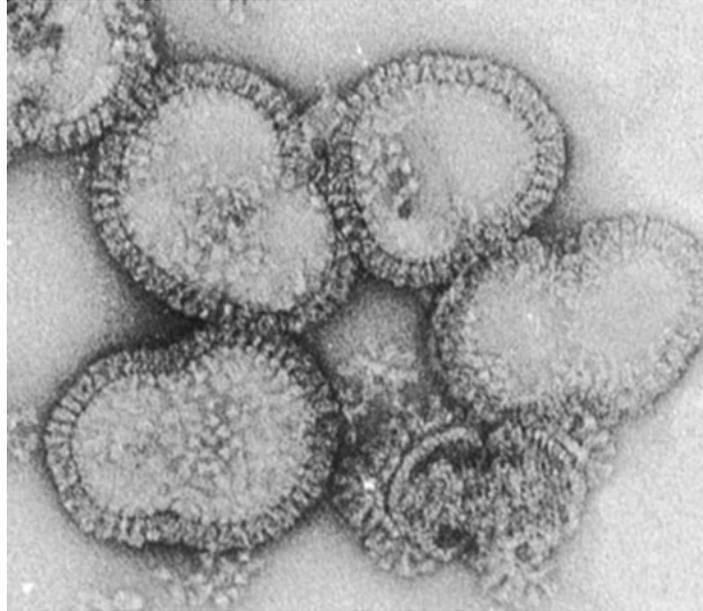


Influenza A/H5N1: Clinical Management



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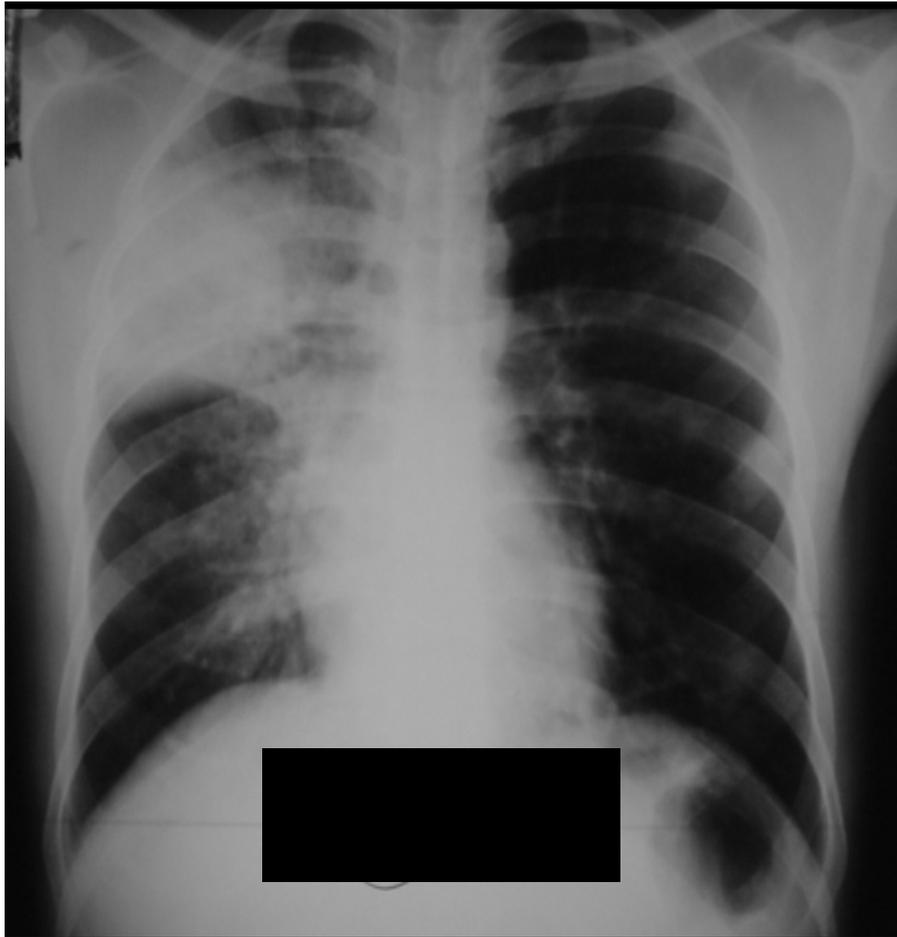


Symptoms:

Fever, sorethroat, cough,
shortness of breath,
diarrhoea, neurological

= non-specific, similar to
most other causes of CAP





Rapid progressive pneumonia and ARDS



CURRENT CONCEPTS

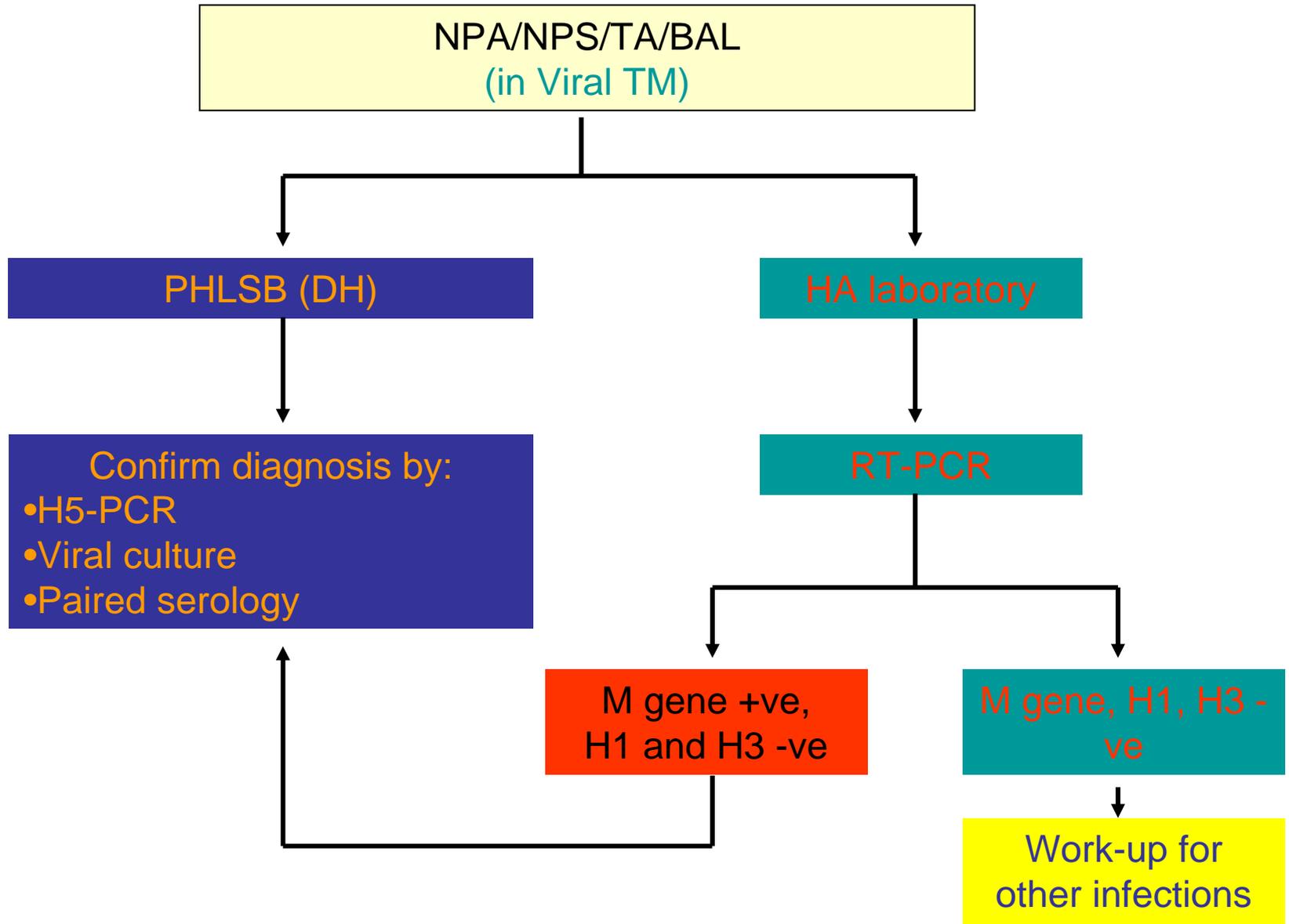
Update on Avian Influenza A (H5N1) Virus Infection in Humans

Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza A (H5N1) Virus*

Table 1. Case Fatality Proportion According to Clade or Subclade and Median Time from Onset of Illness to Hospitalization or Death in Patients with Confirmed Influenza A (H5N1) Illness.

Country	Predominant Clade or Subclade*	Case Fatality Proportion	Onset of Illness to Hospitalization		Onset of Illness to Death	
		<i>no. of patients/total no. (%)</i>	<i>days</i>	<i>no. of patients</i>	<i>days</i>	<i>no. of patients</i>
Cambodia, Thailand, Vietnam†	1	66/123 (54)	4	109	9	65
Indonesia	2.1	76/96 (79)	5	64	9	72
Azerbaijan, Djibouti, Egypt, Iraq, Nigeria, Turkey	2.2	26/59 (44)	3	36	9	24
China, Laos	2.3	17/26 (65)	5	16	10	17

Laboratory Diagnosis of H5 infection



Testing

- RT-PCR
 - TAT 1-2 days
 - Available in each HA cluster & PHLC
- Viral culture
 - TAT 3-7 days
 - Gold standard
 - For genetic and antigenic analysis
- Serology
 - TAT in terms of weeks

Practical Points of Note

- Use only sterile swab with a Dacron/Rayon tip.
 - Calcium alginate swabs, cotton swabs, or swabs with wooden ticks may inhibit PCR testing and should not be used.
- Use of rapid antigen detection is not recommended
 - Low sensitivity and risk of false negative result

Management of H5 infections

1. Supportive management

2. Antiviral use

– **Neuraminidase inhibitors** (Oseltamivir & Zanamivir)

- Zanamivir is active against oseltamivir-resistant variants with H274Y or N294S mutations

– WHO advises against the use of M2 inhibitors (Amantadine, Rimantadine) **alone** due to selection of resistant H5N1 strains

Antiviral Regimes for Treatment & Prophylaxis

Agent, group		Treatment	Chemoprophylaxis
<i>Oseltamivir</i>			
Adults		75mg BD	75mg daily
Children (aged 12 months or older), weight:	≤ 15 kg	30mg BD	30mg daily
	15 – 23 kg	45mg BD	45mg daily
	24 – 40 kg	60mg BD	60mg daily
	> 40 kg	75mg BD	75mg daily
<i>Zanamivir</i>			
Adults		Two 5mg inhalations BD	Two 5mg inhalations (10 mg in total) once per day
Children		Two 5mg inhalations BD (aged ≥ 7 yrs)	Two 5mg inhalations (10 mg in total) once per day (aged ≥ 5 yrs)



衛生防護中心
Centre for Health Protection

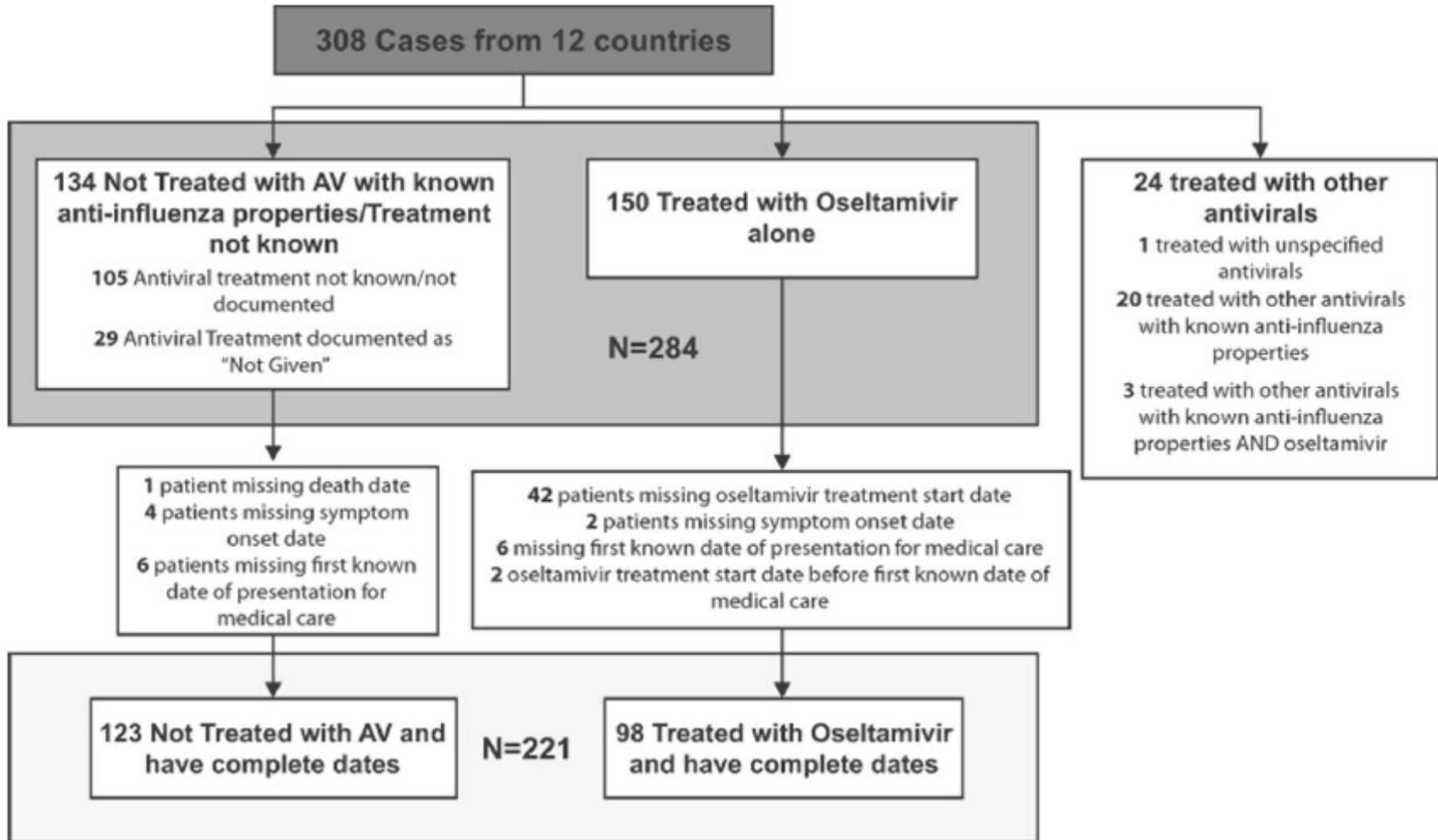
Scientific Committee on Emerging and Zoonotic Diseases

**General Guide to Doctors:
Antiviral Use for Novel Influenza
Treatment and Prophylaxis**

- N.B. Use of modified regimen of oseltamivir for adult, including a two-fold higher dosage (150 mg BD), longer duration (a total of 10 days) and combination therapy with amantadine or rimantadine 100 mg BD may be considered on a case by case basis, especially in patients with pneumonia or progressive disease

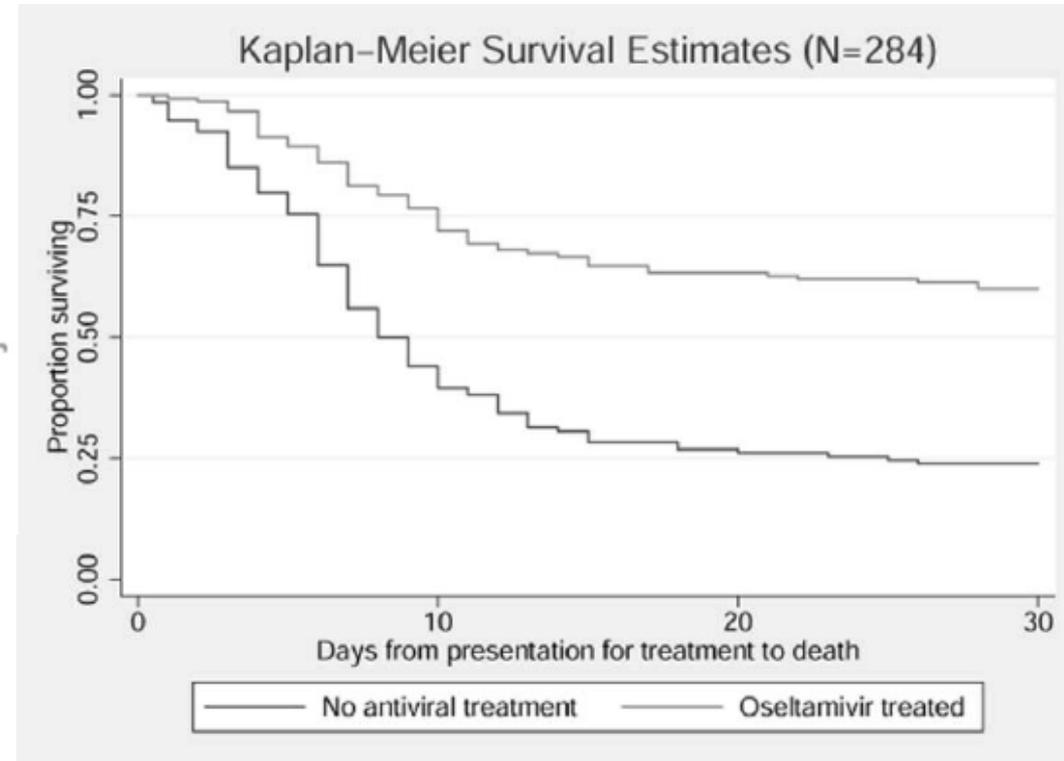
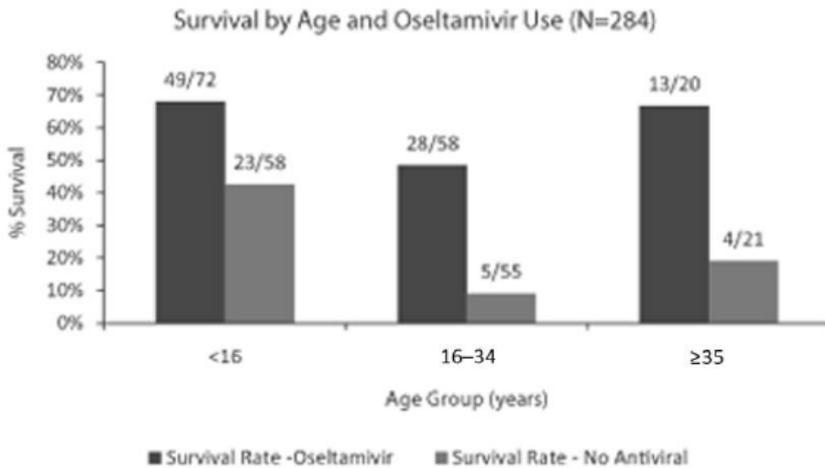
Effectiveness of Antiviral Treatment in Human Influenza A(H5N1) Infections: Analysis of a Global Patient Registry

Journal of Infectious Disease, 2010



Effectiveness of Antiviral Treatment in Human Influenza A(H5N1) Infections: Analysis of a Global Patient Registry

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Antiviral treatment can reduce mortality; the earlier the better.

Convalescent Plasma Therapy in H5N1 Disease

- Case report of 31 yo male who presented with 4 day Hx of fever, cough, and sputum
 - CXR on day 6 showed LLL pneumonia
 - Tracheal aspirate + H5N1 by RT-PCR and culture
 - Oseltamivir 150 mg bid started day 9 of illness but progressive bilateral pneumonia
 - Convalescent plasma infusions from H5 survivor (200 ml X 3) on days 12-13
 - Plasma neutralizing ab titer of 1:80
 - Hospital discharge on day 30

Convalescent Plasma Therapy in H5N1 Disease

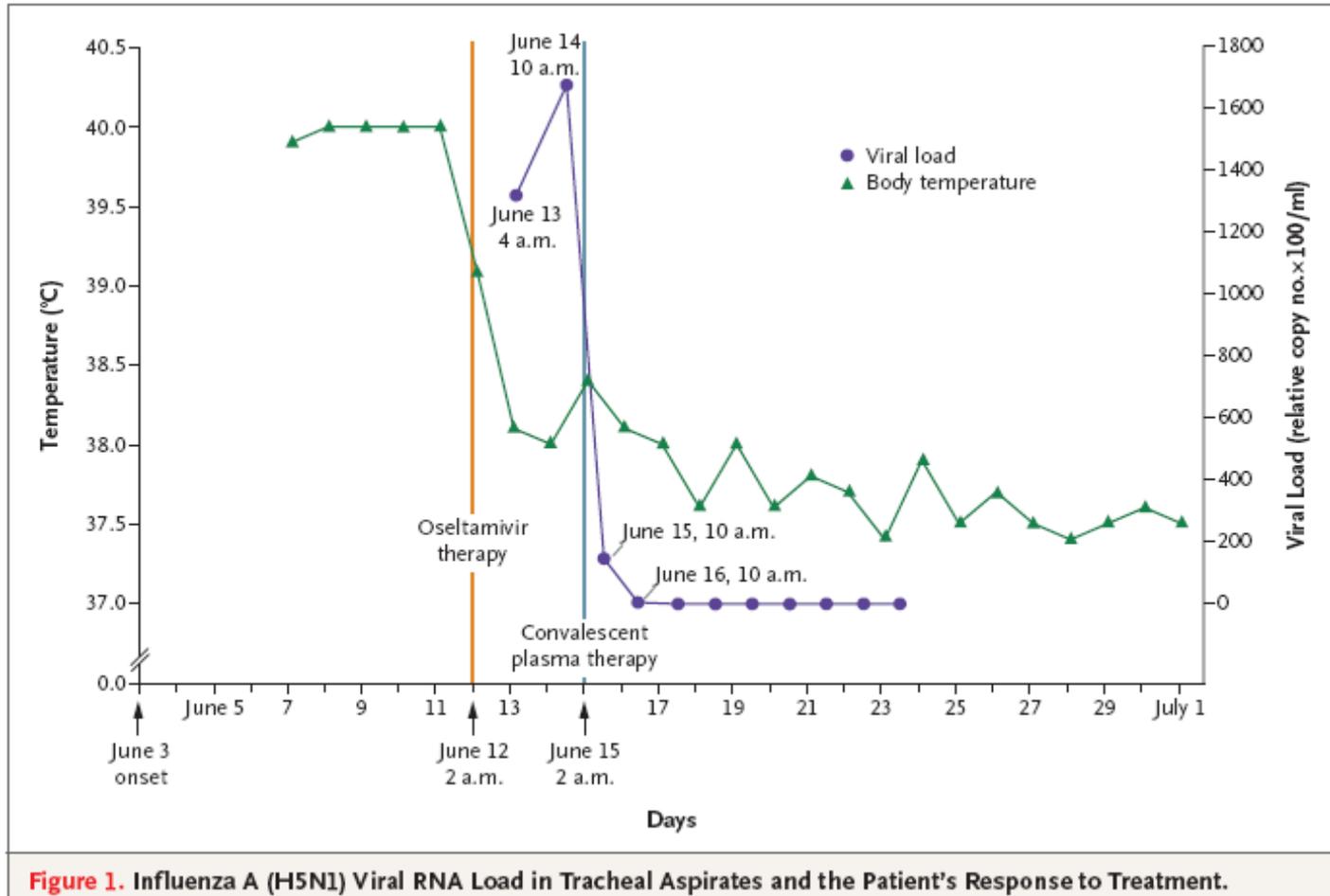


Figure 1. Influenza A (H5N1) Viral RNA Load in Tracheal Aspirates and the Patient's Response to Treatment.

Relative contributions of exogenous plasma, endogenous immune responses, and oseltamivir ?

Clinical Experience Suggests No Role for Corticosteroids in A(H5N1) Treatment

•Vietnam	Survival		
	Steroid Rx	No steroids	P-value
Hanoi^a	12/29 (41%)	29/38 (76%)	0.008
Published cases^b	3/19 (16%)	10/15 (66%)	0.007

^a Cao T, Liem NT. N Engl J Med 2008; 358: 261

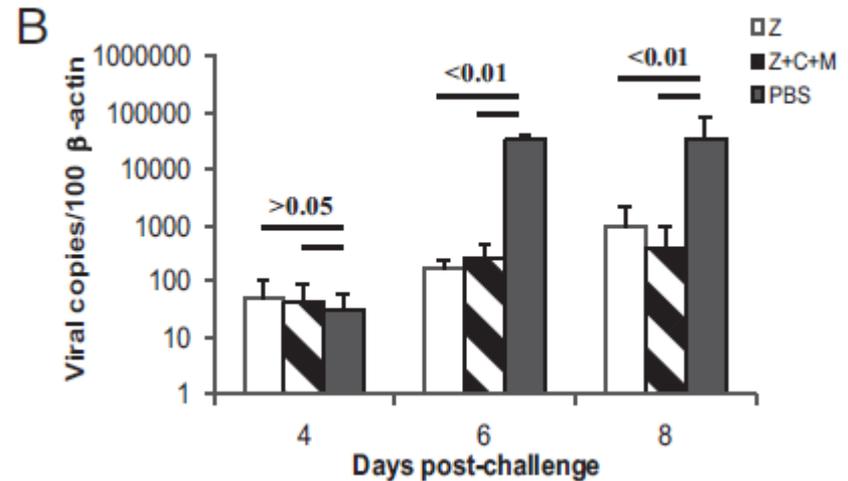
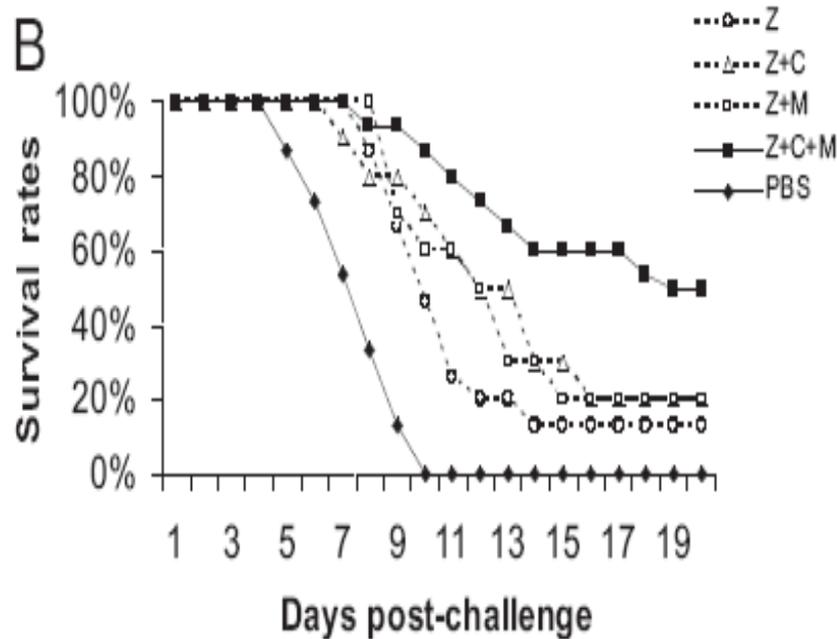
^b Emerg Infect Dis 2005; 11: 201; N Engl J Med 2004; 350: 1179; N Engl J Med 2006; 355: 2186-94.

Delayed antiviral plus immunomodulator treatment still reduces mortality in mice infected by high inoculum of influenza A/H5N1 virus

Bo-Jian Zheng^{*†‡}, Kwok-Wah Chan[§], Yong-Ping Lin[§], Guang-Yu Zhao[§], Chris Chan[§], Hao-Jie Zhang[‡], Hong-Lin Chen^{*†‡}, Samson S. Y. Wong^{*†‡}, Susanna K. P. Lau^{*†‡}, Patrick C. Y. Woo^{*†‡}, Kwok-Hung Chan^{*†‡}, Dong-Yan Jin[¶], and Kwok-Yung Yuen^{*†‡||}

- Comparison of
 - monotherapy with i.p. zanamivir (ZNV),
 - ZNV, celecoxib, mesalazine, or gemfibrozil in various combinations
 - triple regimen of ZNV + celecoxib + mesalazine in mice
- High inoculum of A/Vietnam/1194/04 (10^3 LD50)
- Therapy initiated at 48 hrs post-inoculation

Antiviral + Immunomodulator Therapy for H5N1 in Mice



- \uparrow survival with ZNV + celecoxib + mesalazine
- Even if the viral replication had been suppressed in the mice treated with antiviral, levels of cytokines and chemokines were still similar to the untreated mice, which were significantly higher than those in the mice receiving combination therapy

Influenza Antivirals: *Future Directions*

- Goal: Rapid inhibition of influenza viral replication at all affected sites
- Near-term: parenteral NAIs
 - IV zanamivir or IV/IM peramivir
- Next: antiviral combinations
 - NAI plus M2 inhibitors, polymerase inhibitor (T-705 or ribavirin), Binding site inhibition (Fludase), or neutralizing antibodies
- Longer-term:
 - Antivirals with immunomodulators
 - Host function-targeted agents

Stay tuned to the IC/ ID Training Portal for updated info

Intranet: <http://icidportal.home>

Internet: <http://icidportal.ha.org.hk>

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Avian Influenza

Summary and Situation Updates

General Information

- HA AI contingency plan
- HA AI infection control plan
- HA factsheet on avian influenza
- HA factsheet on antiviral therapy against influenza
- HA guideline on management approach of ILI and CAP suspected of avian influenza

Useful links

- Scientific Committee on Emerging and Zoonotic Diseases: General guide to doctors: antiviral use for novel influenza treatment and prophylaxis (December 2007)
- CHP influenza page
- IEC webpage for Enhanced Surveillance Programme for Influenza A(H5N1)

Training kit on avian influenza

- Supporting Staff
- Non-clinical Staff
- Unit 1 - Background Information
- Unit 2 - Pandemic Risk Assessment
- Unit 3 - Preparedness Plan for Influenza Pandemic
- Unit 4 - Surveillance and Notification Mechanism
- Unit 5 - Clinical Management
- Unit 6 - Infection Control Measures
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