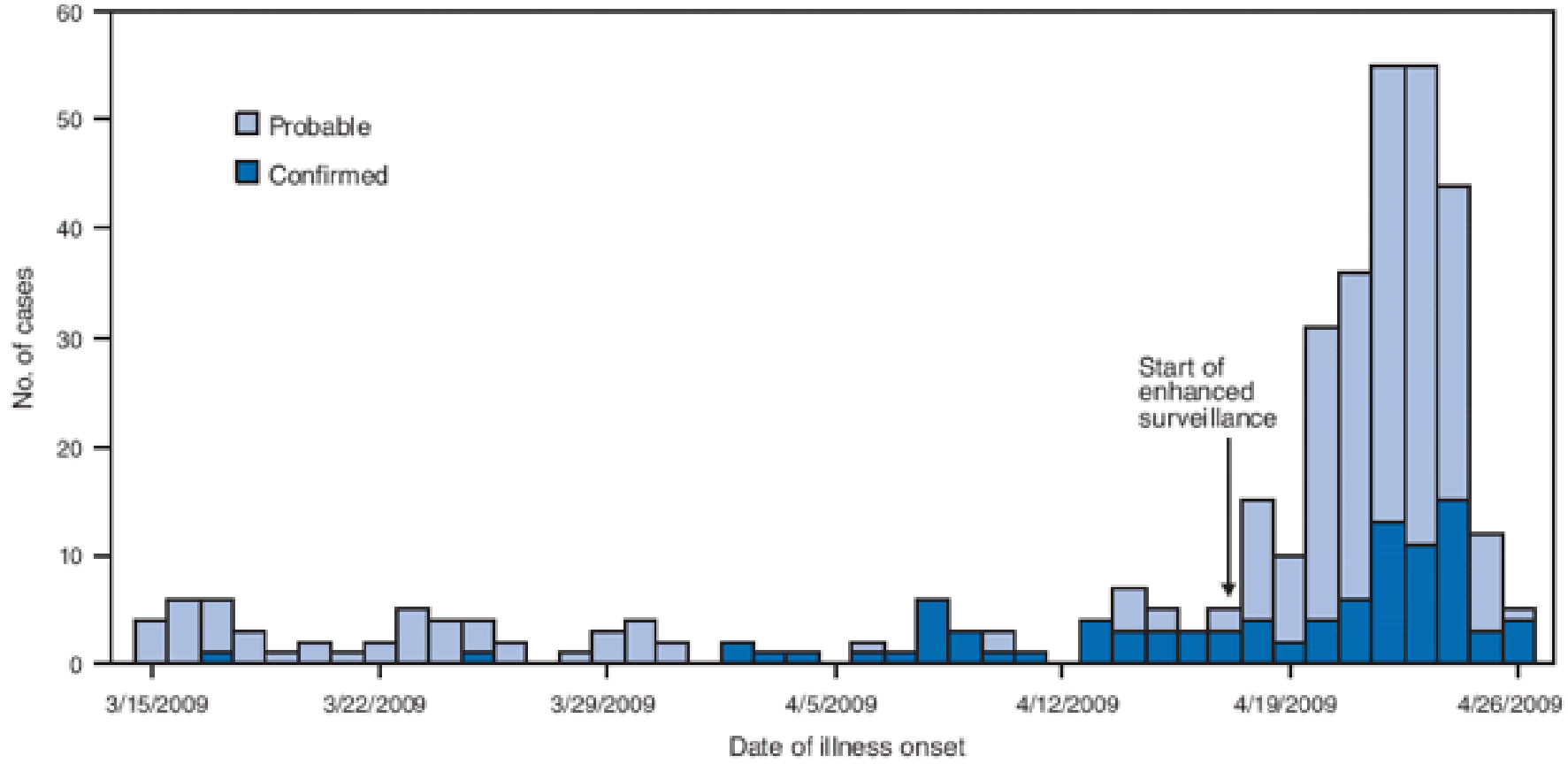
S. pneumoniae
S. aureus
H. influenzae

PNEUMONIA PRIMÁRIA



Influenza

Número de casos confirmados (N=97) e de casos prováveis (N=260)* de Influenza A (H1N1) de origem suína (S-OIV), México – 15 de março a 26 de abril 2009



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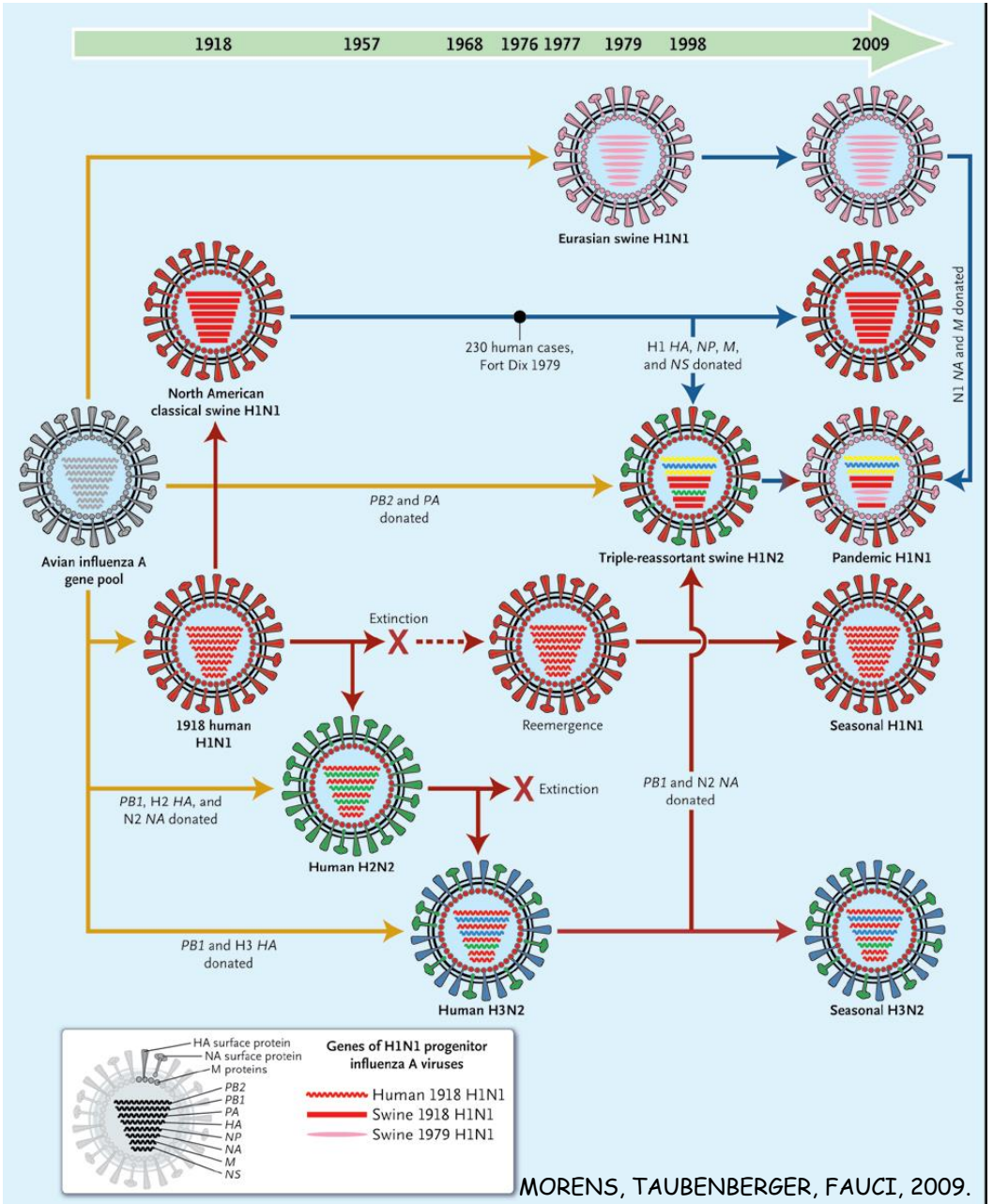
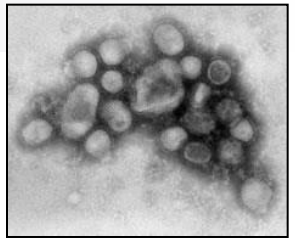
CDC MMWR April 2009

Genesis of swine-origin H1N1 influenza viruses.



MORENS, TAUBENBERGER, FAUCI, 2009.



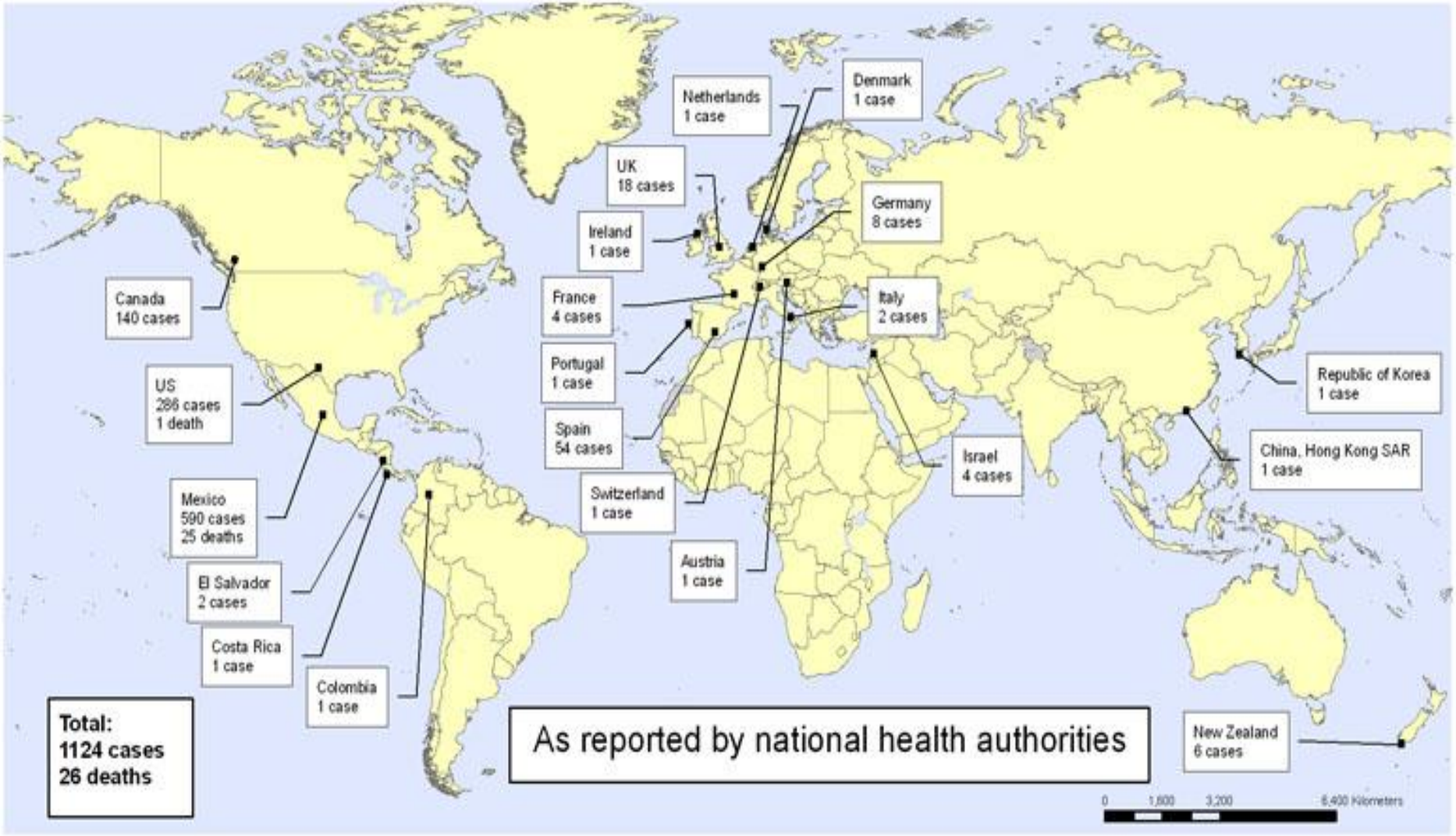
Influenza A/H1N1

- Alerta OMS – 24 de abril
  - EUA – 7 casos confirmados e 9 suspeitos
  - México – 878 casos de pneumonia, 83 mortes. 18 casos confirmados de Influenza A/H1N1
- OMS: 29 Abril 19h - 148 casos confirmados em 9 países
  - EUA: 91
  - México: 26
  - Áustria: 1
  - Canadá: 13
  - UK: 5
  - Alemanha: 3
  - Israel: 2
  - Nova Zelândia: 3
  - Espanha: 4
- 8 mortes confirmadas: 1 EUA e 7 no México
- Nível de Alerta de pandemia – fase 4 → fase 5 →fase 6

www.who.int

New Influenza A (H1N1)
Number of laboratory confirmed cases and deaths

Status as of 5 May 2009
6:30 GMT



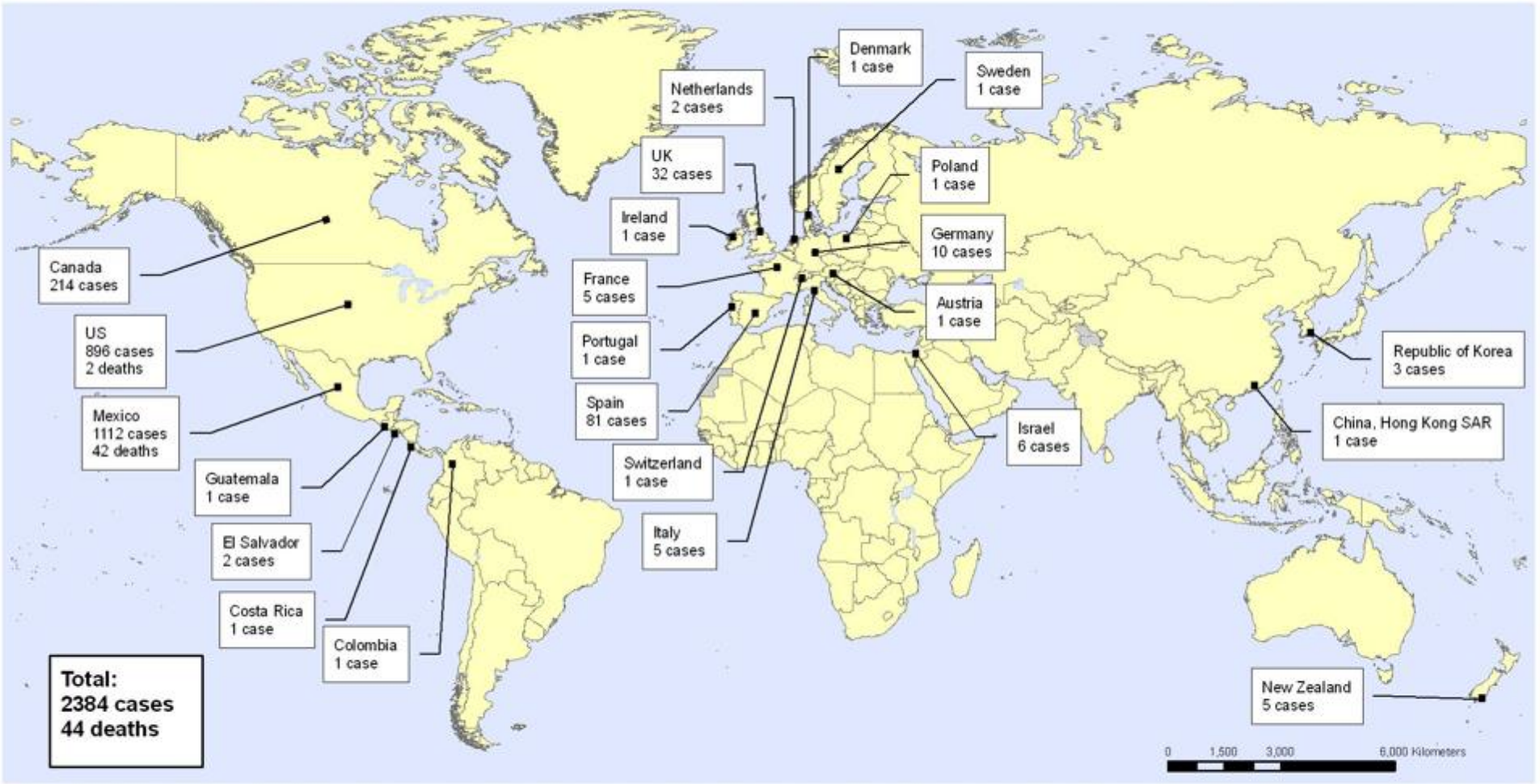
Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Map produced: 5 May 2009 6:30 GMT

New Influenza A (H1N1), Number of laboratory confirmed cases and deaths as reported to WHO

Status as of 8 May 2009 06:00 GMT



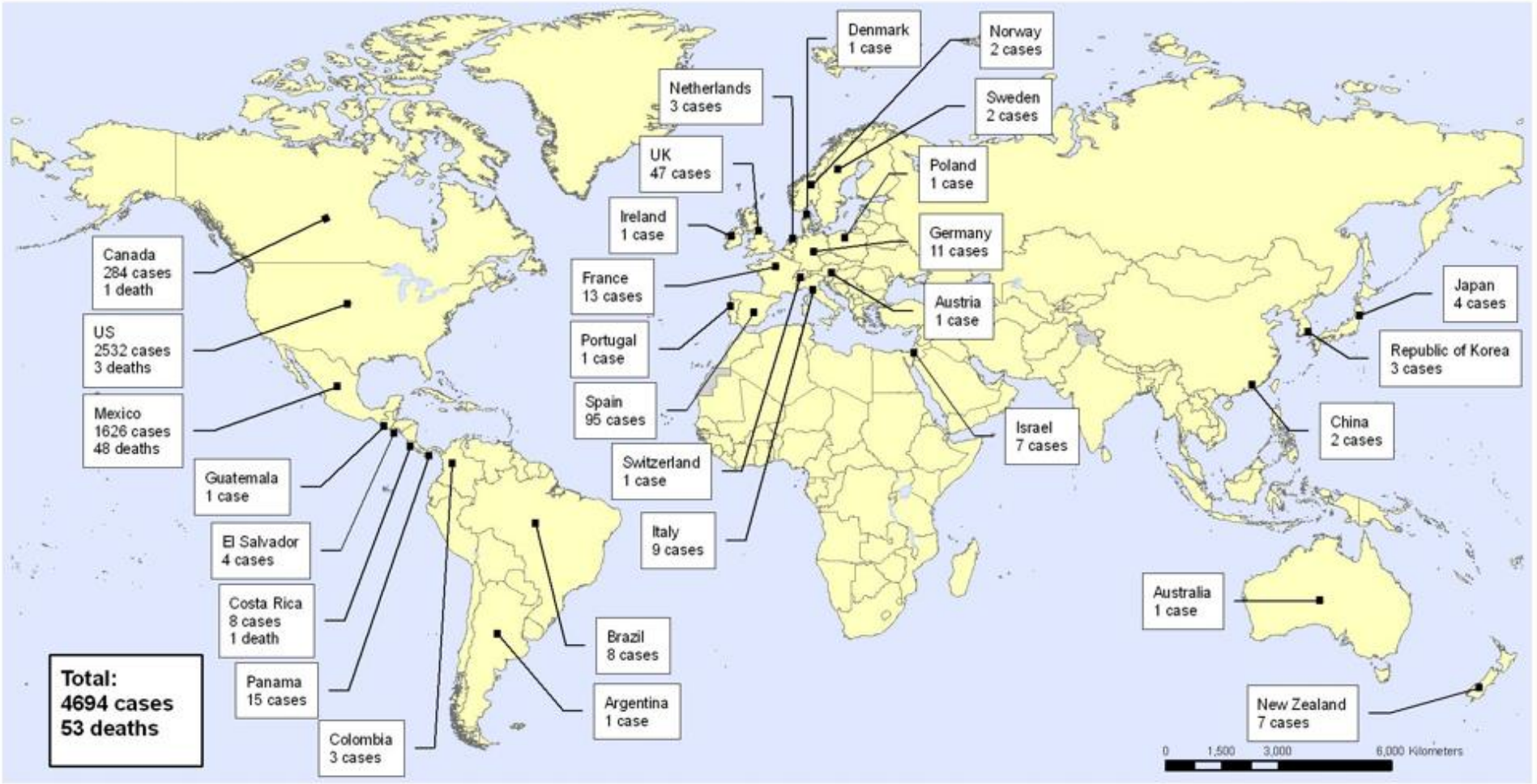
Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Map produced: 8 May 2009 06:00 GMT

New Influenza A (H1N1),
Number of laboratory confirmed cases and deaths as reported to WHO

Status as of 11 May 2009
06:00 GMT



Total:
4694 cases
53 deaths

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

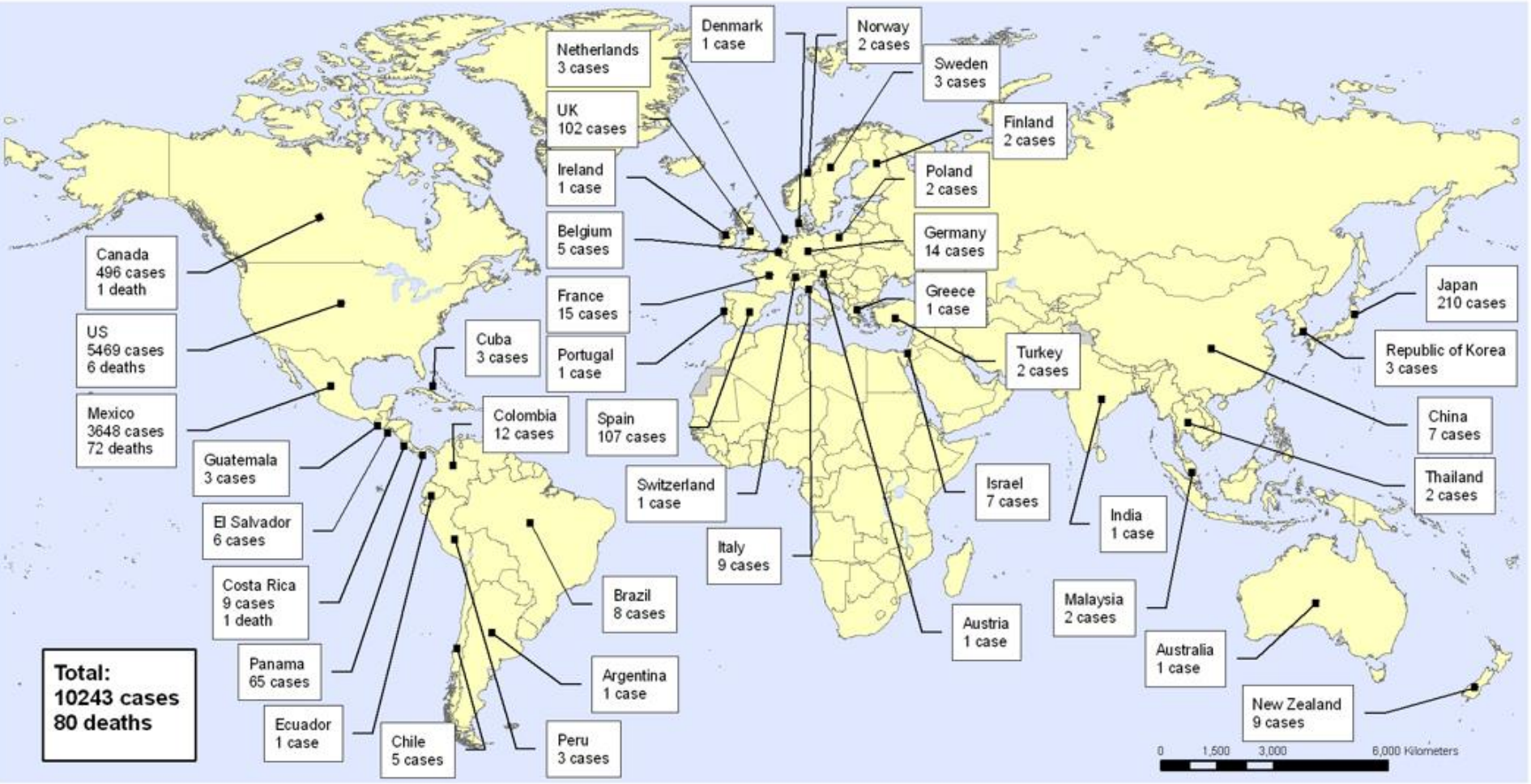
Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Map produced: 11 May 2009 06:00 GMT

New Influenza A (H1N1), Number of laboratory confirmed cases and deaths as reported to WHO

Status as of 20 May 2009 6:00 GMT



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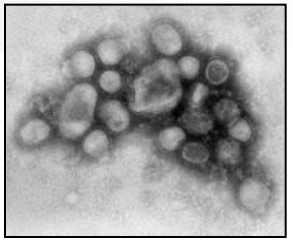
Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Map produced: 20 May 2009 6:00 GMT

Influenza A/H1N1



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  - Nova Zelândia: 3
  - Espanha: 4
- 8 mortes confirmadas: 1 EUA e 7 no México
- Nível de Alerta de pandemia – fase 4 (27/04) → fase 5 29/04)→fase 6 (11/06)

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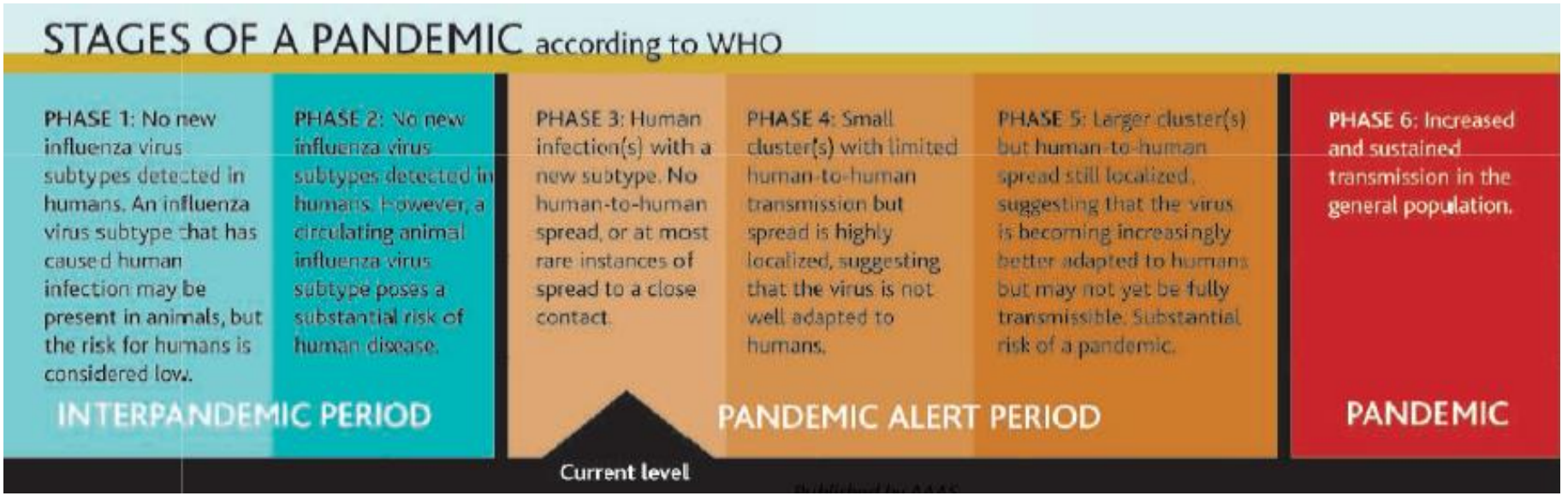
ESTÁGIOS DE UMA PANDEMIA - OMS



Enserink, Ago 2005 Science

1. Não há novo subtipo em humanos – poucas aves mortas;
2. Não há novo subtipo em humanos – muitas aves mortas (risco);
3. Casos em humanos com novo subtipo – contato humano-humano não identificado
4. Transmissão humanos para humanos (poucos casos);
5. Aumento de casos em humanos (transmissão sustentada);
6. Grande número de casos na população mundial – **PANDEMIA!!**

Agosto 2010 – declarada fim da pandemia –Influenza A (H1N1)pdm09

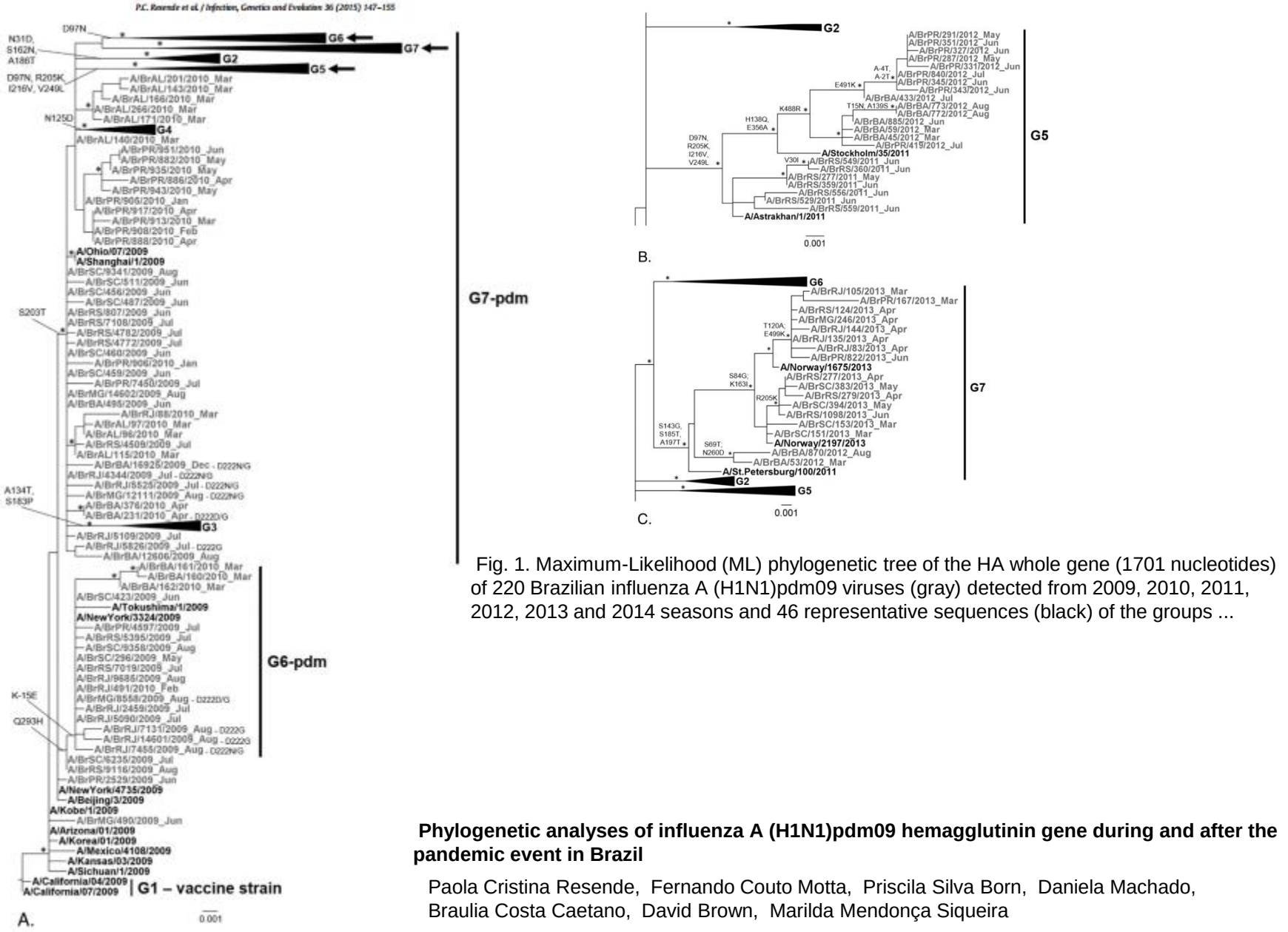


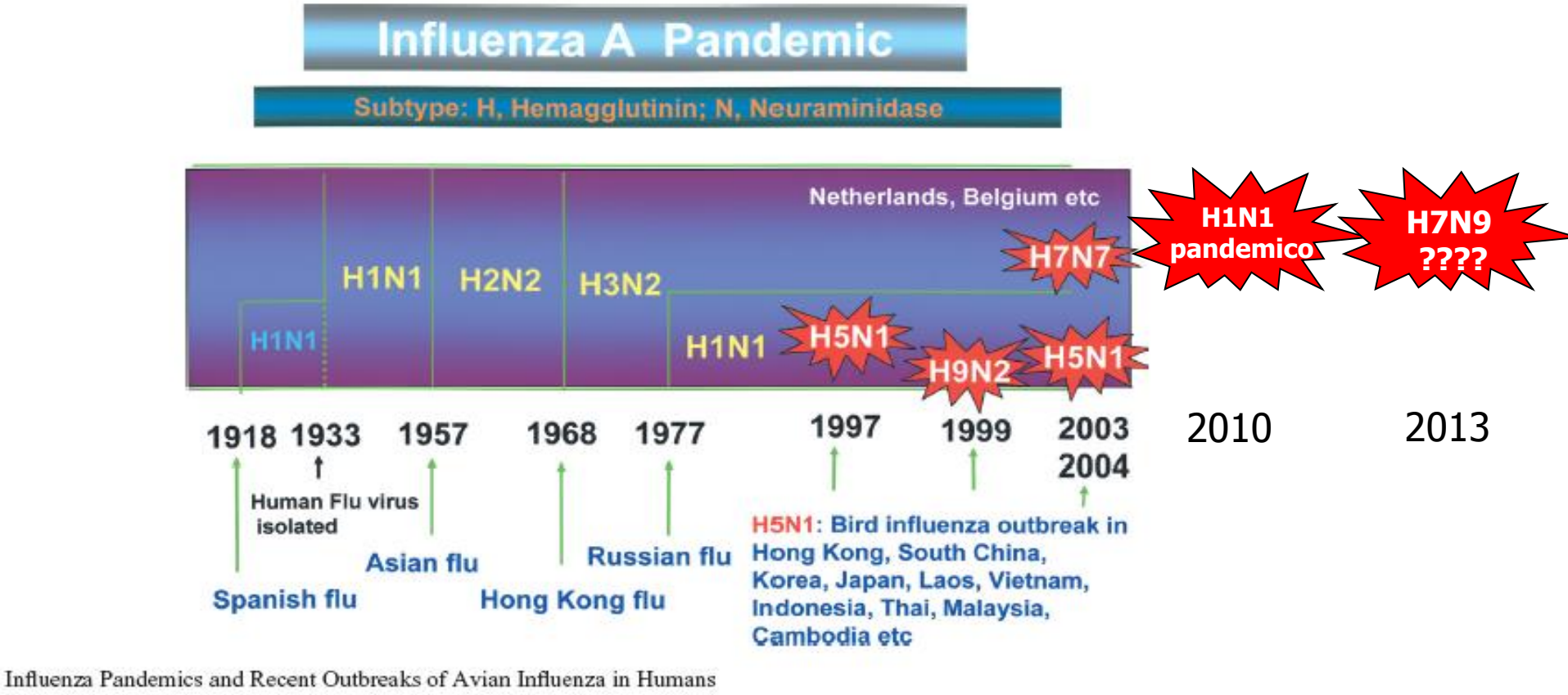
Fig. 1. Maximum-Likelihood (ML) phylogenetic tree of the HA whole gene (1701 nucleotides) of 220 Brazilian influenza A (H1N1)pdm09 viruses (gray) detected from 2009, 2010, 2011, 2012, 2013 and 2014 seasons and 46 representative sequences (black) of the groups ...

Phylogenetic analyses of influenza A (H1N1)pdm09 hemagglutinin gene during and after the pandemic event in Brazil

Paola Cristina Resende, Fernando Couto Motta, Priscila Silva Born, Daniela Machado, Braulia Costa Caetano, David Brown, Marilda Mendonça Siqueira

Infection, Genetics and Evolution, Volume 36, 2015, 147–155 - http://dx.doi.org/10.1016/j.meegid.2015.09.007

HISTÓRICO DAS PANDEMIAS:



Influenza Pandemics and Recent Outbreaks of Avian Influenza in Humans

Recentemente subtipos puramente aviários H5N1, H9N2, H7N7 e H7N9 foram distribuídos diretamente em humanos.

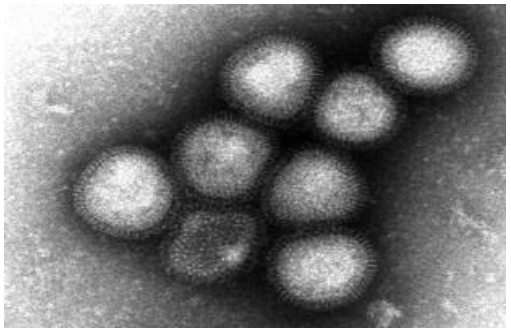
Influenza Aviária A(H7N9) virus

- Fevereiro/2013: primeiro óbito por H7N9 no sudeste da China, de origem aviária, Março/2013: 3 casos
- Adaptação do vírus para se ligar a receptores de células de mamíferos
- Encontrado vírus em aves domésticas: galinhas, patos, pombos
- Fontes de contaminação e reservatório: ? ? ?
- Modo de transmissão: contato com animais ou seu meio ambiente
- **Não tem evidencia de transmissão entre humanos**
- Sintomas: febre, tosse, falta de ar, conjuntivite, pneumonia severa, falência múltipla dos órgãos

cnn.com

Influenza Aviária A(H7N9) virus

- Sensível a inibidores de neuraminidase: oseltamivir e zanamivir
- Virus isolado e caracterizado:
  Genes de 3-4 diferentes virus de Influenza aviária



Who.int

➔ **HA**: sequenciado, geneticamente diferente de outros virus H7, origem provável de patos
➔ **NA**: similar a A (H11N9) detectado em pássaros e patos
➔ **6** genes internos derivados de H9N2 que circula em pássaros no leste da China,

Abril/2013:126 casos (24 óbitos)
Maio/2013: 131 casos (32 óbitos)
Julho/2013:134 casos (43 óbitos) – verão no Hemisf. Norte

H7N9: 803 casos notificados/319 óbitos (Out./16)

Figure 2. *Number of officially reported human cases since February 2013 as of 20 October 2016*

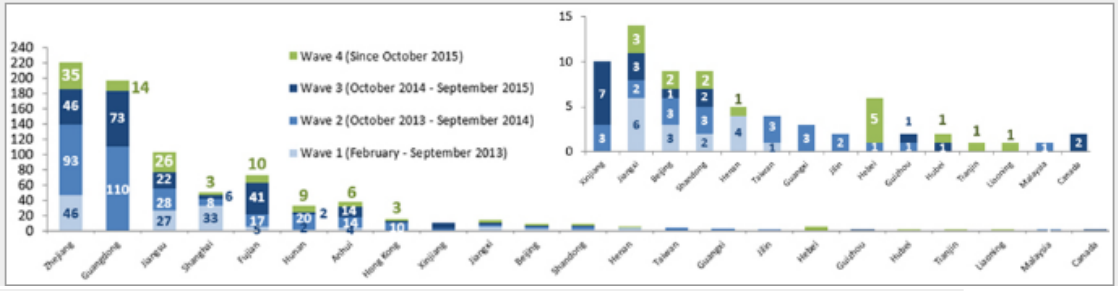
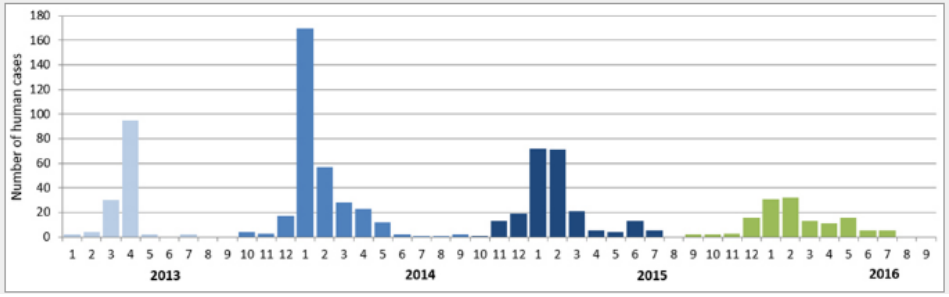


Figure 3. *Incidence of officially reported human cases by month, based on onset date as of 20 October 2016*



http://www.fao.org/ag/againfo/programmes/en/empres/H7N9/situation_update.html

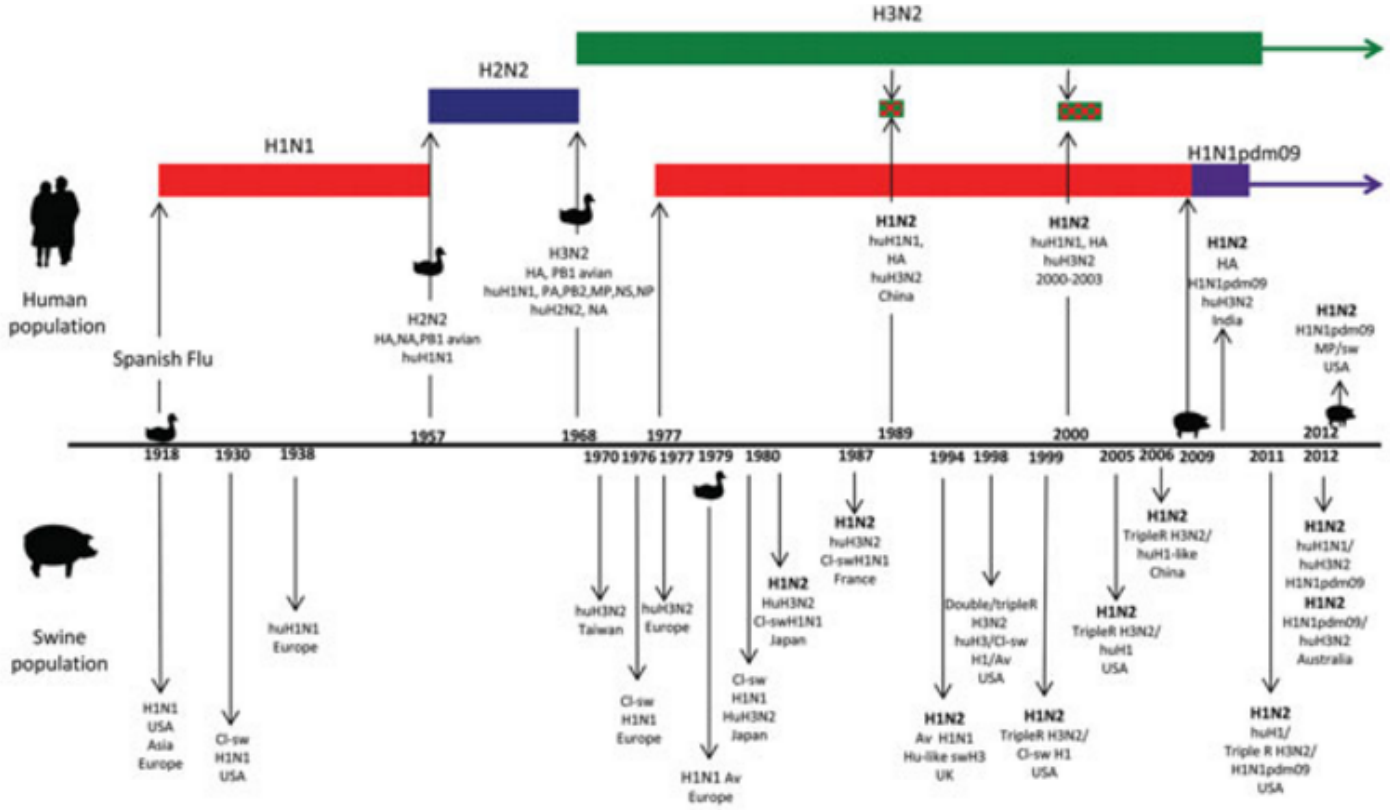
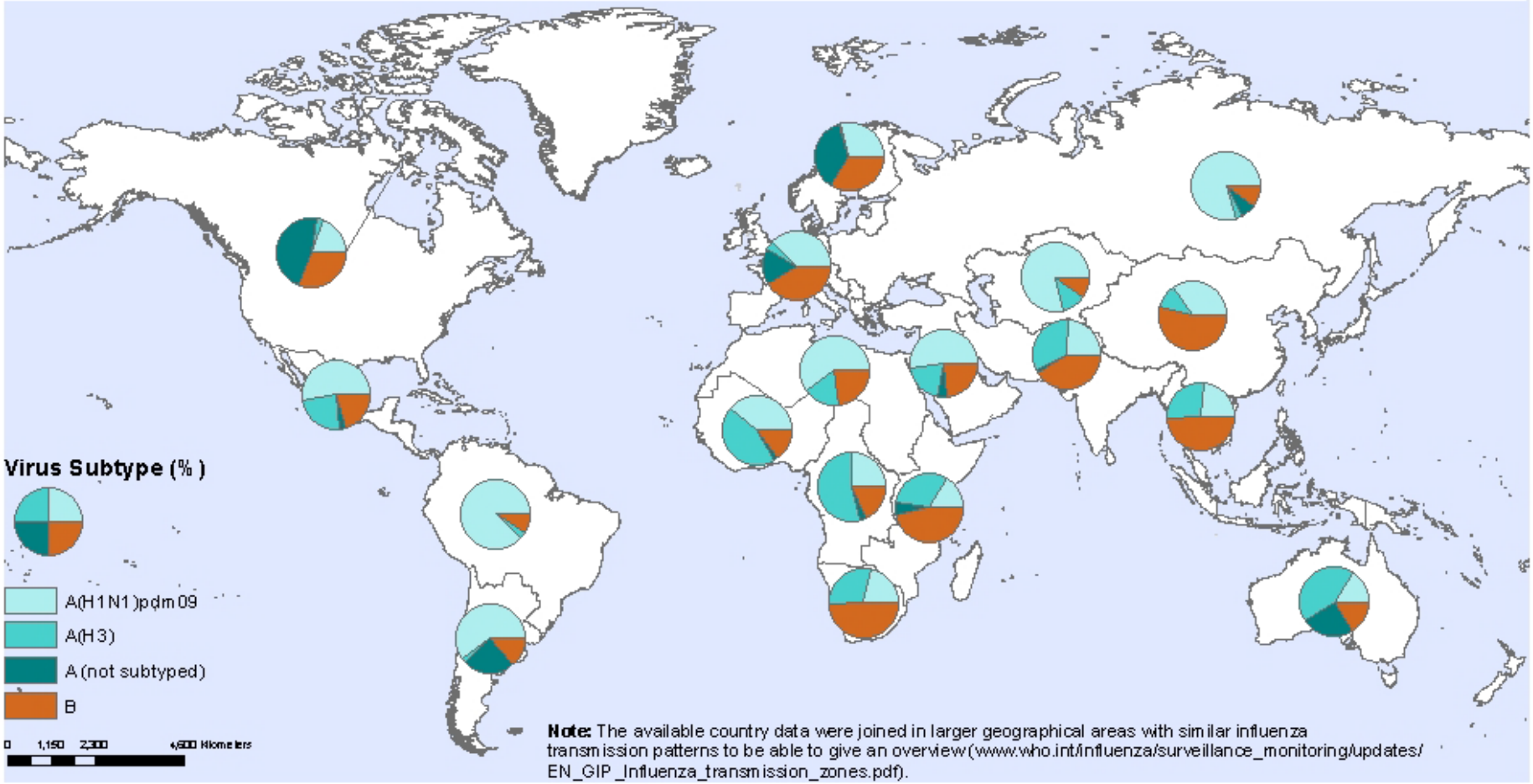


Figure. . Significant points in the history of influenza viruses that have contributed to the emergence of influenza A(H1N2) viruses in human and swine populations. The bird and swine symbols on the timeline indicate when transmission appeared to occur directly from either avian or swine source into the relevant population. The bird symbols on the 1957 and 1968 time-points indicate that the circulating viruses of the time reassorted with viruses of an avian source resulting in novel subtypes. Significant events leading to the emergence of A(H1N2) in the human population are above the timeline and in swine below the timeline. A(H1N2) viruses appearing in both human and swine populations are indicated in boldface. Genotypes of A(H1N2) emerging in the human population are: 1989 (China), human A(H3N2) virus with hemagglutinin (HA) from human A(H1N1); 2000 (worldwide), same genotype as 1989 virus; 2009 (India), human A(H3N2) virus with HA from A(H1N1pdm09); 2012 (United States), human-like H1, A(H1N1pdm09) matrix, remainder swine H3N2 triple reassortant. Virus origins: Cl-sw, classical swine; hu, human; sw, swine; av, avian; hu-like, human like; double, double reassortant, tripleR, triple reassortant.

Distribution of influenza-virus subtypes by influenza transmission zone, January 2016 to September 2016



Note: The available country data were joined in larger geographical areas with similar influenza transmission patterns to be able to give an overview (www.who.int/influenza/surveillance_monitoring/updates/EN_GIP_Influenza_transmission_zones.pdf).

Data Source:
WHO/GIP, FluNet (www.who.int/flunet)
as of 30 September 2016, 04:00 UTC

World Health Organization

Outros vírus circulando no período

Influenza A (H9N2) activity from 24 September 2014 to 23 February 2015
Influenza A(H9N2) viruses are enzootic in poultry populations in parts of Africa, Asia and the Middle East.
3 casos humano – 1 Egito, 2 nas províncias de Sichuan e Guangdong Provinces, China

Influenza A(H1N1)v and A(H1N2)v activity from 24 September 2014 to 23 February 2015
Influenza A(H1N1) and A(H1N2) viruses circulate in swine populations in many regions of the world.

1 caso EUA (H1N1)v. 2 casos humanos (H1N1)v na Suécia .

Influenza A(H3N2)v activity from 24 September 2014 to 23 February 2015
Influenza A(H3N2) viruses are enzootic in swine populations in most regions of the world. Depending on geographic location, the genetic and antigenic characteristics of these viruses differ. Human infections with swine A(H3N2) viruses have been documented in Asia, Europe and North America
1 caso nos EUA

Vacinas???