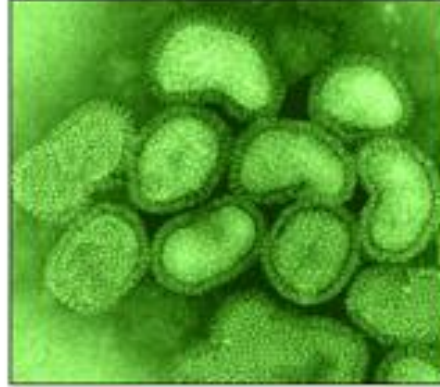


ETİYOLOJİ

ORTHOMYXOVIRUSES

- pleomorphic
- influenza types A,B,C
- febrile, respiratory illness with systemic symptoms



<http://www.uct.ac.za/depts/mmm/stannard/fluovirus.html>
Linda Stannard, of the Department of Medical Microbiology, University of Cape Town

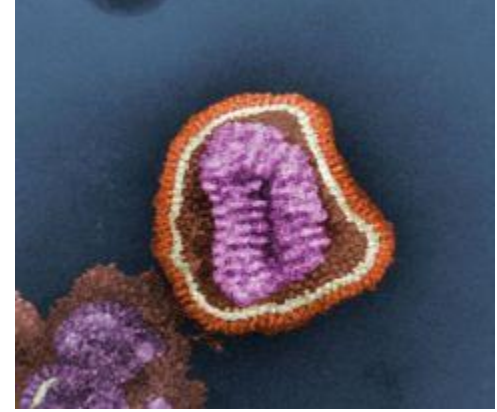


Image by Frederick Murphy courtesy of Public Health Image Library (PHIL)

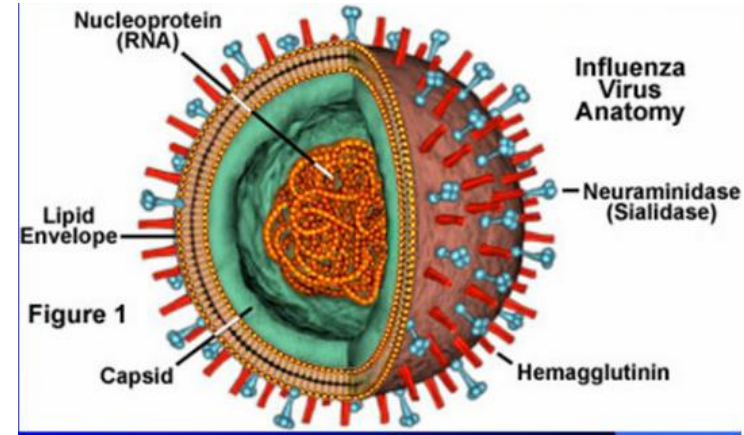
1878 – ilk kez kanatlılarda tanımlandı. (İtalya)
(Avian Influenza)

Segmentli yapı!

Influenza A virusları – insan, at, domuz, kanatlı,
deniz memelileri

Influenza B virusları - insan

Influenza C virusları – insan ve domuz

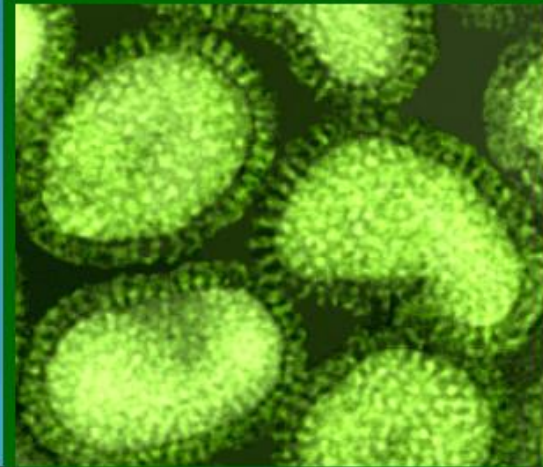
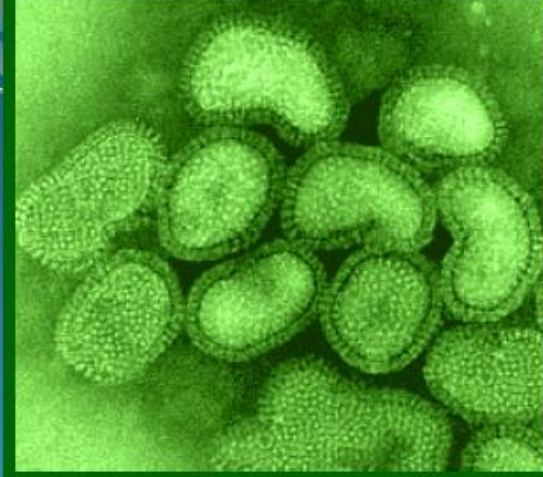


<http://micro.magnet.fsu.edu/cells/viruses/influenzavirus.html>

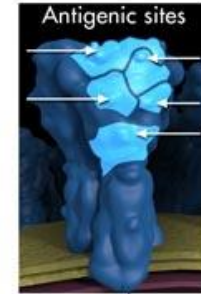
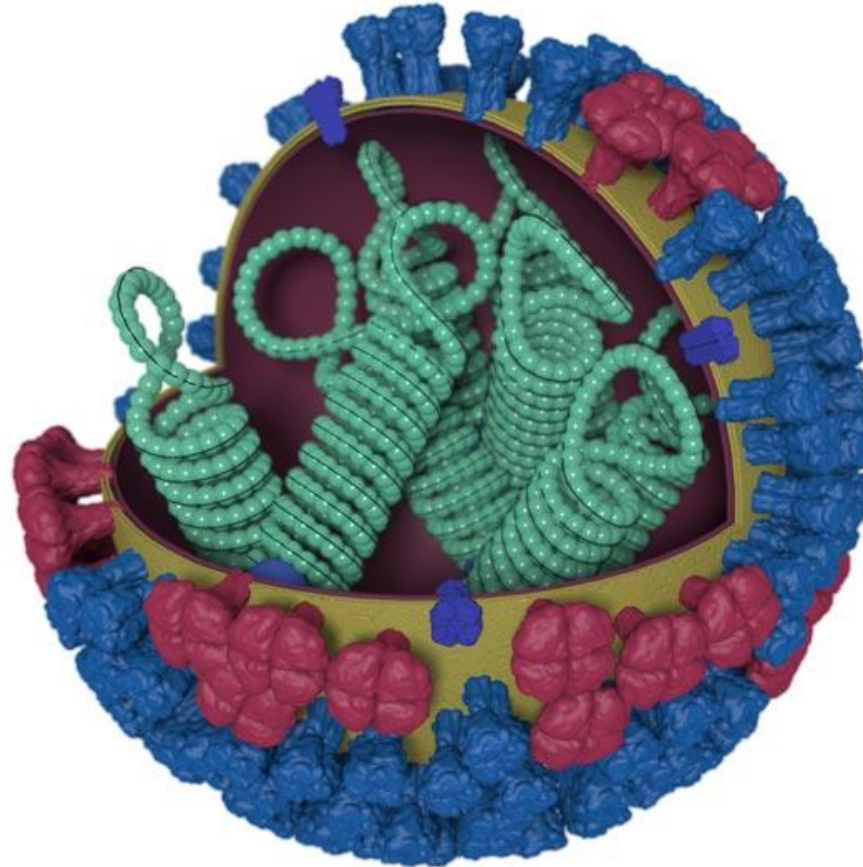
Virus Özellikleri

80-120 nm boyutlarında, negatif polariteli, 8 segmentli ve tek iplikçikli RNA genetik materyali taşıyan zarflı viruslardır.

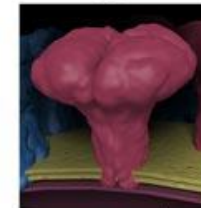
56° C 30 dakika, pH 3 ve lipid solventlere karşı duyarlıdırlar.



AN INFLUENZA VIRUS



Hemagglutinin



Neuraminidase



M2 ion channel



Ribonucleoprotein

<https://www.cdc.gov/flu/professionals/laboratory/antigenic.htm>

<https://www.cdc.gov/h1n1flu/images.htm>

Hemaglutinin (HA) ve Neuraminidaz (NA)

- Membran dışında bulunan yüzey glikoproteinleridir.
- HA, hücreye bağlanma (attachment ve penetrasyon), koruyucu antikor üretimini uyarma, virulensten sorumludur. Hücreye girişte **sialik asit** reseptörlerine bağlanır ve endositozu tetikler.
- NA, virionların hücreden ayrılması sırasında kazanılır. Antikor oluşumunu uyarır. Akciğerlerdeki mucusu hidrolize ederek virusun hücre yüzeyine tutunmasını sağlar.
- Influenza A virusları – 16 tane HA, 9 tane NA alt tipine göre farklı gruplar oluştururlar.

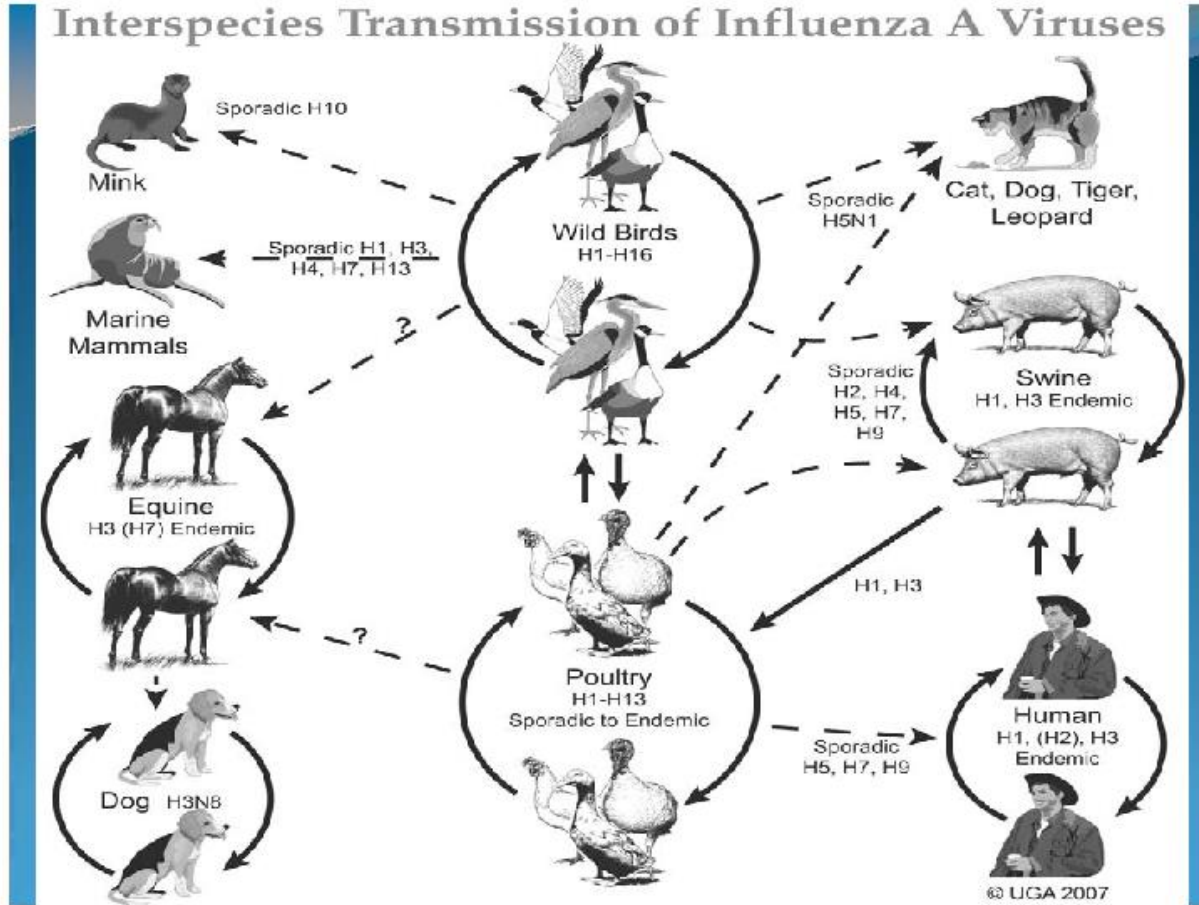
Influenza A yüzey antijenleri ve türlerdeki dağılımı

	Hemaglütinin tipleri															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
İnsan	X	X	X		!											
Domuz	X		X													
At			X				X									
Kuş	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Nöraminidaz tipleri															
	1	2	3	4	5	6	7	8	9							
İnsan	X	X														
Domuz	X	X														
At							X	X								
Kuş	X	X	X	X	X	X	X	X	X							

Influenza A virusları tür bariyerini geçebilirler ve bu nedenle daha tehlikelidirler.

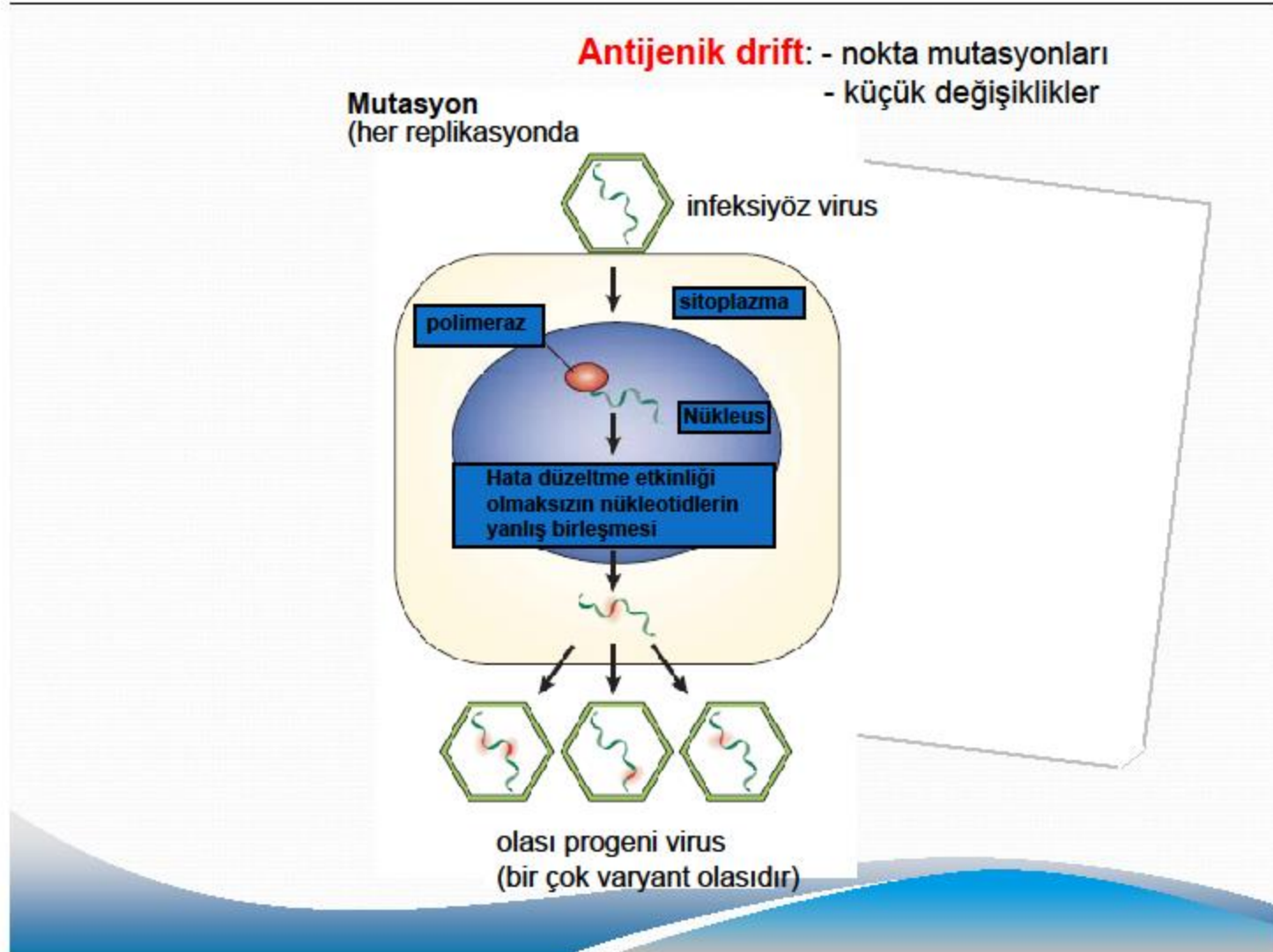
Patogenezde etkili 3 mekanizma vardır:

- Direkt nakil (Türler arası)
- Adaptasyon
- Genetik reassortment



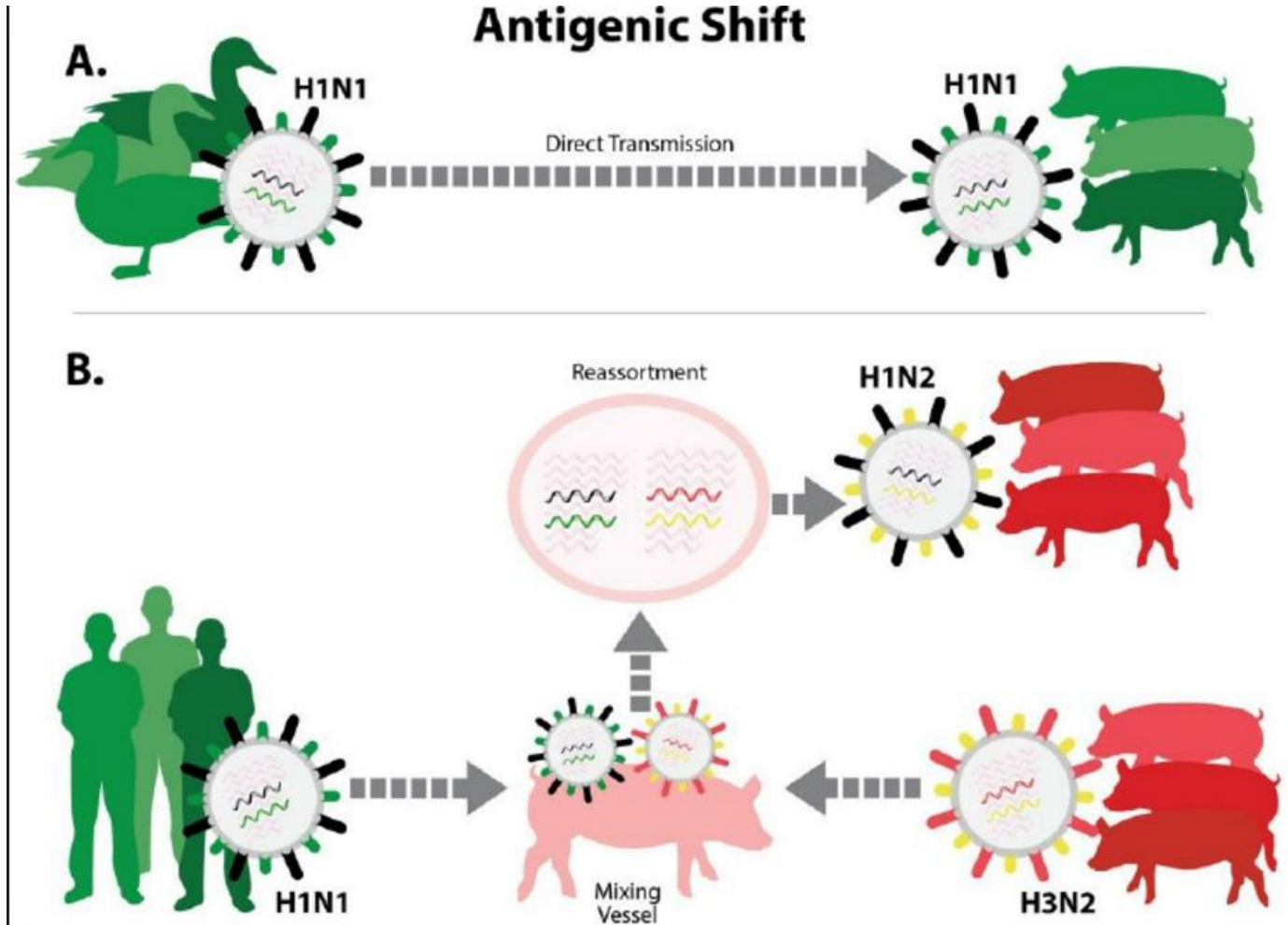
Antijenik Drift (Antijenik kayma) – Mekanizması ve Sonuçları

- Nokta mutasyonlar, yeni viruslar, kross bağıışıklığın kaybı, epidemi



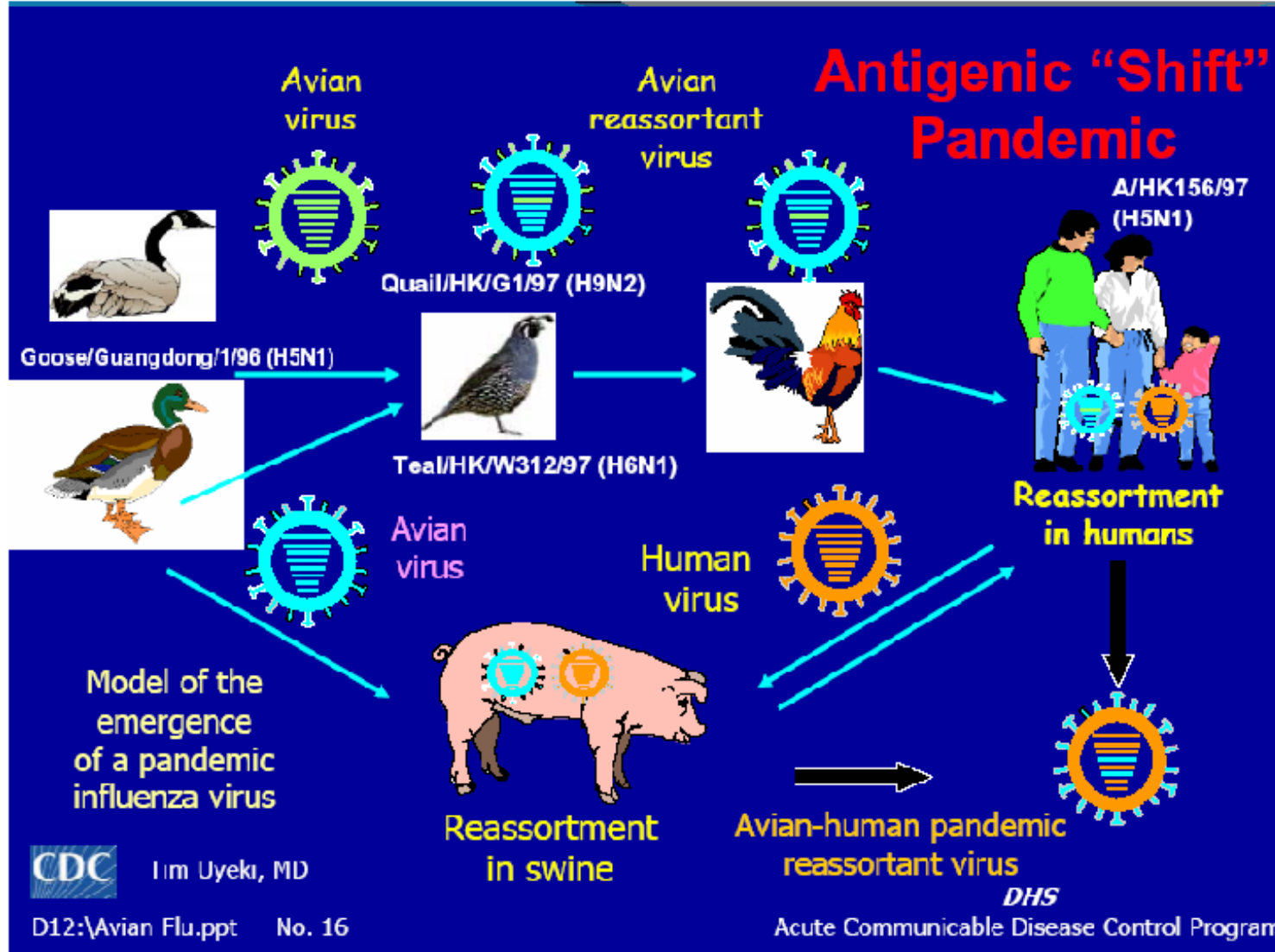
Antijenik Shift (Antijenik sapma) – Mekanizması ve Sonuçları

- Fenotipik deęişiklikler, genetik reassortment (yeniden karışım), yeni HA ve NA alt tipi oluşumu, pandemi



Vaccines, 2015, 3, 22-73.

Farklı antijenik yapıdaki Influenza viruslarının aynı anda, aynı konağı enfekte etmesiyle meydana gelebilecek genetik materyal değişimleri salgınlara yol açabilme özelliğine sahip yeni virusların ortaya çıkmasına neden olmaktadır.



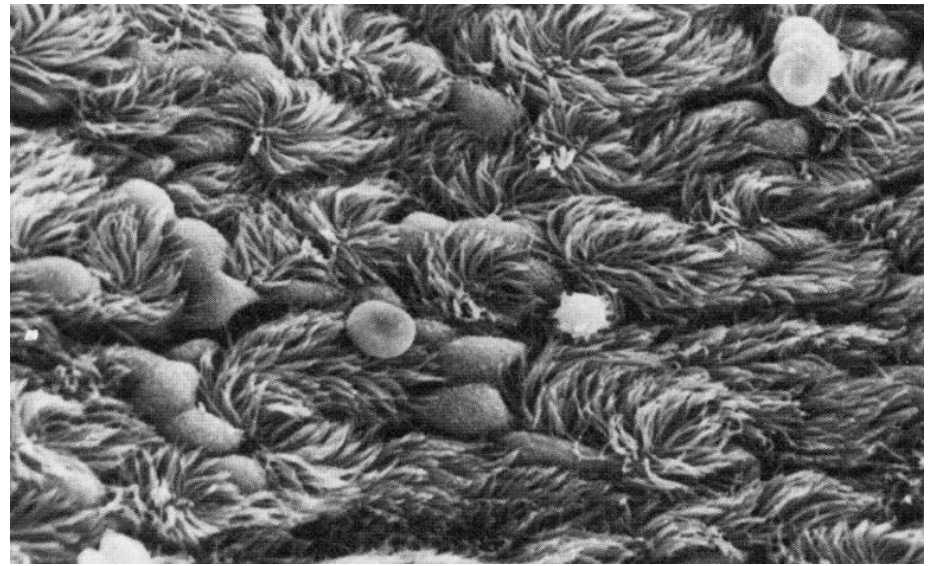
Bulaşma

AEROSOL

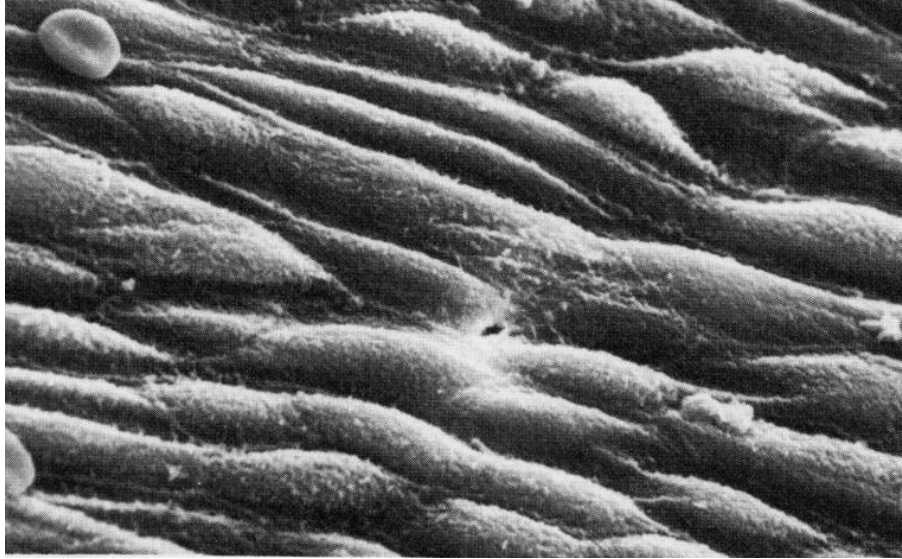
100,000 -1,000,000 VIRIONS
PER DROPLET

18-72 saat inkubasyon

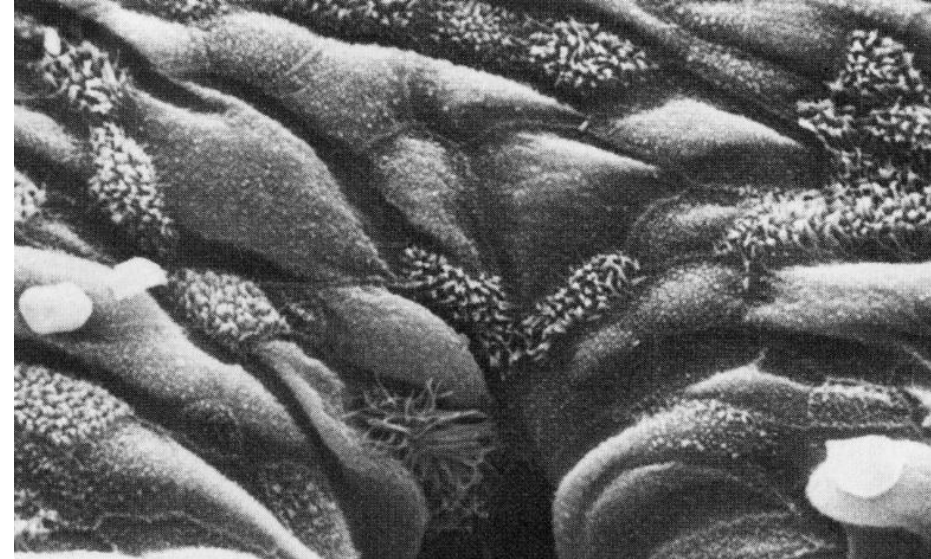
Saçılma



Normal Trachea Mukozası



Enfeksiyondan 3 gün sonra

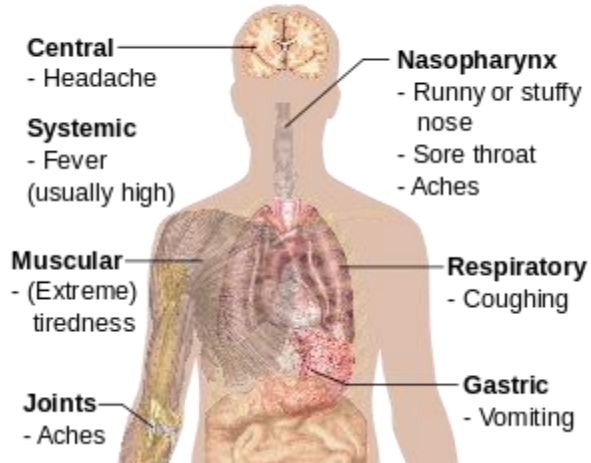


Enfeksiyondan 7 gün sonra

Influenza Viruslarının Patogenez Mekanizması

- Influenza virusları çoğalabilmek için, sialik asitten oluşan spesifik hücre reseptörlerine ihtiyaç duyarlar.
- Avian ve Equine influenza suşları sialik asit bağlantısını α 2,3 galaktoz bağına tercih ederler.
- İnsanlarda, sialik asit reseptörleri α 2,6 bağlanma konfigürasyonunda galaktoz kapsar.
- Domuzlardaki respiratorik kanal epitel hücreleri hem α 2,3 hem de α 2,6 linklerini kapsar. Bunlar hem insan hem avian virusları için duyarlıdır. Yeni reassortant virusların oluşumunda önem taşırlar.

Symptoms of Influenza



Call S, Vollenweider M, Hornung C, Simel D, McKinney W (2005). "Does this patient have influenza?". JAMA. 293 (8): 987–97. doi:10.1001/jama.293.8.987. PMID 15728170.

[Centers for Disease Control and Prevention > Influenza Symptoms](#) Page last updated 16 November 2007. Retrieved 28 April 2009.

Fever and extreme coldness (chills shivering, shaking (rigor))

Cough

Nasal congestion

Body aches, especially joints and throat

Fatigue (yorgunluk)

Headache (baş ağrısı)

Irritated, watering eyes

Reddened eyes, skin (especially face), mouth, throat and nose

Petechial Rash^[24]

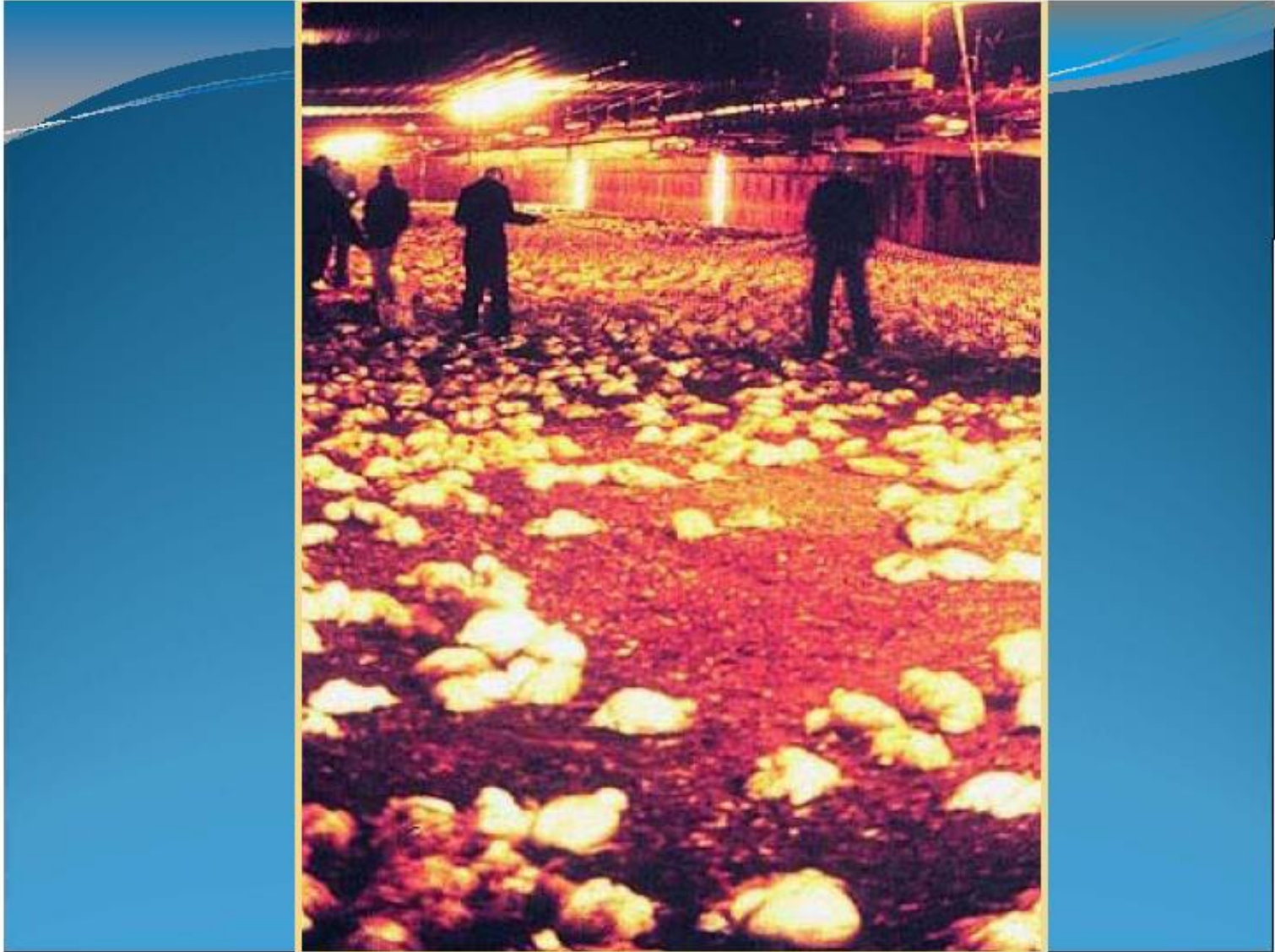
In children, gastrointestinal symptoms such as diarrhea and abdominal pain



Konjesyon ve Hemorajiler



<http://www.cvm.tamu.edu/fadr/disease.aspx?DID=2600>



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

Status as of 12 December 2008
Latest available update

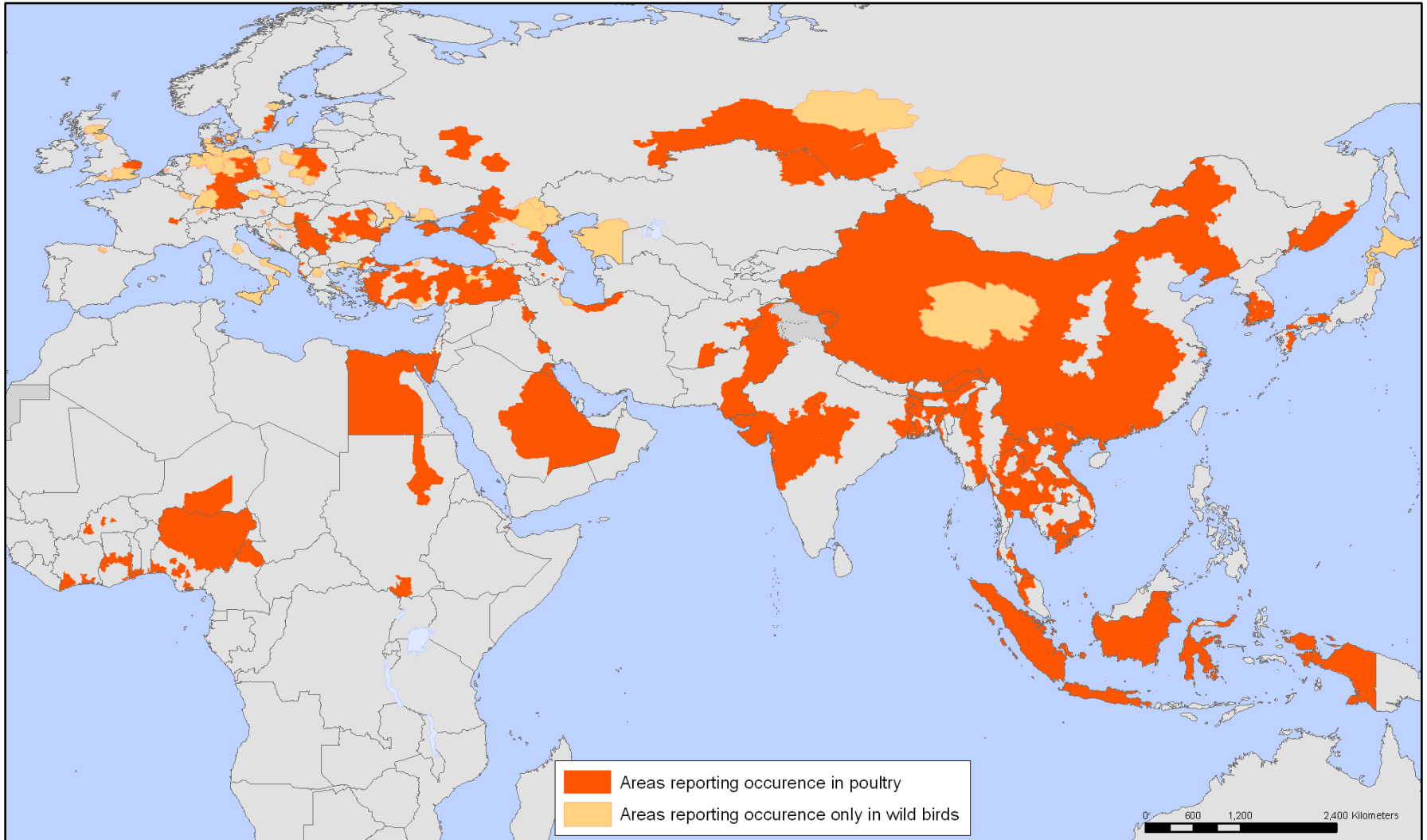




Figure 1. Returning from a shopping trip in Hanoi, Vietnam (photo JM Katz).

Source: Nicholson et al, *Lancet Infect Dis* 4:499-509 (2004)

Bird Flu and the U.A.E. – livestock market in Al Ain





Photo credit: Fabio Frisca (FAO Vietnam)



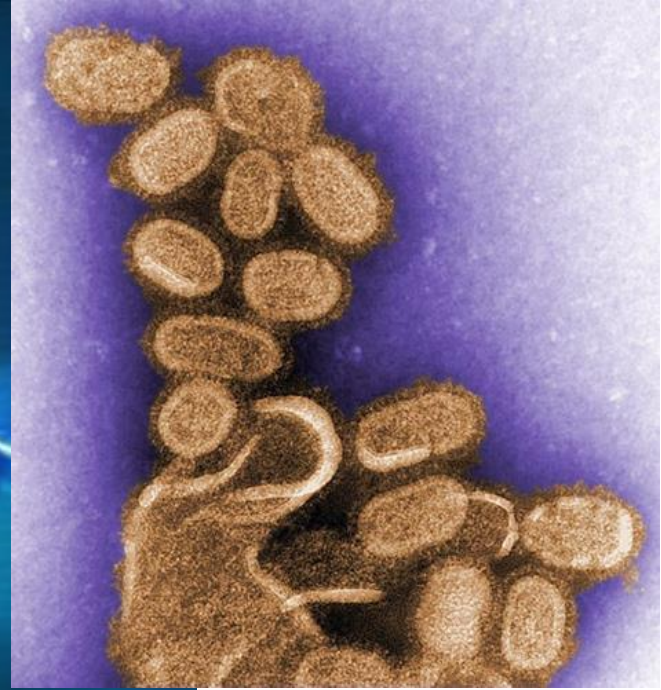
Photo credit: Dr. Ilaria Capua



AVIAN FLU: Are we ready?



SWINE FLU



DOMUZ GRİBİ (A H1N1)

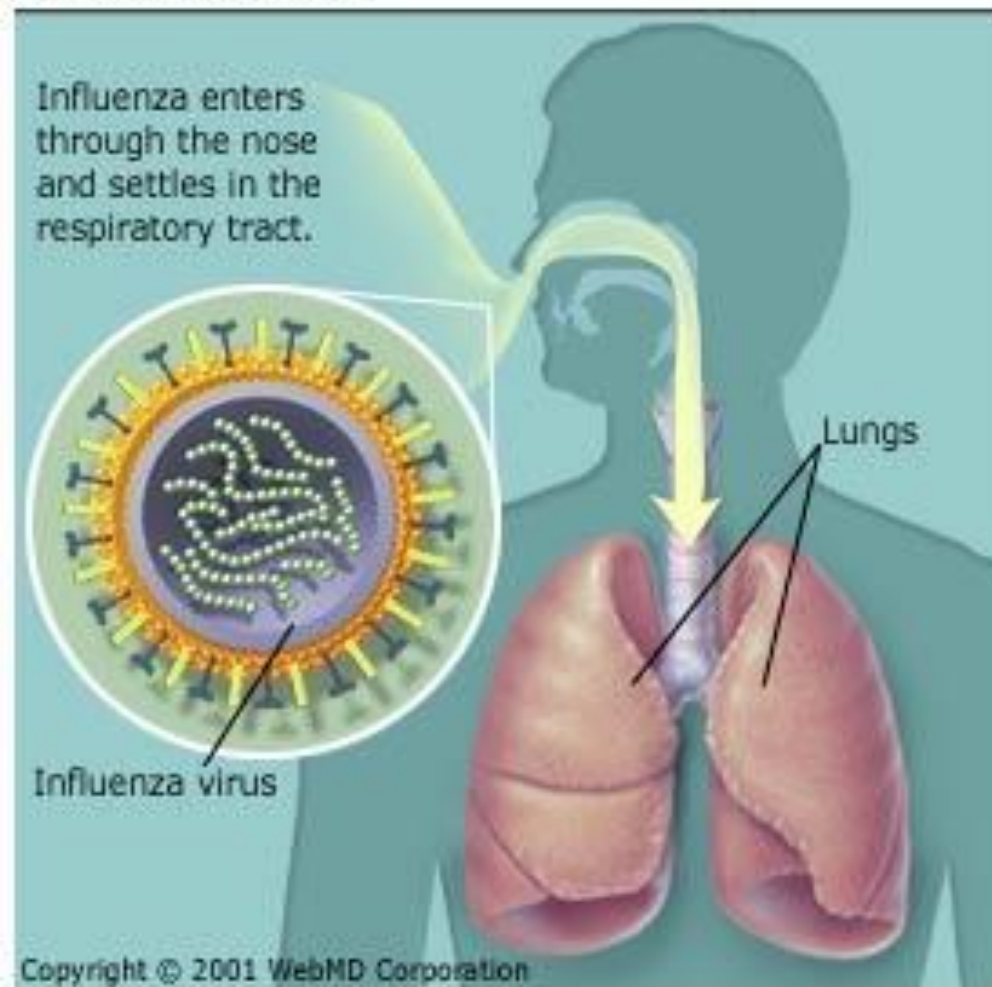
Uzm.Mehmet Aksakal



<https://cisaglobal.wordpress.com/2014/10/>



Influenza Virus



Influenza Pandemileri, insan ölümü

1918 – H1N1, 100 milyon

1957 – H2N2, 100 bin

1968 – H3N2, 700 bin-1 milyon

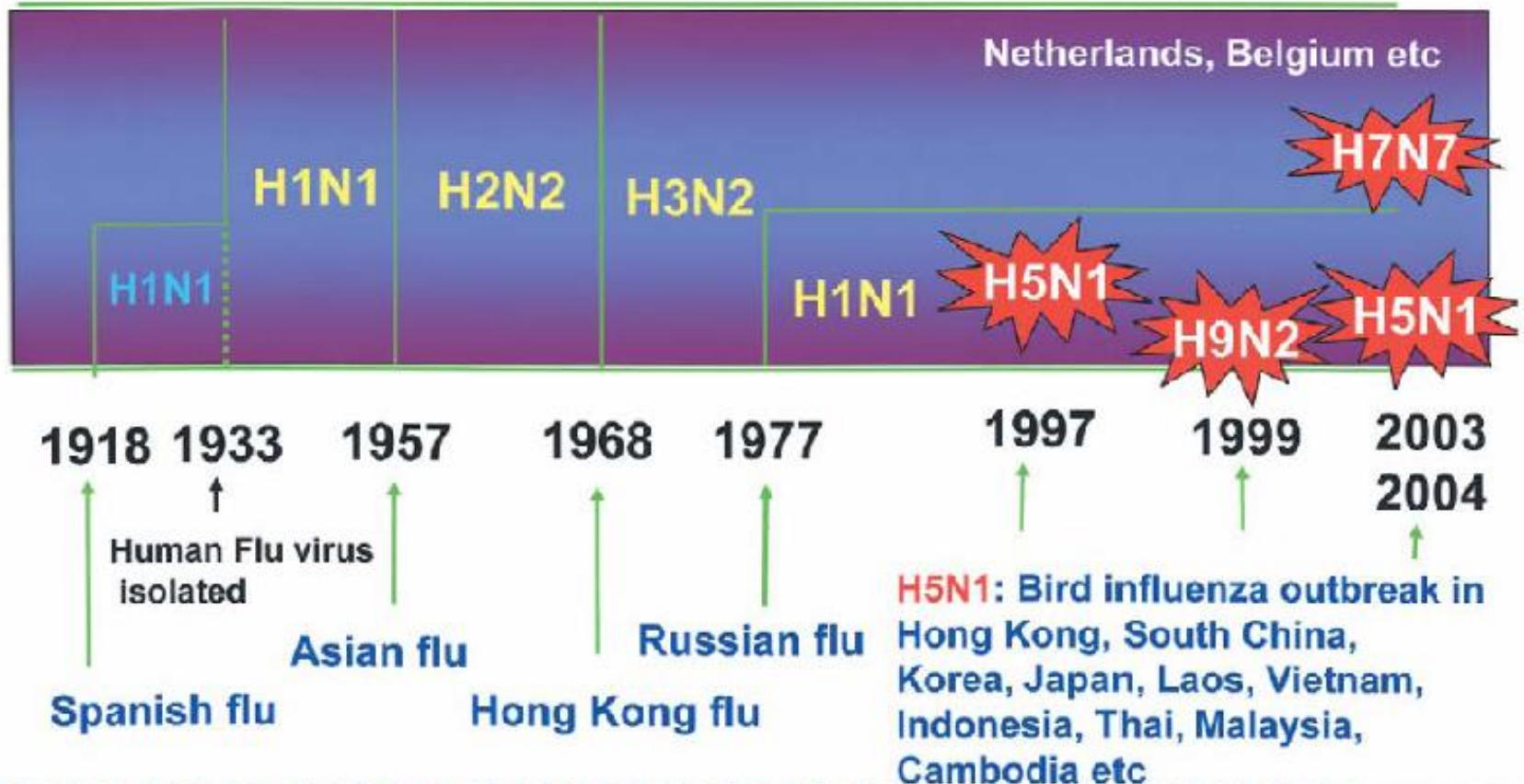
1997 – H5N1, 18 kişi, 18 milyon kanatlı

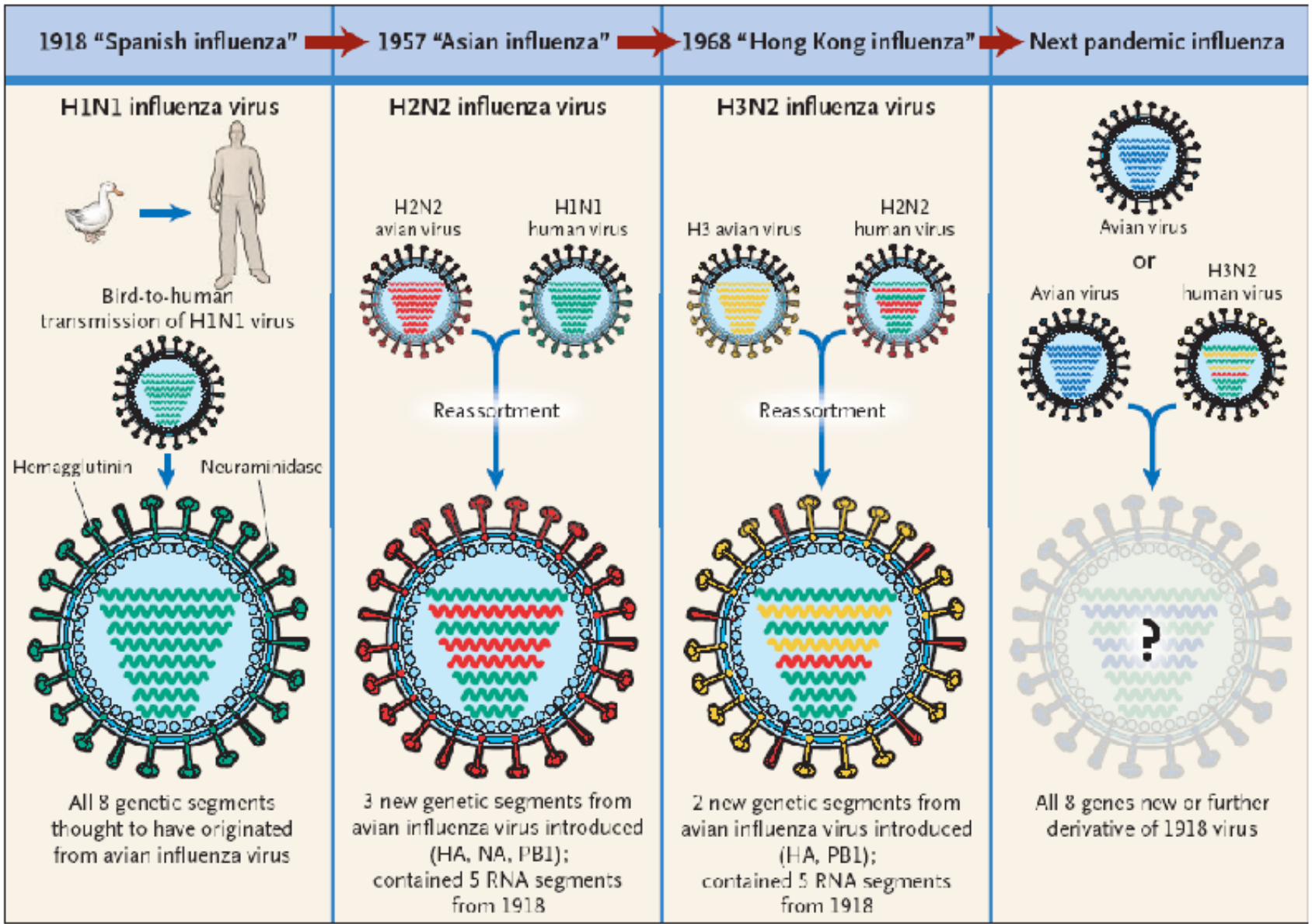
2003-2005 – H5N1, 142 kişi

2009-2010 – H1N1, 18.000

Influenza A Pandemic

Subtype: H, Hemagglutinin; N, Neuraminidase

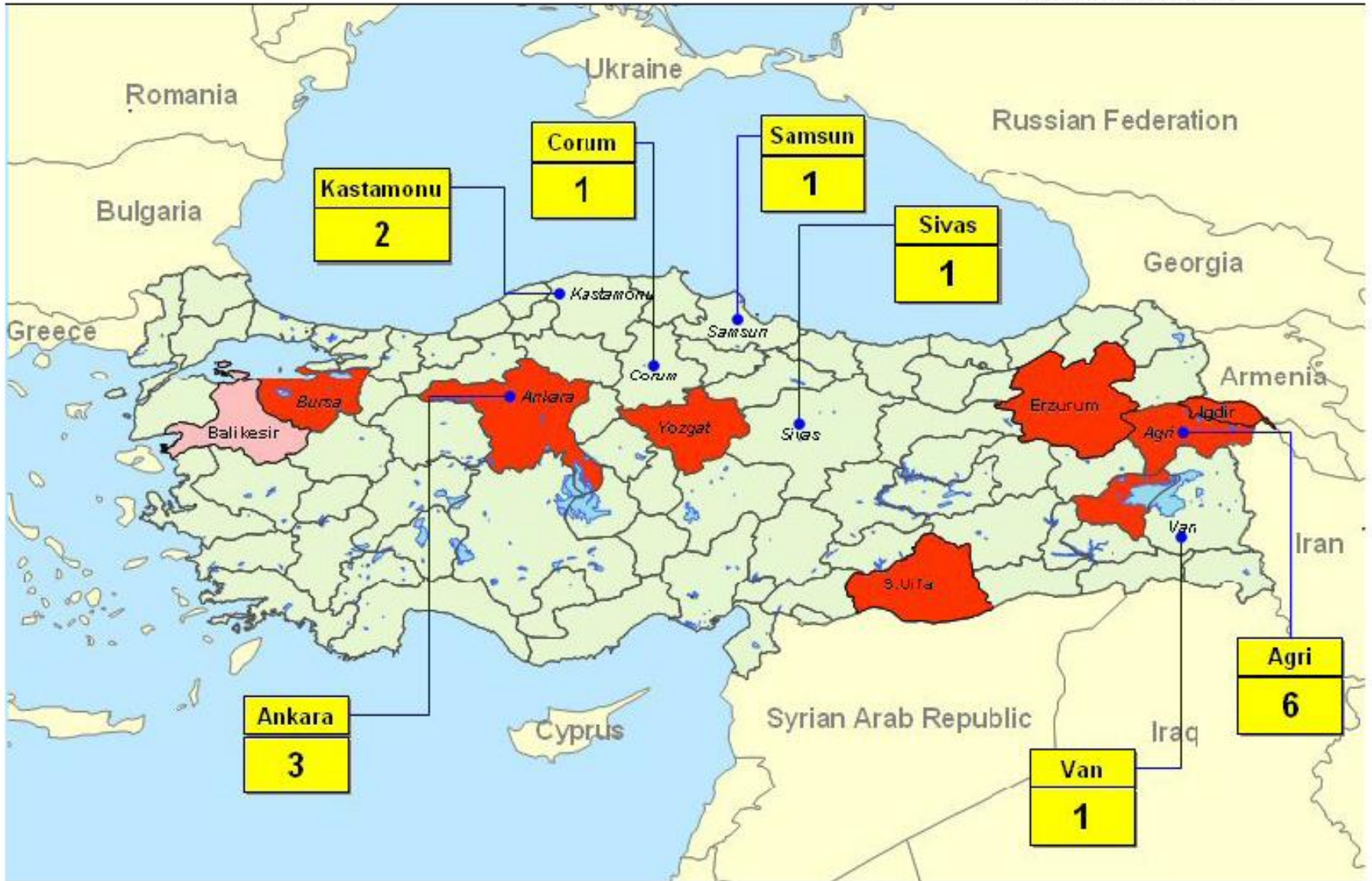




Turkey: Outbreaks of Avian Influenza in birds and humans

As of 11 January 00E

- Provinces with outbreaks in poultry
- Provinces with outbreaks in humans; number of confirmed cases

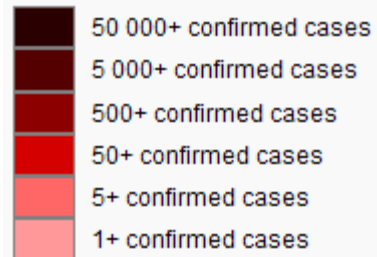
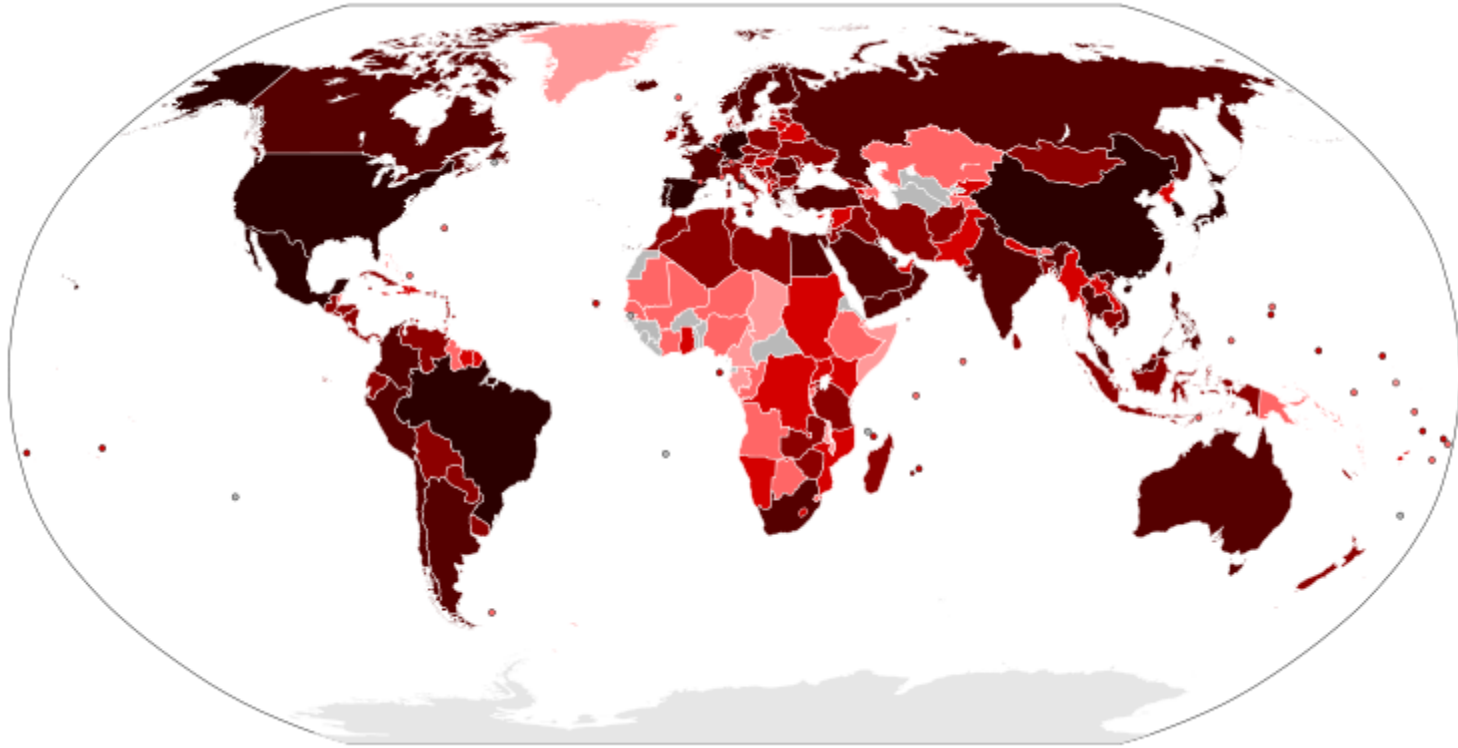


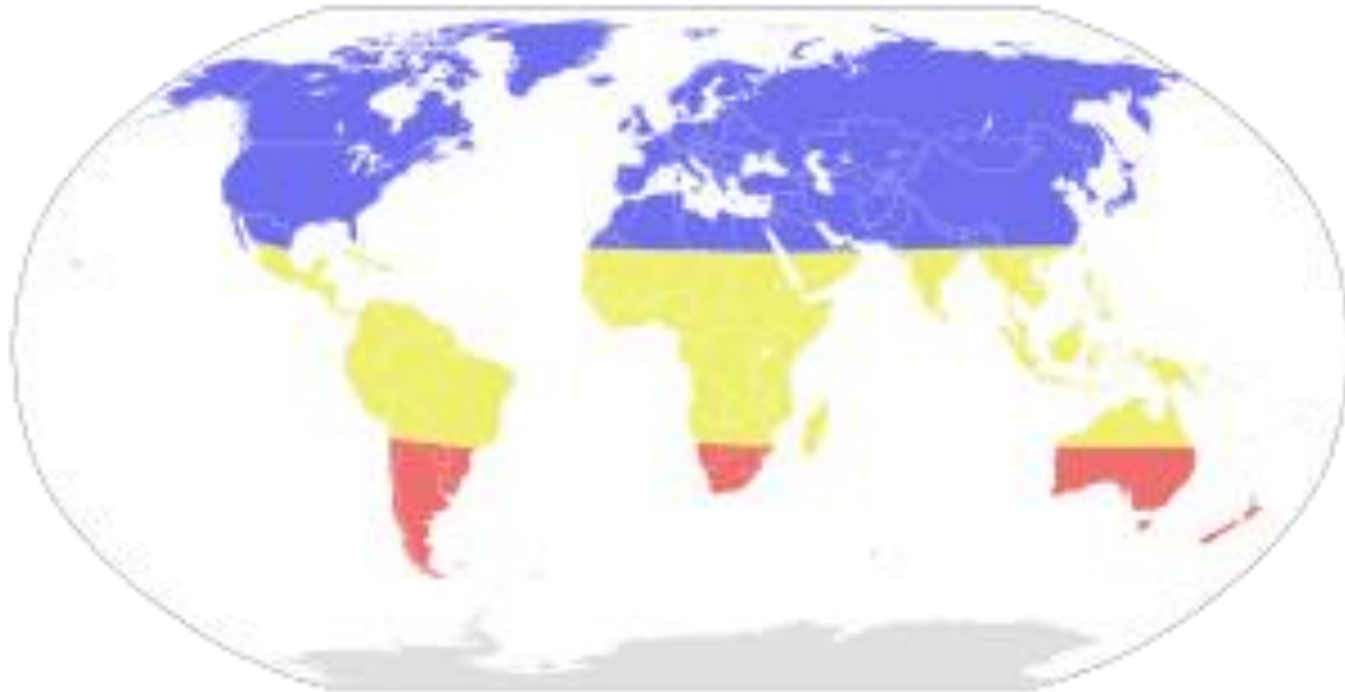
Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO

11 April 2007

Country	2003		2004		2005		2006		2007		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	1	1	7	7
China	1	1	0	0	8	5	13	8	2	1	24	15
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	16	4	34	14
Indonesia	0	0	0	0	20	13	55	45	6	5	81	63
Iraq	0	0	0	0	0	0	3	2	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	2	2	2	2
Nigeria	0	0	0	0	0	0	0	0	1	1	1	1
Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	0	0	93	42
Total	4	4	46	32	98	43	115	79	28	14	291	172

2009 yılı pandemisi-H1N1-postpandemik period





Seasonal risk areas for influenza: November–April (blue), April–November (red), and year-round (yellow).

20th century flu pandemics

Pandemic	Year	Influenza virus type	People infected (approximate)	Estimated deaths worldwide	Case fatality rate
Spanish flu	1918–1919	A/H1N1 ^[183]	33% (500 million) ^[184]	20–100 million ^{[185][186][187]}	>2.5% ^[188]
Asian flu	1956–1958	A/H2N2 ^[183]	?	2 million ^[187]	<0.1% ^[188]
Hong Kong flu	1968–1969	A/H3N2 ^[183]	?	1 million ^[187]	<0.1% ^[188]
Seasonal flu [t 1]	Every year	mainly A/H3N2, A/H1N1, and B	5–15% (340 million – 1 billion) ^[189]	250,000–500,000 per year ^[176]	<0.1% ^[190]
Swine flu	2009–2010	Pandemic H1N1/09	> 622,482 (lab-confirmed) ^[191]	14,286 (lab-confirmed; ^[t 2] ECDC) ^[151] 18,036 (lab-confirmed; ^[t 2] WHO) ^[17]	0.03% ^[192]



İspanyol Pandemisi 1918 (50 - 100 milyon)

Influenza

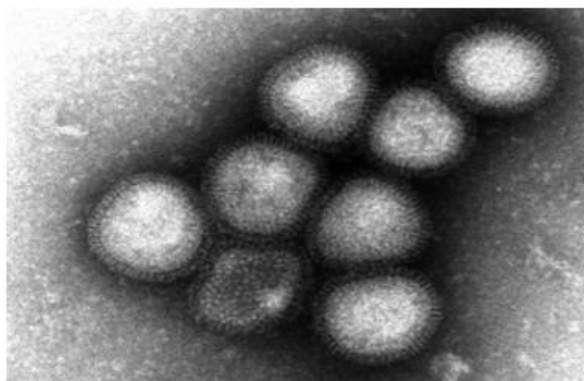
Influenza

- ▶ [Surveillance and monitoring](#)
- ▶ [GISRS and laboratory](#)
- ▶ [PIP Framework](#)
- ▶ [Vaccines](#)
- ▶ [Patient care](#)
- ▼ [Human animal interface](#)

[Avian influenza in humans](#)

[Swine influenza in humans](#)

Avian influenza A(H7N9) virus



Courtesy of WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Japan

Avian influenza A(H7N9) is a subtype of influenza viruses that have been detected in birds in the past. This particular A(H7N9) virus had not previously been seen in either animals or people until it was found in March 2013 in China.

However, since then, infections in both humans and birds have been observed. The disease is of concern because most patients have become severely ill. Most of the cases of human infection with this avian H7N9 virus have reported recent exposure to live poultry or potentially contaminated environments, especially markets where live birds have been sold. This virus does not appear to transmit easily from person to person, and sustained human-to-human transmission has not been reported.

FluNet Summary

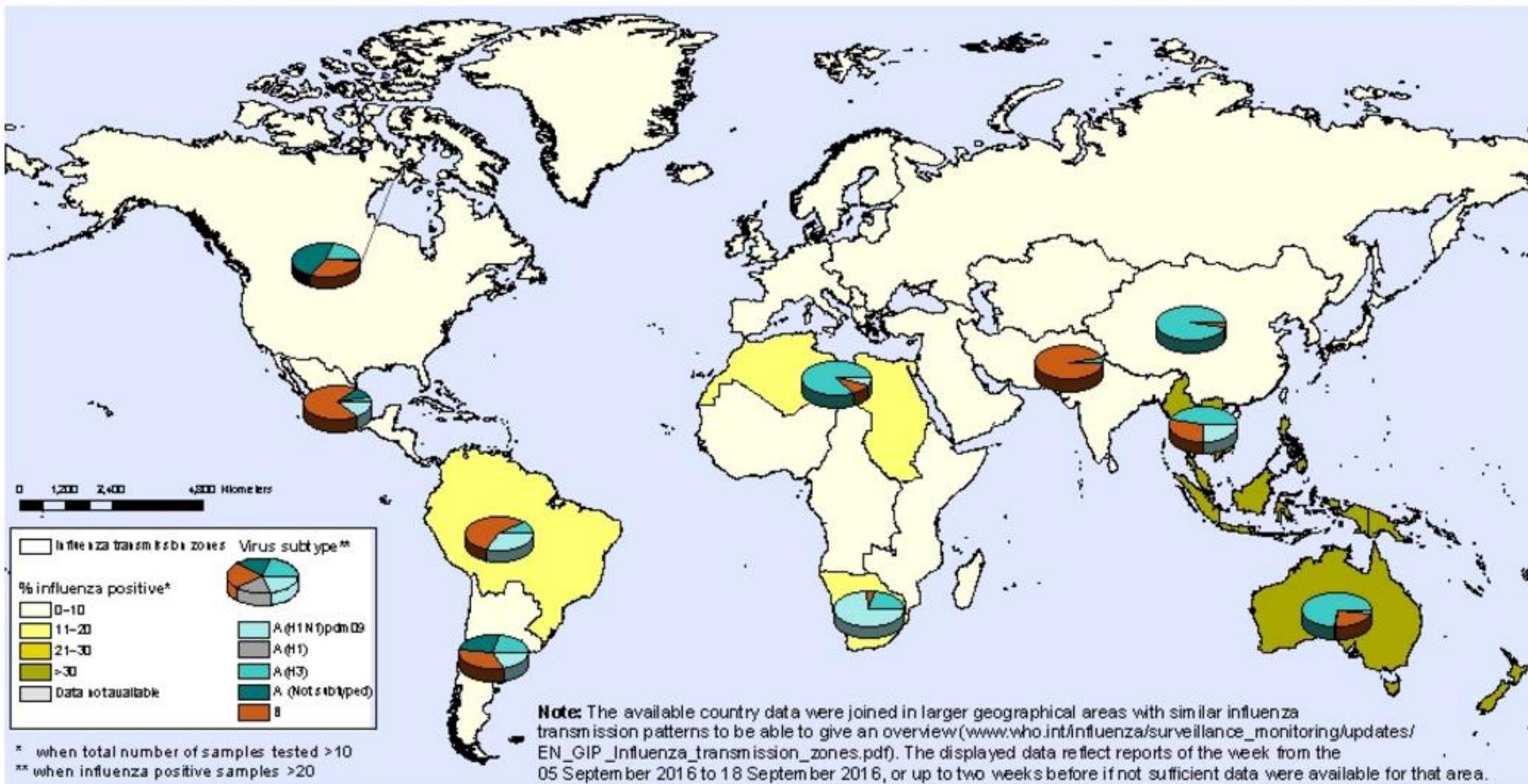
03 October 2016

Source: Laboratory confirmed data from the Global Influenza Surveillance and Response System (GISRS).

National Influenza Centres (NICs) and other national influenza laboratories from 73 countries, areas or territories reported data to FluNet for the time period from 05 September 2016 to 18 September 2016 ^a (data as of 2016-09-30 03:56:53 UTC). The WHO GISRS laboratories tested more than 44178 specimens during that time period. 2763 were positive for influenza viruses, of which 2260 (81.8%) were typed as influenza A and 503 (18.2%) as influenza B. Of the sub-typed influenza A viruses, 246 (12%) were influenza A(H1N1)pdm09 and 1812 (88%) were influenza A(H3N2). Of the characterized B viruses, 31 (24.6%) belonged to the B-Yamagata lineage and 95 (75.4%) to the B-Victoria lineage.

Percentage of respiratory specimens that tested positive for influenza By influenza transmission zone

Status as of 30 September 2016



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 and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/flu-net).



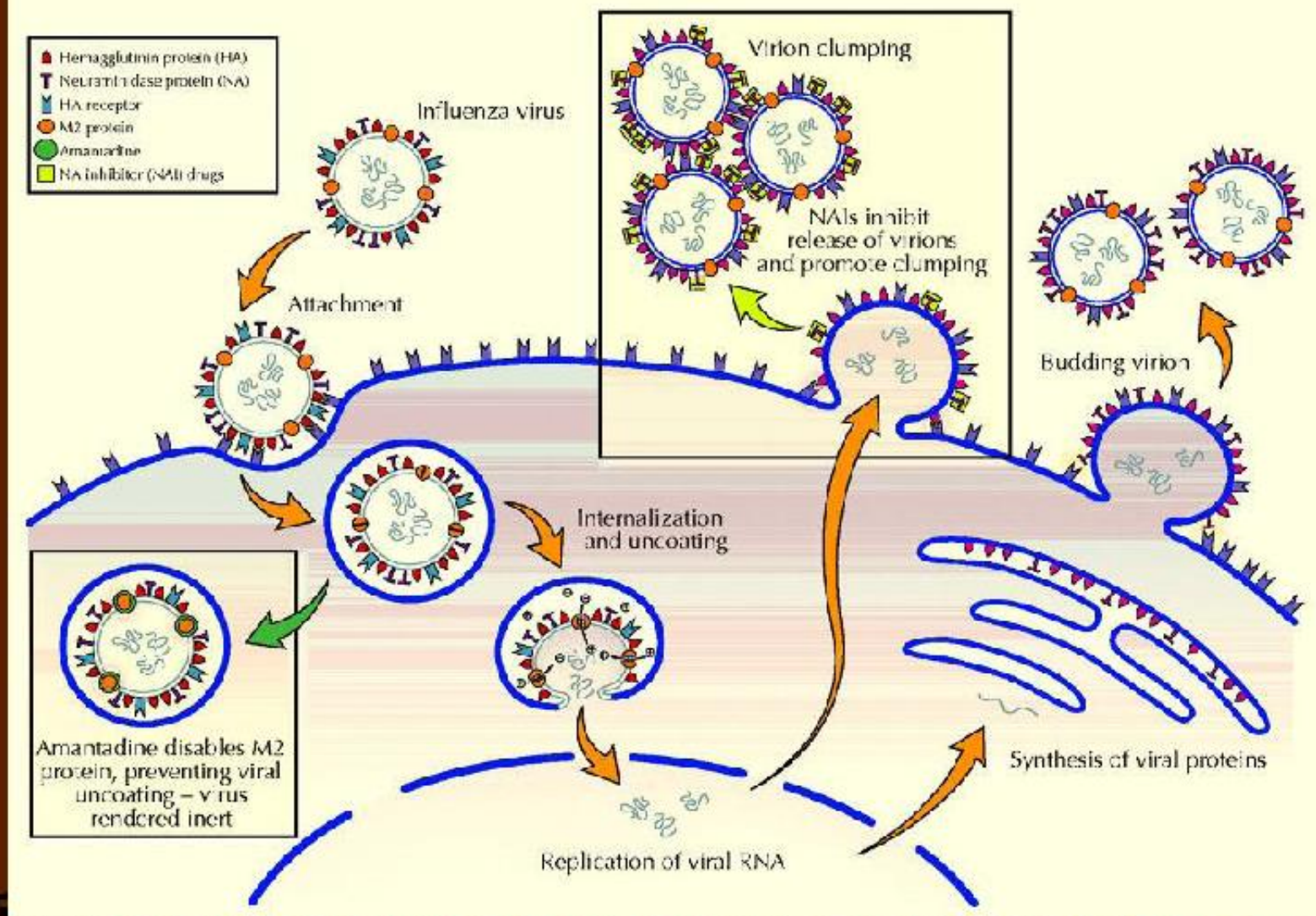
Terapi, Korunma

- Amantadine, Rimantadine – **M2** inhibitörleri
Hücre içine alınan virionun zarından ayrılmasını engelleme,

Viral proteinlerin hücreye girişini engellemek

- Zanamivir, Oseltamivir – **Neuraminidaz** inhibitörü
Virionun hücre dışına salınımını engelleme,
kümeleştirme, yeni hücrelerin enfeksiyonunu engelleme

Mechanism of anti-Influenza viral drugs



Source: Stiver, CMAJ 168:49-56 (2003)

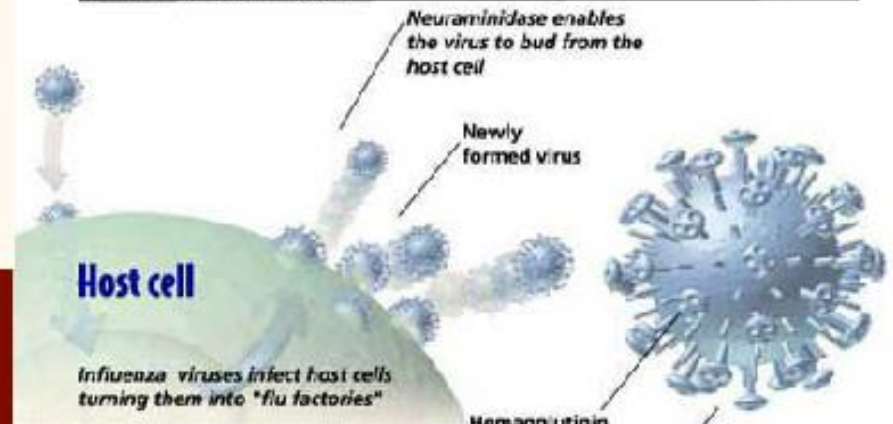


Source: Roche

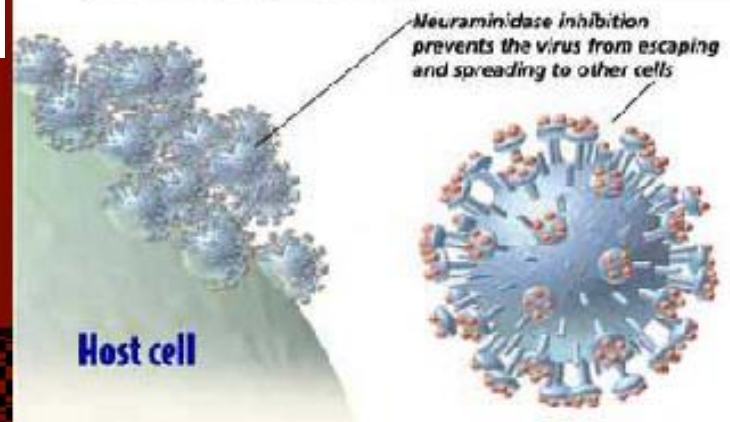
H5N1 viruslarının direnç kazanması!

The concept of neuraminidase inhibition

Influenza infection



Neuraminidase inhibition





2013-2014 Aşı Kompozisyonu

- an A/California/7/2009 (H1N1)pdm09-like virus^a;
- an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011^{b*};
- a B/Massachusetts/2/2012-like virus.

2014-2015 Aşı Kompozisyonu

- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Texas/50/2012 (H3N2)-like virus;
- a B/Massachusetts/2/2012-like virus.





Kaynaklar: www.cdc.gov/flu/avian, www.oie.int www.who.int

Taubenberger JK ve Morens DM (2006). 1918 Influenza: the Mother of All Pandemics. *Em Inf Dis*. Vol 12, 1, 15-22
adlı yayından alıntı: Frost WH (1920). Statistics of influenza morbidity. *Public Health Rep*. 35: 584-97.

Russel CJ ve Webster RG (2005). The Genesis of a Pandemic Influenza Virus. *Cell* 368-371.

Hatta M ve Kawaoka Y (2005). A clue to the molecular mechanism of virulence of highly pathogenic H5N1 avian Influenza viruses isolated in 2004. 55-62

Vranjac A (2006). Avian influenza and human cases. *Rev Saude Publica*. 40 (1) 187-190.

Keawcharoen J ve ark (2004). Avian Influenza H5N1 in Tigers and Leopards. *Emerging Infectious Diseases*. Vol 10, 12, 2189-2191.

Kuiken ve ark (2003). Pathology of Human Influenza A (H5N1) Virus Infection in Cynomolgus Macaques (*Macaca fascicularis*). *Vet Pathol*. 40: 304-310.

“Umarım
insan gribine
yakalanmam”

