

INFLUENZA AVIAR: Clínica y Tratamiento

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Cumulative Number of Virologically Confirmed Cases of Avian Influenza A (H5N1) in Humans Reported to the WHO since 2003

Table 1. Cumulative Number of Virologically Confirmed Cases of Avian Influenza A (H5N1) in Humans Reported to the WHO since 2003.*

Date of Onset	Vietnam		Thailand		Cambodia		Indonesia		Total	
	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths	No. of Cases	No. of Deaths
December 26, 2003, to March 10, 2004	23	16	12	8	0	0	0	0	35	24
July 19, 2004, to October 8, 2004	4	4	5	4	0	0	0	0	9	8
December 16, 2004, to August 5, 2005†	63	20	0	0	4	4	1	1	68	25
Total	90	40	17	12	4	4	1	1	112	57

* Additional details are available at www.who.int/csr/disease/avian_influenza/country/cases_table_2005_08_05/en/print.

† Cases continue to occur. The total number of cases includes fatal ones. This list does not include the 18 patients, 6 of whom died, identified in Hong Kong in 1997 or the 2 patients, 1 of whom died, identified in Fujian Province, China, in 2003.

The Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5, *N Engl J Med* 2005;353:1374-1385

TRANSMISION

- Inhalación de gotas infecciosas, contacto directo, fomites.

Animal a Humano: Contacto directo, manipulación de aves.

Humano a Humano: brotes caseros

Ambiente a Humano, contaminación directa

Outcome or Measure	Hong Kong, 1997 (N=18)	Thailand, 2004 (N=17)	Vietnam, 2004 (N=10)	Ho Chi Minh City, 2005 (N=10)	Cambodia, 2005 (N=4)
Age — yr					
Median	9.5	14	13.7†	19.4†	22
Range	1–60	2–58	5–24	6–35	8–28
Male sex — no. (%)	8 (44)	9 (53)	6 (60)	3 (30)	1 (25)
Time from last presumed exposure to onset of illness — days					
Median	NS	4	3	NS	NS
Range		2–8	2–4		
No. of family clusters		1	2	1	1
Patients with exposure to ill poultry — no./total no. (%)	11/16 (70) visited poultry markets	14/17 (82)	8/9 (89)	6/6 (100) Status of 4 unknown	3/4 (75)
Time from onset of illness to presentation or hospitalization — days					
Median	3	NS	6	6	8‡
Range	1–7		3–8	4–7	5–8
Clinical presentation — no./total no. (%)					
Fever (temperature >38°C)	17/18 (94)	17/17 (100)	10/10 (100)	10/10 (100)	4/4 (100)
Headache	4/18 (22)	NS	NS	1/10 (10)	4/4 (100)
Myalgia	2/18 (11)	9/17 (53)	0	2/10 (20)	NS
Diarrhea	3/18 (17)	7/17 (41)	7/10 (70)	NS	2/4 (50)
Abdominal pain	3/18 (17)	4/17 (24)	NS	NS	2/4 (50)
Vomiting	6/18 (33)	4/17 (24)	NS	1/10 (10)	0
Cough§	12/18 (67)	16/17 (94)	10/10 (100)	10/10 (100)	4/4 (100)
Sputum	NS	13/17 (76)	5/10 (50)	3/10 (30)	NS
Sore throat	4/12 (33)	12/17 (71)	0	0	1/4 (25)
Rhinorrhea	7/12 (58)	9/17 (53)	0	0	NS
Shortness of breath¶	1/18 (6)	13/17 (76)	10/10 (100)	10/10 (100)	NS
Pulmonary infiltrates	11/18 (61)	17/17 (100)	10/10 (100)	10/10 (100)	4/4 (100)
Lymphopenia¶¶	11/18 (61)	7/12 (58)	NS	8/10 (80)	1/2 (50)
Thrombocytopenia	NS	4/12 (33)	NS	8/10 (80)	1/2 (50)
Increased aminotransferase levels	11/18 (61)	8/12 (67)	5/6 (83)	7/10 (70)	NS
Hospital course — no. (%)					
Respiratory failure	8 (44)	13 (76)	9 (90)	7 (70)	4 (100)
Cardiac failure	NS	7 (41)	NS	0	NS
Renal dysfunction	4 (22)	5 (29)	1 (10)	2 (20)	NS
Antiviral therapy					
Amantadine	10 (56)	0	0	0	NS
Ribavirin	1 (6)	0	2 (20)	0	
Oseltamivir	0	10 (59)	5 (50)	10 (100)	
Corticosteroids**	5 (28)	8 (47)	7 (70)	5 (50)	NS
Inotropic agents	NS	8 (47)	2 (20)	NS	
Time from onset of illness to death — days					
Median	23	12	9	12.8†	8
Range	8–29	9–30	4–17	4–21	6–10
Deaths — no. (%)	6 (33)	12 (71)	8 (80)	8 (80)	4 (100)

* Data from Hong Kong are from Yuen et al.¹³ and Chan,¹⁴ data on Thailand are from Chotpitayasonondh et al.,¹⁵ data on Vietnam are from Hien et al.,¹⁶ or data were presented at the WHO Consultation. NS denotes not stated.

† The median was unavailable, and the mean is given.

‡ Some patients had multiple outpatient illness visits before hospitalization.

§ In Hong Kong, shortness of breath later developed in 11 of 18 patients (61 percent) during hospitalization. In Thailand, all patients had cough and shortness of breath at hospitalization.

¶ In Vietnam, the median lymphocyte count was 700 per cubic millimeter (range, 250 to 1100), and the median leukocyte count was 2100 per cubic millimeter (range, 1200 to 3400).¹⁶ In Thailand, the mean leukocyte count was 4900 per cubic millimeter (range, 1200 to 13,600),¹⁵ and the lymphocyte count was 1453 per cubic millimeter (range, 454 to 3400).

¶¶ In Thailand, 7 of 10 patients given oseltamivir died a mean of 11 days after the onset of symptoms (range, 5 to 22 days), as compared with 5 of 7 untreated patients. Oseltamivir was used in conventional doses (75 mg orally, twice daily for 5 to 10 days with a weight-based dose reduction in children) in the majority of recipients. In Vietnam, one of five recipients of oseltamivir recovered, as compared with one of five untreated patients.¹⁶ The use of relatively low doses of oral ribavirin in two patients was not associated with obvious effectiveness.

** Initial patients in Vietnam received methylprednisolone (5 mg per kilogram of body weight per day or 1 to 2 mg per kilogram) for one to four days¹⁶; subsequent patients in Ho Chi Minh City received dexamethasone at 0.4 mg per kilogram per day for five days in a randomized trial. In Thailand, methylprednisolone (2 mg per kilogram per day) was administered for two to five days.

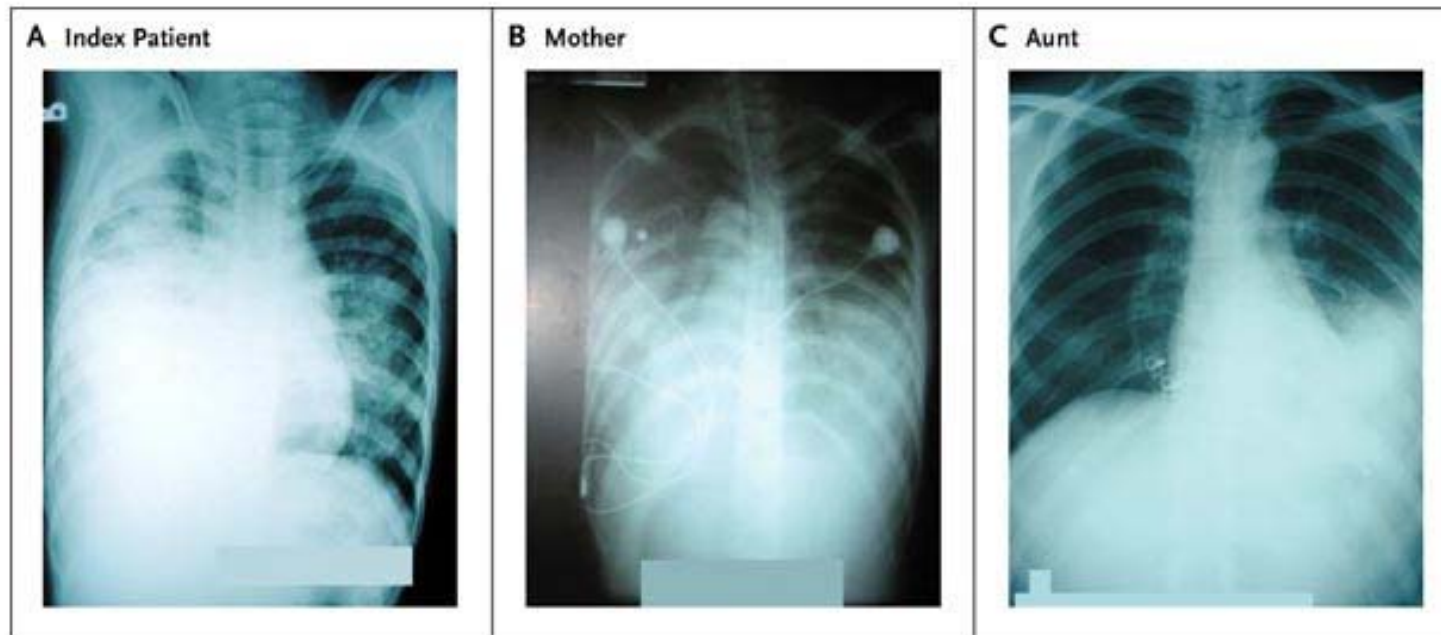
Síntomas iniciales

- Debuta con fiebre alta ($>38^{\circ}\text{C}$) y síntomas respiratorios bajos (SRBs).
- Síntomas respiratorios altos son infrecuentes
- La conjuntivitis es rara
- Diarrea acuosa (puede estar sola una semana antes), vómitos, dolor abdominal, dolor pleurítico y sangrado por encías y nariz

Curso Clínico

- SRBs son el debut. Disnea, taquipnea y crépitos son comunes.
- Espujo es variable y puede ser sanguinolento.
- Clínica es de Neumonía
- Rx tórax: infiltrados difusos, multifocales, en parche, intersticiales, consolidación lobar o segmentaria. Se presentan en una mediana de 7 días luego del inicio de fiebre.
- Efusión pleural no es común

Chest Radiographs from the Three Patients with Avian Influenza A (H5N1)



Ungchusak, K. et al. N Engl J Med 2005;352:333-340

Complicaciones

- Progresión a falla respiratoria Asociada a ARDS e imágenes Rx difusas, bilaterales como vidrio esmerilado. Mediana 6 días.
- Falla multiorgánica: disfunción renal, compromiso cardiaco (dilatación cardiaca y arritmias supraventriculares)
- Hemorragia pulmonar
- Neumotórax
- Sepsis

Laboratorio

- Leucopenia (linfopenia)*
- Trombocitopenia*
- Aumento de TGO/TGP
- Aumento de Creatinina.
- Hiperglicemia

* Aumento de riesgo de muerte si presentes a la admisión

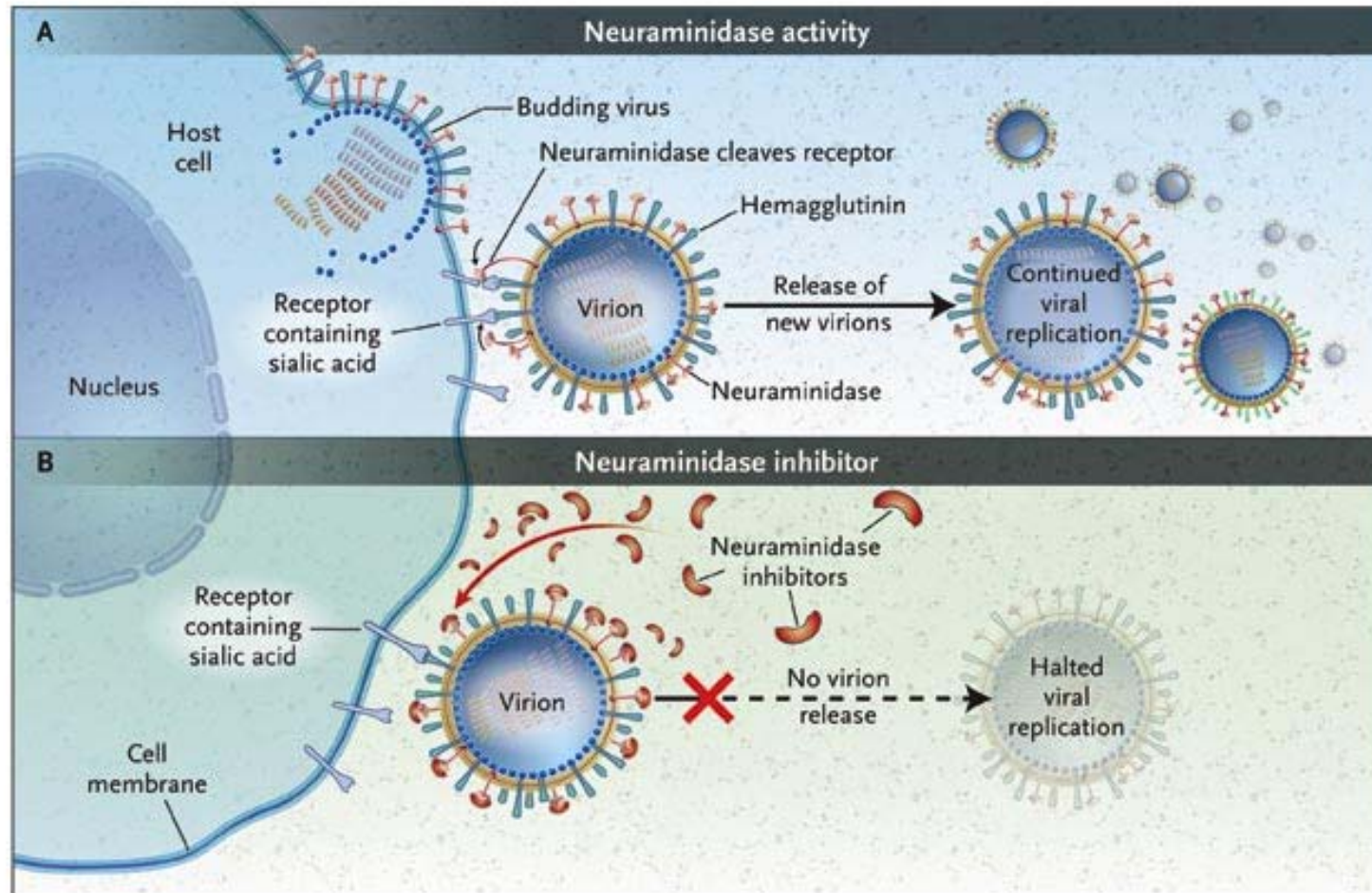
MORTALIDAD

- La tasa de fatalidad es cercana al 100%.
- Casos recientes son más severos en niños.
- Ocurre entre 9 a 10 días luego del inicio de los síntomas.
- La mayoría fallece de insuficiencia respiratoria progresiva.

MANEJO

- Muchos requieren soporte ventilatorio en las 48 horas de la admisión.
- Ingresan a UCI
- Tratamiento empírico con antibióticos, antivirales (sólos o con esteroides).
- Introducción temprana de Oseltamivir es de beneficio.
- Oxígeno suplementario
- Nebulizadores no están indicados.

Mechanism of Action of Neuraminidase Inhibitors



Moscona, A. N Engl J Med 2005;353:1363-1373

Dosing Schedule of Neuraminidase Inhibitors for the Treatment and Prevention of Influenza, According to Patient's Age and Coexisting Illnesses

Table 1. Dosing Schedule of Neuraminidase Inhibitors for the Treatment and Prevention of Influenza, According to Patient's Age and Coexisting Illnesses.*

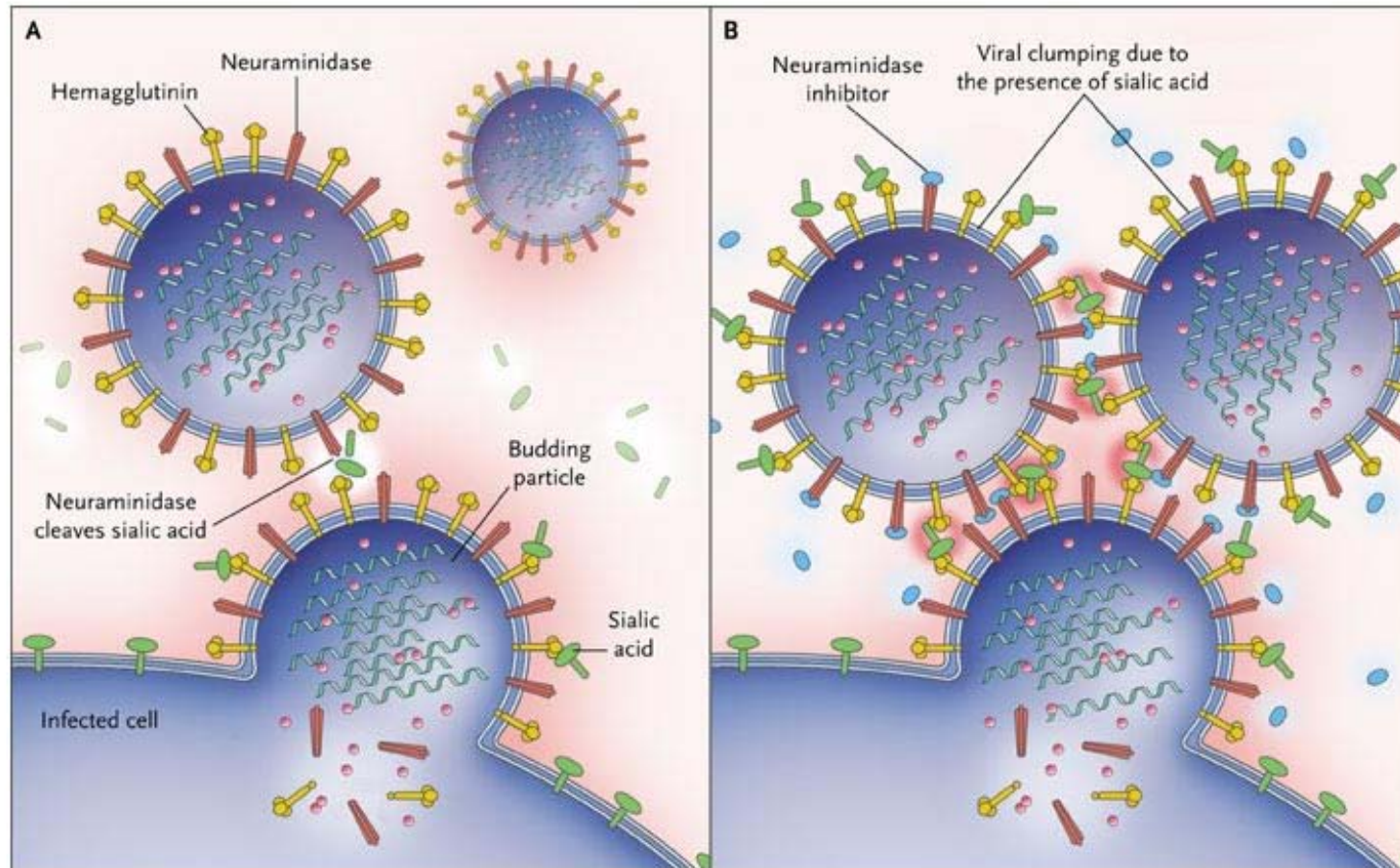
Antiviral Drug	Recommended Dose According to Age				Coexisting Illness	
	1–6 yr	7–12 yr	13–64 yr	≥65 yr	Renal Disease	Hepatic Disease
Treatment						
Zanamivir	NA	10 mg (equivalent to 2 inhalations) twice daily for 5 days	10 mg (equivalent to 2 inhalations) twice daily for 5 days	10 mg (equivalent to 2 inhalations) twice daily for 5 days	10 mg (equivalent to 2 inhalations) twice daily for 5 days	—
Oseltamivir	Weight <15 kg: 30 mg twice daily for 5 days; 15–23 kg: 45 mg twice daily for 5 days; >23–40 kg: 60 mg twice daily for 5 days; >40 kg: 75 mg twice daily for 5 days	Weight <15 kg: 30 mg twice daily for 5 days; 15–23 kg: 45 mg twice daily for 5 days; >23–40 kg: 60 mg twice daily for 5 days; >40 kg: 75 mg twice daily for 5 days	75 mg twice daily for 5 days	75 mg twice daily for 5 days	For adults, reduce dose if creatinine clearance is ≤30 ml/min; if creatinine clearance is 10–30 ml/min, 75 mg once daily†	Not evaluated
Prevention						
Oseltamivir	NA	NA	75 mg once daily for >7 days (up to 6 wk)	75 mg once daily for >7 days (up to 6 wk)	If creatinine clearance is 10–30 ml/min, 75 mg every other day†	Not evaluated

* The doses listed are those currently approved in the United States. NA denotes not applicable.

† No regimen is available for patients with end-stage renal disease.

Moscona, A. N Engl J Med 2005;353:1363-1373

Restricted by a Neuraminidase Inhibitor (Panel B)

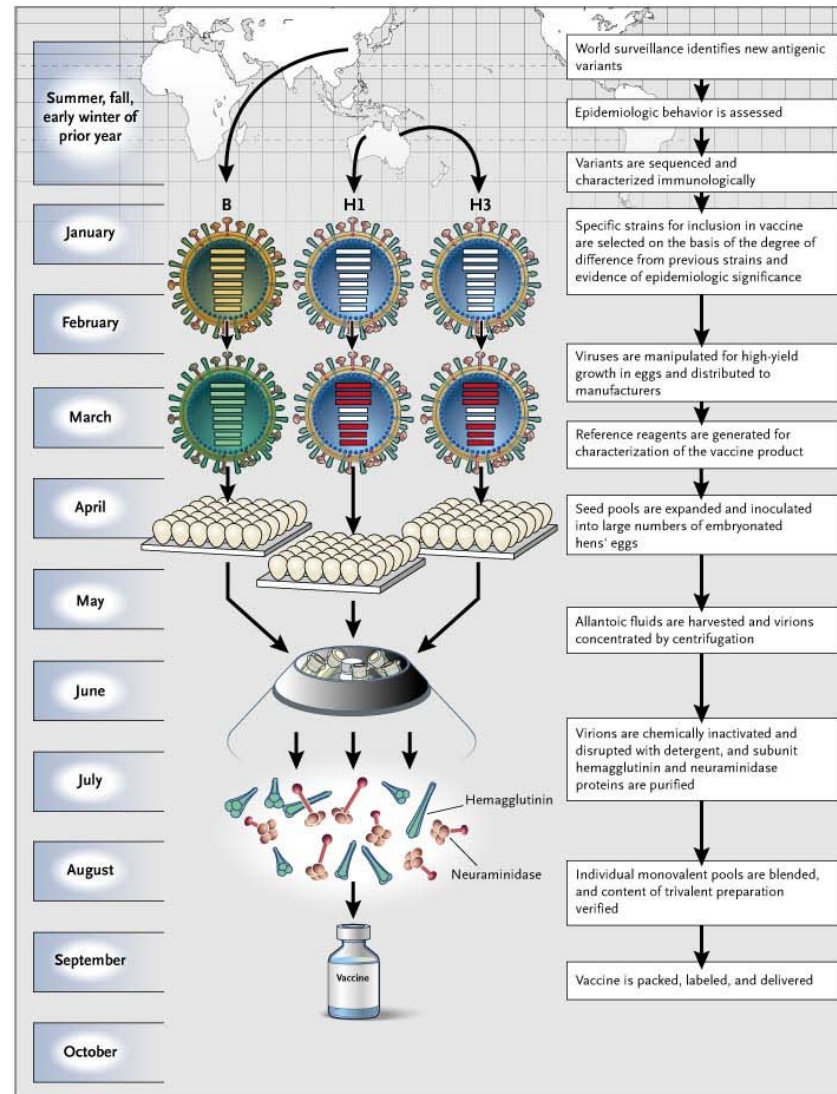


Monto, A. S. N Engl J Med 2005;352:323-325

Detección de casos

- **Sospechar en todo paciente con insuficiencia respiratoria en territorios con gripe aviar (H5N1).**
- **Sobre todo si tiene encefalopatía o diarrea.**
- **El hisopado de faringe da mejor resultado que el de fosas nasales.**
- **Confirmación:**
 - Cultivo +**
 - PCR H5N1 +**
 - IF + H5**
 - 4x Ab H5 sobre el basal**

Outline of the Annual Process of Development, Manufacturing, and Distribution of Influenza Vaccine



Treanor, J. N Engl J Med 2004;351:2037-2040

PREVENCION

- **Vacunas**, no hay vacunas comerciales disponibles.
- **Control de Transmisión Nosocomial**, respiradores N95 o múltiples mascarillas quirúrgicas
- **Contactos cercanos y de casa**, debe recibir profilaxis post exposición (Oseltamivir 75mg PO QD x 7 a 10 días). **Cuarentena**, en los casos de potencial transmisión humana

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SPMI