Emerging Infectious Diseases in Southeast Asia....

Paul Ananth Tambyah

National University Hospital

NUS National University of Singapore

Broadcast live from the 2010 conference of the Australian Infection Control Association

www.webbertraining.com October 5, 2010

Case presentation

- 24 year old pig chaser
- Admitted February 1999
- 4 day history of fever and confusion
- Initial temperature 39C
- Neck stiff, drowsy
- Became comatose
- Treated with ceftriaxone, Acyclovir, RHEZ

Progress II

- Fifth hospital day:
  - Began to improve spontaneously
  - Able to respond to simple commands
  - Intermittently confused
- Tenth hospital day:
  - Alert and oriented
  - Repeat CSF exam normal

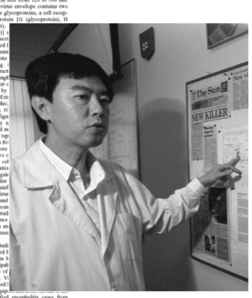
Discharge

- Discharged on 14^{th} hospital day
- Well
- Diagnosis:
  - "Viral encephalitis of unknown etiology"

Nipah Virus: A Recently Emergent Deadly Paramyxovirus

K. B. Chua,[1] W. J. Bellini,[2*] P. A. Rota,[2] B. H. Harcourt,[2] A. Tamin,[2] S. K. Lam,[1] T. G. Ksiazek,[2] P. E. Rollin,[2] S. R. Zaki,[2] W.-J. Shieh,[2] C. S. Goldsmith,[2] D. J. Gubler,[3] J. T. Roehrig,[3] B. Eaton,[4] A. R. Gould,[4] J. Olson,[2] H. Field,[5] P. Daniels,[4] A. E. Ling,[6] C. J. Peters,[2] L. J. Anderson,[2] B. W. J. Mahy[2]

A paramyxovirus virus termed Nipah virus has been identified as the etiologic agent of an outbreak of severe encephalitis in people with close contact exposure to pigs in Malaysia and Singapore. The outbreak was first noted in late September 1998 and by mid-June 1999, more than 265 encephalitis cases, including 105 deaths, had been reported in Malaysia, and 11 cases of encephalitis or respiratory illness with one death had been reported in Singapore. Electron microscopic, serologic, and genetic studies indicate that this virus belongs to the family *Paramyxoviridae* and is most closely related to the recently discovered Hendra virus. We suggest that these two viruses are representative of a new genus within the family *Paramyxoviridae*. Like Hendra virus, Nipah virus is unusual among the paramyxoviruses in its ability to infect and cause potentially fatal disease in a number of host species, including humans.



26 MAY 2000 VOL 288 SCIENCE www.sciencemag.org

Patient was called back...

Internal Medicine Journal 2001; 31: 132–133

CASE REPORT

First case of Nipah virus encephalitis in Singapore

P. A. TAMBYAH,[1] J. H. TAN,[1] B. K. C. ONG,[1] K. H. HO[1] and K. P. CHAN[2]

[1]*Department of Medicine, National University Hospital and* [2]*Department of Pathology, Singapore General Hospital, Singapore*

In March 1999, an outbreak of Nipah virus encephalitis was recognized among slaughterhouse workers in Singapore.[1] One month prior, a 24-year-old pig auction worker presented to the National University Hospital with a 4-day history of fever and confusion. He had a temperature of 39°C, neck stiffness and drowsiness. His full blood count and

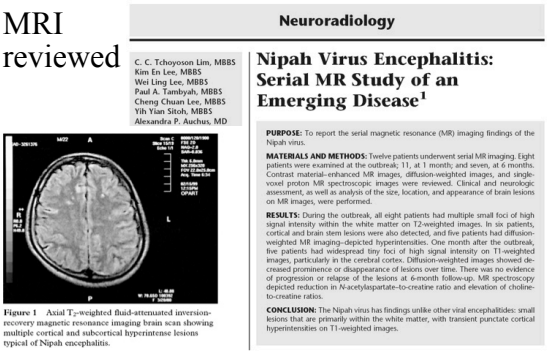
Subsequently, two separate serum specimens from our patient obtained during follow up 6 weeks and 10 weeks after the onset of illness were tested according to a protocol developed by the Centers for Disease Control[1] and were found to be strongly positive for IgG and IgM antibodies to the Nipah virus by enzyme-linked immunosorbent assay. This was

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)

MRI reviewed



Neuroradiology

C. C. Tchoyoson Lim, MBBS
Kim En Lee, MBBS
Wei Ling Lee, MBBS
Paul A. Tambyah, MBBS
Cheng Chuan Lee, MBBS
Yih Yian Sitoh, MBBS
Alexandra P. Auchus, MD

Nipah Virus Encephalitis: Serial MR Study of an Emerging Disease[1]

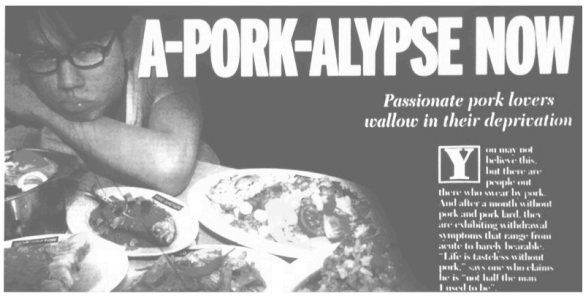
PURPOSE: To report the serial magnetic resonance (MR) imaging findings of the Nipah virus.

MATERIALS AND METHODS: Twelve patients underwent serial MR imaging. Eight patients were examined at the outbreak; 11, at 1 month; and seven, at 6 months. Contrast material–enhanced MR images, diffusion-weighted images, and single-voxel proton MR spectroscopic images were reviewed. Clinical and neurologic assessment, as well as analysis of the size, location, and appearance of brain lesions on MR images, were performed.

RESULTS: During the outbreak, all eight patients had multiple small foci of high signal intensity within the white matter on T2-weighted images. In six patients, cortical and brain stem lesions were also detected, and five patients had diffusion-weighted MR imaging–depicted hyperintensities. One month after the outbreak, five patients had widespread tiny foci of high signal intensity on T1-weighted images, particularly in the cerebral cortex. Diffusion-weighted images showed decreased prominence or disappearance of lesions over time. There was no evidence of progression or relapse of the lesions at 6-month follow-up. MR spectroscopy depicted reduction in *N*-acetylaspartate–to-creatine ratio and elevation of choline-to-creatine ratios.

CONCLUSION: The Nipah virus has findings unlike other viral encephalitides: small lesions that are primarily within the white matter, with transient punctate cortical hyperintensities on T1-weighted images.

Figure 1 Axial T_2-weighted fluid-attenuated inversion-recovery magnetic resonance imaging brain scan showing multiple cortical and subcortical hyperintense lesions typical of Nipah encephalitis.



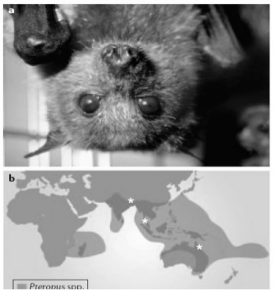


Figure 1 | **Flying foxes, their distribution and the locations of disease outbreaks caused by Hendra virus and Nipah virus. a** | *Pteropus poliocephalus* is an Australian flying fox and member of the family Pteropodidae, one of 18 bat families in the order Chiroptera. There are four *Pteropus* species in Australia[4]. **b** | Sixty-five *Pteropus* species are distributed from Madagascar through the Indian subcontinent to south-eastern Asia and Australia and as far east as the Cook Islands[4]. Some *Pteropus* species are among the largest of all bats, weighing as much as 1.2 kg and displaying a wing span of up to 1.7 m. *Pteropus* species are unique because they lack the complex neural and behavioural mechanisms required for echolocation that characterize the vast majority of bat species. Instead, they have large eyes and they navigate visually, feeding mainly on fruit and flowers, which they locate by smell. The sites of disease outbreaks caused by henipaviruses are indicated. Map modified with permission from REF 4 © (2002) University of New South Wales Press.

Eaton et al Nat Rev Micro 2006;4:23-35

Don't mess with Nature

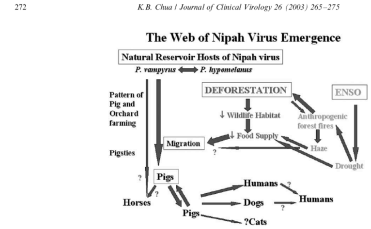


Fig. 2. A flow chart representing the proposed sequence of events leading to the spillover of Nipah from its reservoir hosts (*P. vampyrus*) into the swine population and subsequent transmission to other animal hosts including humans.

Ending the Outbreak

- >1.5 million pigs killed
- Industry devastated
- Pork ban in SG continues (!)

Scientific American 1999

A Webber Training Teleclass www.webbertraining.com

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)


CONTROVERSIAL ROMAN RULING: Sex-starved husband wins Supreme Court support PAGE 6

The Sunday Times

Chinese elite is no cause for worry

THE SILENCE OF THE PIGS

No squeals, no machinery noise, no workers' yells

DPM Lee gives the reassurance that the Government will promote the cultures of all ethnic communities

SPECIAL REPORTS by Sharon Yeow, Leslie Koh and Douglas Wong

MOVE TO ENSURE NO ONE ELSE HAS ENCEPHALITIS


Natural Selections: The Potential Pandemic You've Never Heard Of | Infectious Diseases | DISCOVER Magazine - Netscape Browser

DISCOVER

Health & Medicine / Infectious Diseases

Daily Dose

Natural Selections: The Potential Pandemic You've Never Heard Of

How the connections between pigs, bats, and people could threaten your health.

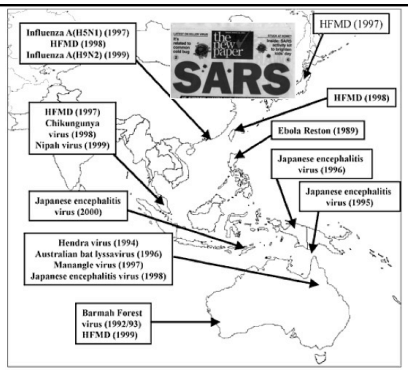
by Mary C. Pearl

FREE GIFT WITH YOUR PAID ORDER! DISCOVER

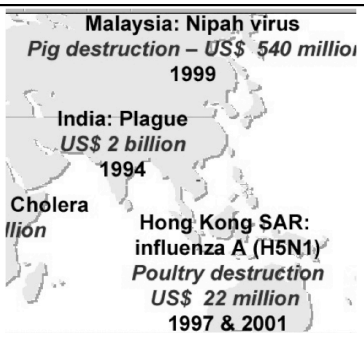
Related Articles

What is an Emerging Infectious Disease?

- "new, re-emerging or drug-resistant infections whose incidence in humans has increased within the past two decades or whose incidence threatens to increase in the near future."
  - Lederberg et al Institute of Medicine 1992



McKenzie et al EID June 2001



http://www.apec.org/infectious/NoN/Rodier.pdf

Targetted surveillance?

- Early warning
- Most vulnerable
- Most controlled environment

A Webber Training Teleclass www.webbertraining.com

Watch out
for the
Canaries.....

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 6, 2008 VOL. 358 NO. 10

A New Arenavirus in a Cluster of Fatal Transplant-Associated Diseases

Gustavo Palacios, Ph.D., Julian Druce, Ph.D., Lei Du, Ph.D., Thomas Tran, Ph.D., Chris Birch, Ph.D., Thomas Briese, Ph.D., Sean Conlan, Ph.D., Phenix-Lan Quan, Ph.D., Jeffrey Hui, B.Sc., John Marshall, Ph.D., Jan Fredrik Simons, Ph.D., Michael Egholm, Ph.D., Christopher D. Paddock, M.D., M.P.H.T.M., Wun-Ju Shieh, M.D., Ph.D., M.P.H., Cynthia S. Goldsmith, M.G.S., Sherif R. Zaki, M.D., Ph.D., Mike Catton, M.D., and W. Ian Lipkin, M.D.

ABSTRACT

BACKGROUND
Three patients who received visceral-organ transplants from a single donor on the same day died of a febrile illness 4 to 6 weeks after transplantation. Culture, polymerase-chain-reaction (PCR) and serologic assays, and oligonucleotide microarray analysis for a wide range of infectious agents were not informative.

METHODS
We evaluated RNA obtained from the liver and kidney transplant recipients. Unbiased high-throughput sequencing was used to identify microbial sequences not found by means of other methods. The specificity of sequences for a new candidate pathogen was confirmed by means of culture and by means of PCR, immunohistochemical, and serologic analyses.

RESULTS
High-throughput sequencing yielded 103,632 sequences, of which 14 represented an Old World arenavirus. Additional sequence analysis showed that this new arenavirus was related to lymphocytic choriomeningitis viruses. Specific PCR assays based on a unique sequence confirmed the presence of the virus in the kidneys, liver, blood, and cerebrospinal fluid of the recipients. Immunohistochemical analysis revealed arenavirus antigen in the liver and kidney transplants in the recipients. IgM and IgG antiviral antibodies were detected in the serum of the donor. Seroconversion was evident in serum specimens obtained from one recipient at two time points.

CONCLUSIONS
Unbiased high-throughput sequencing is a powerful tool for the discovery of pathogens. The use of this method during an outbreak of disease facilitated the identification of a new arenavirus transmitted through solid-organ transplantation.

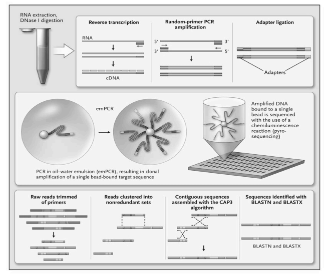
From the Center for Infection and Immunity, Mailman School of Public Health, Columbia University, New York (G.P., T.B., S.C., P.-L.Q., J.H., W.I.L.); Victorian Infectious Diseases Reference Laboratory, Victoria, Australia (J.D., T.T., C.B., J.M., M.C.); 454 Life Sciences, Branford, CT (L.D., J.F.S., M.E.); and the Centers for Disease Control and Prevention, Atlanta (C.D.P., W.-J.S., C.S.G., S.R.Z.). Address reprint requests to Dr. Lipkin at the Center for Infection and Immunity, Mailman School of Public Health, Columbia University, 722 W. 168th St., New York, NY 10032, or at wil2001@columbia.edu, or to Dr. Catton at the Victorian Infectious Diseases Reference Laboratory, Locked Bag 815, Carlton South, Victoria 3053, Australia, or at mike.catton@mh.org.au.

Drs. Palacios and Druce contributed equally to this article.

This article (10.1056/NEJMoa073785) was published at www.nejm.org on February 6, 2008.

N Engl J Med 2008;358:991-8.
Copyright © 2008 Massachusetts Medical Society.

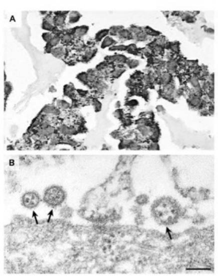
High-Throughput Sequencing Method



Palacios G et al. N Engl J Med 2008;358:991-998

The NEW ENGLAND JOURNAL of MEDICINE

Propagation of the New Arenavirus in Tissue Culture



Palacios G et al. N Engl J Med 2008;358:991-998

The NEW ENGLAND JOURNAL of MEDICINE

A large outbreak of acute encephalitis with high fatality rate in children in Andhra Pradesh, India, in 2003, associated with Chandipura virus

B L Rao, Atanu Basu, Niteen S Wairagkar, Milind M Gore, Vidya A Arankalle, Jyotsna P Thakare, Ramesh S Jadi, K A Rao, A C Mishra

Lancet 2004; 364: 869–74
See Comment page 821

Summary
Background An outbreak of acute encephalitis of unknown origin with high case fatality
reported in children from Andhra Pradesh state in southern India during 2003. We investig

Methods Cell lines and peripheral blood lymphocyte co-cultures were used to isolate the caus
samples. Identity of the agent was established by electron microscopy and serological and n

Findings Clinical samples tested negative for IgM antibodies to Japanese encephalitis,
measles viruses, and for RNA of coronavirus, paramyxovirus, enterovirus, and influenza vi
from six patients with encephalitis and was identified as Chandipura virus by electron n
fixation, and neutralisation tests. Chandipura virus RNA was detected in clinical samp
Sequencing of five of these RNA samples showed 96·7–97·5% identity with the re
Chandipura viral antigen and RNA were detected in brain tissue of a deceased child by imm
test and PCR. Neutralising, IgG, and IgM antibodies to Chandipura virus were present i
samples. Serum samples obtained after 4 days of illness were more frequently positive for I
than were those obtained earlier (p<0·001). A similar trend was noted for neutralising antib

Interpretation Our findings suggest that this outbreak of acute encephalitis in Andhra Prad
Chandipura virus, adding to the evidence suggesting that this virus should be considered as
pathogen.

RT-PCR for Chandipura virus RNA was done on the basis of the G gene sequence for an Indian Chandipura virus isolate (CHPI-653514, Genebank accession number J04350) The primers shown in the panel were synthesised and used in hemi-nested format for the detection of Chandipura viral RNA in clinical specimens.

PCR products were purified by use of Wizard PCR preps DNA purification Kit (Promega, Madison, USA) according to the manufacturer's instructions, and sequenced with Big Dye Terminator cycle sequencing

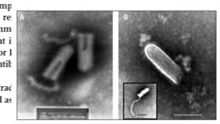


Figure 2: Transmission electron micrographs of primary Chandipura virus isolates from culture

Jpn. J. Infect. Dis., 60, 2007

Comprehensive
Surveillance
Is the key
To
Detecting Emerging
Infectious Diseases

Table 3. Detection of West Nile virus (WNV) and Japanese eucephalitis virus (JEV) antibody from crow sera

	Year of sampling	JEV HI antibody titer (JaGAr01)	JEV Neutralizing antibody (JaGAr01)	WNV HI antibody titer (FCG)	WNV Neutralizing antibody (FCG)
Crow serum 1	1995	10	10	<10	<40
Crow serum 2	1995	10	10	<10	<40
Crow serum 3	1995	10	12	<10	<40
Crow serum 4	1995	10	12	<10	<40
Crow serum 5	1995	10	13	<10	<40
Crow serum 6	1995	10	13	<10	<40
Crow serum 7	1995	10	16	<10	<40
Crow serum 8	1995	10	16	<10	<40
Crow serum 9	1995	10	18	<10	<40
Crow serum 10	1995	20	10	<10	<40
Crow serum 11	1995	40	13	<10	<40
Crow serum 12	2002	10	10	10	<40
Crow serum 13	1995	80	11	10	<40
Crow serum 14	1995	80	21	10	<40
Crow serum 15	1995	160	21	10	<40
Crow serum 16	1995	320	39	10	<40
Crow serum 17	2003	<10	<10	10	<40
Crow serum 18	2003	<10	243	10	<40
WNV-immune serum 1		320	102	80	≧1,280
WNV-immune serum 2		1.280	191	80	≧1,280

Laboratory and Epidemiology Communications

Surveillance of Mosquitoes and Crows for West Nile Virus in the Tokyo Metropolitan Area

Yukiko Tabei*, Michiya Hasegawa, Noriko Iwasaki, Terue Okazaki, Yasuko Yoshida and Kazuyoshi Yano

Department of Microbiology, Tokyo Metropolitan Institute of Public Health, Tokyo 169-0073, Japan

Communicated by Mutsuo Kobayashi

(Accepted October 11, 2007)

West Nile virus (WNV) is a member of the genus *flaviviridae*, which is antigenically close to the Japanese encephalitis virus (JEV). Since human cases of WNV infection were first confirmed in North America in 1999, WNV No invasion of WNV into Japan has been confirmed. However, WNV could invade Japan in the near future under the current circumstances, in which many people and materials enter and leave the country within a short period of time, the

DSO NATIONAL LABORATORIES

Biological Defence Programme
DMERI@DSO
DSO(Kent Ridge) Building
27 Medical Drive #13-01
Singapore 117510
Tel: 64857242 Fax: 64857262
Website: http://www.dso.org.sg

REAL-TIME PCR TESTS AVAILABLE FROM CDSL (wef 15 June 06)

PATHOGEN	REMARKS
Bacillus anthracis	Published PCR, ISO 15189 accreditation soon
Francisella tularensis	Published PCR, ISO 15189 accreditation soon
Yersinia pestis	Published PCR, ISO 15189 accreditation soon
Burkholderia pseudomallei	Published PCR, ISO 15189 accreditation soon
Varicella zoster virus	Published PCR, ISO 15189 accreditation soon
Legionella pneumophila	Published PCR, ISO 15189 accreditation soon
Plasmodium species	Published PCR, ISO 15189 accreditation soon
Salmonella species	Published PCR, ISO 15189 accreditation soon
Shigella species	In-house developed and validated, ISO 15189 accreditation soon
Vibrio cholerae	In-house developed and validated, ISO 15189 accreditation soon
Influenza A	Published PCR, ISO 15189 accreditation soon
Influenza B	Published PCR, ISO 15189 accreditation soon
Adenovirus	Published PCR, ISO 15189 accreditation soon
Respiratory syncytial virus	Published PCR, validated in-house
Human metapneumovirus	Published PCR, validated in-house
Dengue virus generic	Published PCR, validated in-house
Japanese encephalitis virus	Published PCR, validated in-house
Chikungunya virus	Published PCR, validated in-house
Yellow fever virus	Published PCR, validated in-house

Please send test requests to CDSL, DMERI@DSO, 27 Medical Drive, #13-00, S(117510).
Tel: 64857242 (Jimmy Loh), 64857257 (Janet Chew). Hp: 97965585 (Jimmy Loh).

Could we have prevented the Singapore Nipah outbreak??

Internal Medicine Journal 2001; 31: 132–133

CASE REPORT

First case of Nipah virus encephalitis in Singapore

P. A. TAMBYAH,[1] J. H. TAN,[1] B. K. C. ONG,[1] K. H. HO[1] and K. P. CHAN[2]

[1]*Department of Medicine, National University Hospital and* [2]*Department of Pathology, Singapore General Hospital, Singapore*

In March 1999, an outbreak of Nipah virus encephalitis was recognized among slaughterhouse workers in Singapore.[1] One month prior, a 24-year-old pig auction worker presented to the National University Hospital with a 4-day history of fever and confusion. He had a temperature of 39°C, neck stiffness and drowsiness. His full blood count and Subsequently, two separate serum specimens from our patient obtained during follow up 6 weeks and 10 weeks after the onset of illness were tested according to a protocol developed by the Centers for Disease Control[1] and were found to be strongly positive for IgG and IgM antibodies to the Nipah virus by enzyme-linked immunosorbent assay. This was

DAILY EPIDEMIOLOGY REPORT		
21-Feb-2007 Wednesday		Level of Alert - Green
International Surveillance		
1. HEPATITIS A, RESTAURANT - USA (TEXAS): [1] Harris County Public Health and Environmental Services (HCPHES) has been notified that a member of the waiter staff of a restaurant located in north Harris County has tested positive for hepatitis A. The employee is reported to have only worked at the Pappasito's Cantina located at 15280 I-45 North (at Airtex) Houston, TX, 77090 while he was still infectious. Employees and customers who were at this restaurant on the following dates may have been exposed to hepatitis A: 23-27 Jan 2007, 30-31 Jan, 1-3 Feb 2007, and 7-9 Feb 2007. [2] We're learning as many as 12 000 people in Houston may have been exposed to hepatitis A at the Pappasito's restaurant on I-45. The health department is planning to treat 3000 people with an antibiotic [?] shot. And all of this is costing taxpayers here big money. In terms of the cost to the county, it's being quoted as $88 500, all for this one confirmed case. The biggest cost of the hepatitis case was for the immune globulin shots. The county had to get a special shipment from the manufacturer to treat the 3000 people who could benefit from the treatment.		
MOH Update Singapore		
No Unusual Updates		
NPATIENT SURVEILLANCE	Inpatient Surveillance over the last 24 hours: submission compliance rate : 100% No unusual fever clusters or undiagnosed febrile cases at Day 3	% Ward
Cases of alert via Inpatient Surveillance	Number of cases	Details/ Remarks
Pneumonia	NIL	<16 years old: NIL; >16 years old: NIL
Fever for Investigation	1	Ward 48 Bed 4. 6 years old. TW: 9.98. D1 Fever: 39.7. Malarial Microscopy: No Malarial parasite seen. Blood c/s: No growth after 1 day incubation Final report to follow. Travel Hx: Pt just came from Indonesia to seek treatment.
None of these fulfill MOH Directive MH34:24/6-82 for Surveillance of SARS)		
ESRF, ? Chicken Pox	1	Ward 62 Bed 18. 49 years old.
Case Report Form (CRF) – A Nil Return was submitted on 21-Feb.	Please note: Effective 7 October 2004, EPIU ceases to monitor dengue and DHF cases. EPIU does not monitor STI. Effective 11 October 2004, all cases of atypical pneumonia, unexplained fever >72 hours and sudden deaths with acute respiratory symptoms will be reported to MOH via the CRF system by EPIU	
STAFF SURVEILLANCE	Number of cases	No fever clusters among health care staff defined as clusters of 3 or more healthcare staff in the same work area with fever >38C within 48 hours
Staff admission to Isolation wards	NIL	
Staff admission to General Wards	2	
Case(s) under observation	NIL	
Total number of MC - 18 Feb to 20 Feb	9	
Iew MC on 20 Feb	2	
ncludes old MC within the surveillance period		
VRE SURVEILLANCE	Number of cases	Details/ Remarks

OUTPATIENT SURVEILLANCE		
NIL		
LABORATORY SURVEILLANCE	Number of cases	Details/ Remarks
AFB Smear from rt submandibular node Tissue seen : 1+	1	Outpt, on TB treatment.
AFB c/s from Pleural Fluid	1	D/c, Dr In Charge Notified
AFB c/s from Sputum	1	D/c, on TB Treatment
AFB c/s from Lymph Node	1	D/c, on TB Treatment
AFB c/s from ETTAS		
AFB Smear from Sputum seen : 1+		
MORTALITY SURVEILLANCE		

		29 years old. RIP on 17-Feb. Pri. Dx.: Viral Fever of unknown origin.Previously well. Now admitted for -- 1. generally feeling unwell x 3/7 , - with fever, runny nose, dry cough, - no hemoptysis/headache/abdominal pain/urinary symptoms. 2. transient syncopal episode on day of admission - lightheadedness, postural related. Had seen GP x2 - 1st given Anarex, then amoxycillin. Had travelled to Hong Kong 1/52 ago - no contact with illness while there. No h/o TCM use. Admitted through EMD - was hypotensive with BP 71/60 - improved to 85/65 with IV fluids. Had received 4L of IV fluids by the time she reached inpatient ward. BP was 90/60 at time of admission to ward. No PMH. COD. pending.
		87 years old. RIP on 17-Feb. Pri. Dx.: ACUTE CHOLECYSTITIS WITH LARGE GALLSTONE. PMH: Recent NSTEMI, Dementia, Mild renal impairment.
		90 years old. RIP on 17-Feb. Standby collapse case -- Asystole @ presentation 25 mins ago. A/t relatives, collapsed ?1 hour ago. Stopped breathing @ 1/2 hour ago. Asystole o/a paramedics. No Spont. Response. No trauma. PMH: Hpt.
		60 years old. RIP on 18-Feb. Chest pain since yest. Night, epigastric pain a/w sweating , pt then became drowsy, while preparing to bring pt to hospital. PMH: Hpt.
		66 years old. RIP on 19-Feb. RTA.
		79 years old. RIP on 20-Feb. Pri. Dx.: NSTEMI. PMH: post HI seizures on phenytoin.
Non coroner	11	
Pneumonia	4	88 years old RIP on 18-Feb. PMH: HPT, IHD, DM, diverticular disease, appendicitis 2000, hypothyroidism, multiple drug allergiespenicillin, voltaren, phenylbutazone, beserol, carbimazole, borpyrin, penbiotin
		78 years old. RIP on 19-Feb. PMH: ESRF on HD 1,3,5, IHD, DM, HTN, hyperlipidemia, bilat AKA sec to peripheral vascular disease.
		73 years old. RIP on 19-Feb. PMH: Hypertension, Hyperlipidaemia, Chronic renal failure, Right basal ganglia bleed.
		50 years old. RIP on 19-Feb. PMH: DM, Hyperlipidaemia, Multisystem atrophy with long tract involvement and postural instability, and erectile dysfunction, Right frontal stroke, Small left Frontoparietal acute on chronic subdural haematoma, Recurrent falls, Post subcapsular cataract, Bilateral infected trochanteric pressure sores.
PM Report Requested	NIL	
Details of report available at request.		

NG@nuh.com.sg, Song_Khim_CHUA@nuh.com.sg, "Benjamin ONG - CMB" , Khean_Teik_GOH@nuh.com.sg, mdcfda@nus.e...

Transfer Special Tools Window Help

Search Web

<none> MIME QP Send

To: CONTACT_TRACING@nuh.com.sg, Song_Khim_CHUA@nuh.com.sg, "Benjamin ONG - CMB" <mdcongkc@nus.edu.sg>, Khean_Teik_GOH@nuh.com.sg, mdcfda@nus.edu.sg, Yi_Ann_CHAI@nuh.com.sg, Gamini_KUMARASINGHE@nuh.com.sg, Raymond_LIN@nuh.com.sg, "Tow Keang LIM" <mdclimtk@nus.edu.sg>, Siu_Yin_LEE@nuh.com.sg, Shirley_OOI@nuh.com.sg, "Pao-Tang KAO" <paev4@nus.edu.sg>
From: Paul Ananth Tambyah <mdcpat@nus.edu.sg>
Subject: Re: EPIU Update For 21-Feb, 2007, Wednesday.
Cc: Toon_Mae_NG@nuh.com.sg, Candy_John_LIEW@nuh.com.sg, Xiuying_SUN@nuh.com.sg, CONTACT_TRACING@nuh.com.sg, Epidemiology@nuh.com.sg
Bcc:

Dear Mabel

Can you call me as soon as you read this at 98126960. We need to alert MOH ASAP about the 29 year old with the travel history to Hongkong who presented with URTI symptoms, was diagnosed as viral fever of unknown origin and died suddenly

It seems too deja-vu!!!

Paul Ananth

At 05:58 PM 21/02/2007, CONTACT_TRACING@nuh.com.sg wrote:

> Regards:
> Mabel Leong
> Tel No: 6772 2112
> Epidemiology Unit (EPIU)
> NUH

At 08:14 AM 22/02/2007, CONTACT_TRACING@nuh.com.sg wrote:

Dear All,

There is a coroners case whose pri. Dx. is : viral fever of unknown origin.

details from HIDS notes:
29 yr old Chinese lady
Previously well
Now admitted for
1. generally feeling unwell x 3/7
- with fever, runny nose, dry cough
- no hemoptysis/headache/abdominal pain/urinary symptoms
2. transient syncopal episode on day of admission
- lightheadedness, postural related
Had seen GP x2 - 1st given Anarex, then amoxycillin
Had travelled to Hong Kong 1/52 ago - no contact with illness while there. No h/o TCM use
Admitted through EMD - was hypotensive with BP 71/60 - improved to 85/65 with IV fluids
Had received 4L of IV fluids by the time she reached inpatient ward. BP was 90/60 at time of admission to ward
Never tachypneic - pulse 80.
Patient had mild dizziness on rising to walk but denied other symptoms
O/E alert, oriented Afebrile, BP 90/60, HR 80, RR 16
H S1S2 L clear A soft NT, BS active neuro grossly normal
FBC: Tw 7.07 Hb 13.3 Plt 131 RP#1: Na 134 K 3 urea 2.4 Cr 77 Glu 7.4 Lactate 1.7
CXR - no active lung lesion, heart size normal
Imp: likely viral fever- of uncertain origin

Placed on hourly monitoring with further IV fluids given in ward. Started IV ceftriaxone
Bloods repeated in ward:ABG: pH 7.35 pCO2 31.1 pO2 8=95.1 HCO3 16.7 BE -7.6 SaO2 97%
FBC - falling plt count to 98. Thus dengue serology added; pending at patient's demise
Renal panel remained stable However Mg and Ca low - given IV replacement
17/2/07 0400h: Patient's BP decreased to 80/60. Tachycardic and tachypneic, sweating ++
Ran fluids fast. ECG then showed no hyperacut echanges nor changes characteristic of pericarditis. Sinus tachycardia recorded
Decision to start IV dopamine as inotrope
However patient collapsed at 0515h - no spontaneous respirations, pulse not palpable; ECG - pulseless electrical activity
Givne 2.4mg atropine, 1mg adrenaline. CPR commenced
Intubated and manual ventilation given
Cardiology reg on call contacted - bedside 2D echo showed no pericardial effusion or tamponade
Given 10mg adrenaline total - refractory PEA on cardiac monitor
F/b 10ml CaCl2, 250ml HCO3, 1 unit Hartmann's, 1 unit gelofundin
Labs: Na 141, K 5.2, urea 3.7, Cr 81. total Ca 1.54
Rhythm subsequently evolved into asystole
CPR stopped at 0630h. Have updated consultant on call re: above events
To be made coroner's case.

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)

From: Paul Ananth Tambyah [mailto:mdcpat@nus.edu.sg]
Sent: Thursday, February 22, 2007 6:42 PM
To: Chua Song Khim (NUH)
Cc: Goh Khean Teik (NUH); Dale Fisher; Lim Tow Keang; Benjamin K C Ong (Medicine); Raymond_LIN@nuh.com.sg; Toon_Mae_NG@nuh.com.sg
Subject: Re: EPIU Update For 21-Feb, 2007, Wednesday.

Hi CEO

I have spoken with Raymond (who was in Frankfurtll) and the reg who saw the patient (Rahul). The case was very unusual and Raymond is going to try to get some specimens from our lab to see if diagnostic tests can be run. He is also going to speak with someone at MOH to ensure that appropriate specimens are sent from CFM.

Khean Teik, can you help chase up the prelim PM report? I think that MOH will be interested

Paul Ananth

At 10:24 AM 22/02/2007, Song_Khim_CHUA@nuh.com.sg wrote:

> Paul
>
> plse keep CMB and I updated on this case. ty
>
> Paul Ananth Tambyah <mdcpat@nus.edu.sg>
>
> 22-02-07 07:10 AM

Subject: Re: Coroners Case (Fever of unknown origin)
Cc: Ai Lian NG <NG_Ai_Lian@moh.gov.sg>, CONTACT_TRACING@nuh.com.sg, Gamini_KUMARASINGHE@nuh.com.sg, Khean_Teik_GOH@nuh.com.sg, mdcfda@nus.edu.sg, Raymond_LIN@nuh.com.sg, Toon_Mae_NG@nuh.com.sg, Tun YE <YE_Tun@moh.gov.sg>

Thanks [redacted]

At 09:25 AM 23/02/2007, [redacted] wrote:

> Good Morning Prof
>
> Ive checked with HSA, Forensic medicine
>
> Autopsy was done on 18 Feb 2007 by Pathologist Dr [redacted]
> His contact no. is 63130638, I was not able to get hold of him the whole of yesterday, will try again.
> SGH virology had received the following autopsy samples:
> Lung tissues and broncho swab were sent to SGH for respiratory viruses culture and IF
> Brain and CSF were sent for neurotropic virus CFT
> Heart tissue was sent for enterovirus culture and isolation
> There was no dengue PCR or serology requested by NUH or HSA
>
> Cause of death is pending the above results
> Body was released with Cardio-pulmonary failure as cause of demise.
>
> Will check whether patient had returned work after her Hong Kong trip

Denouement

To: mdcpat@nus.edu.sg
Cc: Raymond LIN <Raymond_LIN@moh.gov.sg>
Subject: Fw: Sudden death with URTI
From: [redacted]
Date: Sat, 24 Feb 2007 21:18:58 +0800
X-MIMETrack: Serialize by Router on SEHUBM003/GOV/H/SINEXTRA(Release 6.65FP1HF50 | June29, 2006) at 02/24/2007 21:18:58,Serialize complete at 02/24/2007 21:18:58
X-imss-version: 2.046
X-imss-result: Passed
X-imss-scanInfo: M:B L:E SM:3
X-imss-tmaseResult: TT:1 TS:-14.9524 TC:1F TRN:60 TV:3.6.1039(15016.001)
X-imss-scores: Clean:99.90000 C:2 M:3 S:5 R:5
X-imss-settings: Baseline:3 C:1 M:1 S:1 R:1 (0.5000 0.5000)
X-OriginalArrivalTime: 24 Feb 2007 13:18:59.0790 (UTC) FILETIME=[5855EEE0:01C75816]

Dear Paul

Not sure whether you know this already...
Patient's resp IF was positive for Flu A.
Was any testing for flu done at NUH?

Thanks

[redacted]

ELSEVIER

Burns 28 (2002) 349–357

BURNS

www.elsevier.com/locate/burns

Multi-resistant *Acinetobacter baumannii* on a burns unit—clinical risk factors and prognosis

Ting Hway Wong, Ban Hock Tan*, Moi Lin Ling, Colin Song

Departments of Plastic Surgery, Internal Medicine and Infectious Diseases and Pathology, Singapore General Hospital, Outram Road, Singapore 169608, Singapore

Accepted 27 November 2001

Abstract

Burns patients are highly susceptible to infection, and preventing and treating infection are integral to the successful management of severe burns.

Multi-resistant *Acinetobacter baumannii* (MR-AB) strains are becoming increasingly important in nosocomial infections. We conducted a retrospective study of all adult admissions to the Singapore General Hospital (SGH) National Burns Center over an 18-month period.

The only independent risk factors for the acquisition of MR-AB were the APACHE II score on admission and the number of intravascular lines placed. The only independent predictor of infection with MR-AB was the number of intravascular lines placed. The only independent predictors of longer length of stay were the total number of operations required and infection with MR-AB. The only independent predictor of mortality was the APACHE II score. This is in contrast to other studies that have suggested that the acquisition of MR-AB is an independent risk factor for mortality.

Keywords: *Acinetobacter baumannii*; Burns; Multi-resistant; Risk factors

Responding to Emerging Infections: March 14 2003 Straits Times

Straits Times Mar 14, 2003

IN SINGAPORE

Three women ill after HK trips

By LEE HUI CHIEH

THREE women who visited Hongkong late last month have come down with pneumonia since returning here.

But the Ministry of Health said that no link has been established between their illnesses and the recent outbreak of severe pneumonia in Asia which has claimed six lives.

Two of the Singaporean women have already been discharged — one from Singapore General Hospital and the

The Ministry of Health said in a statement yesterday. "Investigations suggest a viral origin, however no causative organism has been identified."

Pneumonia has more than 30 known causes, including infection by bacteria, fungi or chemicals.

The ministry also said that there had not been any increase in the incidence of acute respiratory infections here. Pneumonia, or inflammation of the lungs, comes under this category.

fever and a cough with a lot of phlegm — as well as flu-like symptoms such as headaches, muscle aches and sore throat.

The ministry has been in touch with family and friends of the three women and advised them to seek medical attention if they develop such symptoms.

It gave the same advice to members of the public, especially those who have returned recently from Guangdong in southern China, Hanoi in northern Vietnam and Hongkong.

"You should seek medical attention, especially if, in addition to the flu-like symptoms, you start coughing and feel breathless."

She added that atypical pneumonia is not uncommon, making up about 10 per cent to 30 per cent of pneumonia cases, but there was no need to worry unless this proportion rocketed.

Following guidelines from WHO and the ministry, hospitals here will be taking precautions.

These include isolating pa-

Taking no chances, Hongkong hospital staff keep their

Very early in the outbreak, the MOH stopped briefing doctors and started using the mass media extensively

A Webber Training Teleclass www.webbertraining.com

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)

Everyone had to follow the rules

Even if we disagreed with them!

Important decisions needed to be made in response to the outbreak:
A major hospital was closed

5th person to die was in both TTSH and NUH

THE fifth person to die from severe acute respiratory syndrome (Sars) was probably infected when she was a patient at Tan Tock Seng Hospital (TTSH) from March 20 to 24.

Madam [redacted] was there for an inflamed stomach lining, caused by steroids, and doctors believe she may have caught the virus from one of the nurses who was looking after her.

The day after being discharged, she fell ill again. This time, the problem was chest pains. But, by then, TTSH had been designated the Sars treatment hospital and was no longer accepting other patients.

So Madam Seah went to the National University Hospital (NUH) on March 25 and was discharged two days later.

On Monday, she fell ill again. This time, the problem was a lung disease. She was again warded at NUH.

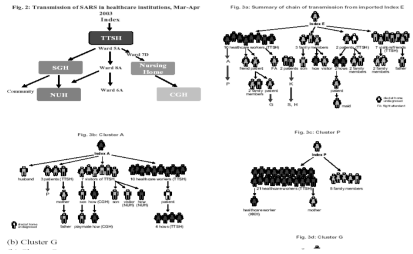
The Straits Times INTERACTIVE

Football | Women Only | Your Health | Movie Mania | Education | Pocket Mon

APRIL 4, 2003 FRI

Patients still were sick

Ultimately, the outbreak spread to almost all the hospitals



Heng BH, Lim SW. Epi News Bulletin 2003;29:42-7

Most people with SARS in Singapore were infected in hospital

Table 3
Distribution of probable SARS cases by place of infection

	No.	%
Hospital/nursing home	155	75.2
Household	32	15.5
Overseas (imported)	7	3.4
Community	4	1.9
Market	3	1.5
Taxi	2	1.0
Aircraft	1	0.5
Undefined	2	1.0
All cases	206	100

Table 4
Distribution of probable SARS cases by various population groups

	No.	%
Healthcare worker	84	40.8
Family member	49	23.8
Inpatient	25	12.2
Visitor to hospital	19	9.2
Friend/social contact	14	6.8
Imported	7	3.4
Co-worker in market	3	1.5
Taxi driver	2	1.0
Flight attendant	1	0.5
Undefined	2	1.0
All groups	206	100

Heng BH, Lim SW. Epi News Bulletin 2003;29:42-7

We worked with WHO and CDC to analyse the data quickly

MMWR™
Morbidity and Mortality Weekly Report

Weekly May 9, 2003 / Vol. 52 / No. 18

Severe Acute Respiratory Syndrome — Singapore, 2003

The Singapore Ministry of Health (MOH), with assistance from the World Health Organization (WHO), has been investigating an outbreak of severe acute respiratory syndrome (SARS). This is a novel condition caused by the SARS-associated coronavirus (SARS-CoV) and is characterized by both an atypical pneumonia and efficient nosocomial transmission. This report summarizes epidemiologic features of

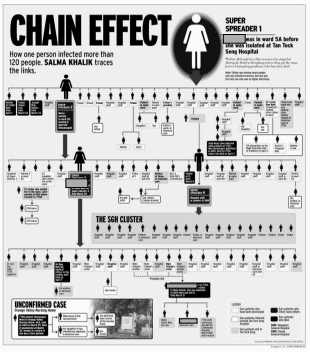
community-acquired pneumonia, unexplained respiratory deaths, and individual cases with no contact but that are clinically suspicious for SARS. An independent, hospital-based surveillance system is being established for community-acquired pneumonia, but the threshold to monitor and investigate any unexplained febrile illness or pneumonia with laboratory testing for SARS-CoV and other etiologies is

A Webber Training Teleclass www.webbertraining.com

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

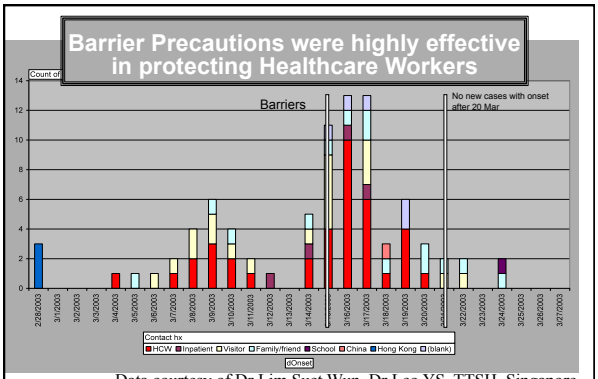
Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)



The newspapers did their own investigations

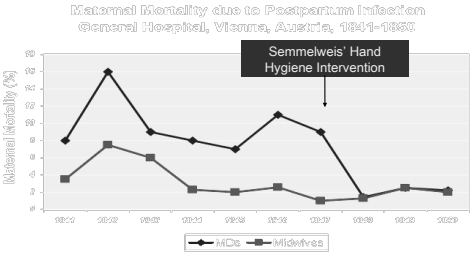
Healthcare worker protection was a top priority. The CEO visited all infected healthcare workers initially

Straits Times Mar 20, 2003



Data courtesy of Dr Lim Suet Wun, Dr Leo YS, TTSH, Singapore

Hand Hygiene: Not a New Concept



~ Hand antisepsis reduces the frequency of patient infections ~

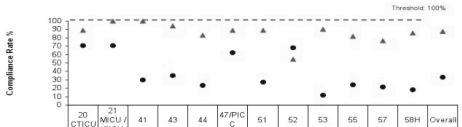
http://www.cdc.gov/handhygiene/materials.htm

Adapted from: *Hosp Epidemiol Infect Control*, 2nd Edition, 1999.

Hand Hygiene Audit

February - March & June 2003

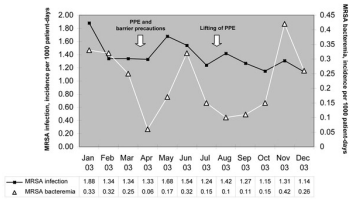
Compliance Rate



	20 CTICU	21 MICU / SICU	41	43	44	47/PIC C	51	52	53	55	57	58H	Overall
◆ Compliance (%) (Pre-SARS)	70.6	71	29.7	35.1	23.6	62.5	27.4	68.5	12.0	24	21.3	18	33.4
Compliance #	12	53	22	26	17	21	20	50	9	18	16	13	277
Sample Size	17	75	74	74	72	74	73	73	75	75	75	72	829
▲ Compliance (%) (Post-SARS)	88.9	100	100.0	94.4	83.3	88.9	88.9	54.5	90.0	82	76.9	85.7	87.4
Compliance #	16	18	14	17	10	16	16	6	9	9	10	12	153
Sample Size	18	18	14	18	12	18	18	11	10	11	13	14	175

Courtesy of Deborah & QIU team

Hand hygiene needs a comprehensive approach



Chai et al *Clinical Infectious Diseases* *2005;40:632-633*

A Webber Training Teleclass www.webbertraining.com

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)

Efficacy of Soap and Water and Alcohol-Based Hand-Rub Preparations against Live H1N1 Influenza Virus on the Hands of Human Volunteers

M. Lindsay Grayson,[1,2,3] Sharmila Melvani,[1] Julian Druce,[4] Ian G. Barr,[5] Susan A. Ballard,[1] Paul D. R. Johnson,[1,3,4] Tasoula Mastorakos,[1] and Christopher Birch[4]

[1]Infectious Diseases Department, Austin Health, [2]Department of Epidemiology and Preventive Medicine, Monash University, [3]Department of Medicine, University of Melbourne, and [4]Victorian Infectious Diseases Reference Laboratory, Melbourne Health, and [5]World Health Organization Collaborating Centre for Influenza, Melb

Table 2. Assessment, by PCR and culture, of the efficacy of various hand hygiene (HH) protocols against live H1N1 influenza virus on the hands of 14 human volunteers who were culture-positive at baseline.

HH product	Real-time RT-PCR[a] mean Ct value ± SD (range)		Culture $TCID_{50}$/0.1 mL level, mean ± SD (range)	
	Palm	Glove juice	Palm	Glove juice
Control	24.0 ± 3.4[b] (19.8–32.2)	24.3 ± 3.8[b] (18.6–32.4)	3325 ± 8352[b] (0–32,000)	1041 ± 1701[b] (0–5600)
SW	37.6 ± 3.2[c] (30.9–40.1)	39.4 ± 1.1[c] (37.0–40.1)	0 (0–0)	0 (0–0)
ETOH only	34.8 ± 2.6[c] (30.4–40.1)	33.3 ± 2.1[c] (30.1–36.3)	0 (0–0)	0 (0–0)
ISOP-CHX	35.7 ± 2.2[c] (32.8–40.1)	33.5 ± 2.5[c] (30.5–39.8)	0 (0–0)	0 (0–0)
ETOH-CHX	34.4 ± 2.9[c] (28.3–38.2)	33.3 ± 3.0[c] (28.9–38.6)	0 (0–0)	0 (0–0)

NOTE. Control, no product was used; Ct, cycle threshold; ETOH-CHX, ethanol 70% plus 0.5% chlorhexidine solution; ETOH only, ethanol 61.5% gel; glove juice, right hand glove juice; ISOP-CHX, isopropanol 70% plus 0.5% chlorhexidine solution ; palm, right palm; SW, soap and water.

[a] Ct values increase with decreasing quantities of detectable virus copies per microliter. Baseline left-hand fingertip (control) RT-PCR results (mean ± SD) were similar for the assessment using no product and all HH protocol assessments: no product (control), 23.2 ± 3.5; range, 19.5–31.0; SW, 21.9 ± 2.2; range, 18.4–27.1; ETOH only, 23.3 ± 2.8; range, 19.8–30.3; ISOP-CHX, 24.9 ± 3.3, range, 20.7–30.7; ETOH-CHX, 24.4 ± 2.9; range, 20.8–31.1.

[b] Significant change in Ct values for each HH product compared with no product (control) ($P < .001$).

[c] Difference between SW and other HH protocols: ETOH only, $P = .02$; ETOH-CHX, $P = .01$; ISOP-CHX, $P = .09$.

[d] Significant difference between SW and other HH protocols, $P < .001$ for all.

[e] Significant difference between no product (control) and each HH protocol: palm culture, $P < .002$; glove juice, $P < .002$, by Wilcoxon signed-rank test.

Clinical Infectious Diseases 2009; 48:285–91

Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings 2007

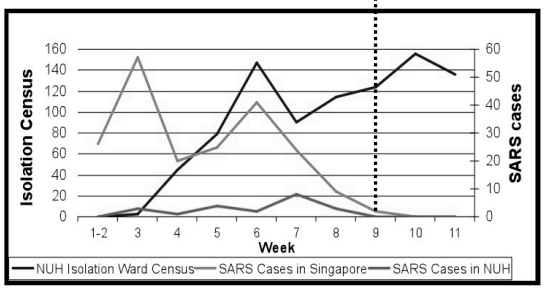
Jane D. Siegel, MD; Emily Rhinehart, RN MPH CIC; Marguerite Jackson, PhD; Linda Chiarello, RN MS; the Healthcare Infection Control Practices Advisory Committee

Acknowledgement: The authors and HICPAC gratefully acknowledge Dr. Larry Strausbaugh for his many contributions and valued guidance in the preparation of this guideline.

Suggested citation: Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings, ***June 2007*** *http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf*

http://www.cdc.gov/ncidod/dhqp/pdf/guidelines/Isolation2007.pdf

Isolation ward utilisation



Facillities needed to be created

A liberal isolation policy:

	Confirmed SARS	Non SARS	Total
No of Cases Admitted to Isolation Wards	13	465	478
No of Cases Admitted to General Wards	1	3949	3950
Total	14	4414	4428

Chai et al ICEID 2004

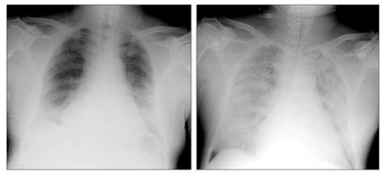
Efficacy of NUH Isolation Criteria

Test	Value (95 % C I)
Sensitivity	92.9 % (64.3 – 99.6)
Specificity	89.5 % (89.4 – 89.5)
Positive Predictive Value	0.027
Number Needed to Isolate	37
Positive Likelihood Ratio	8.1 (7.445 – 10.435)
Negative Likelihood Ratio	0.080 (0.012 – 0.528)

Chai et al ICEID 2004

A "super spreader"

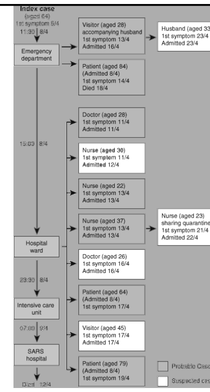
- 63 year old veg seller
- Breathless, afebrile
- Admitted as "heart failure"



1: Chest x-ray performed on 8 April at 12:06 showing non-specific bibasal infiltrates

2: Chest x-ray performed on 9 April at 02:34 showing extensive progression

Fisher, Chew, Lim, Tambyah. Med J Aust. 2003 Jun 2;178(11):555-8



Index case
(aged 64)
1st symptom 5/4
11:30 8/4
Emergency department
15:00 8/4
Hospital ward
23:30 8/4
Intensive care unit
07:00 9/4
SARS hospital
Died 12/4
Visitor (aged 28) accompanying husband 1st symptom 13/4 Admitted 16/4
Husband (aged 33) 1st symptom 23/4 Admitted 23/4
Patient (aged 84) (Admitted 8/4) 1st symptom 14/4 Died 18/4
Doctor (aged 28) 1st symptom 11/4 Admitted 11/4
Nurse (aged 30) 1st symptom 11/4 Admitted 12/4
Nurse (aged 22) 1st symptom 13/4 Admitted 13/4
Nurse (aged 37) 1st symptom 13/4 Admitted 13/4
Nurse (aged 23) sharing quarantine 1st symptom 21/4 Admitted 22/4
Doctor (aged 26) 1st symptom 16/4 Admitted 16/4
Patient (aged 64) (Admitted 8/4) 1st symptom 17/4
Visitor (aged 45) 1st symptom 17/4 Admitted 17/4
Patient (aged 79) (Admitted 8/4) 1st symptom 19/4
Probable Case
Suspected case

Fisher, Chew, Lim, Tambyah. Med J Aust. 2003 Jun 2;178(11):555-8

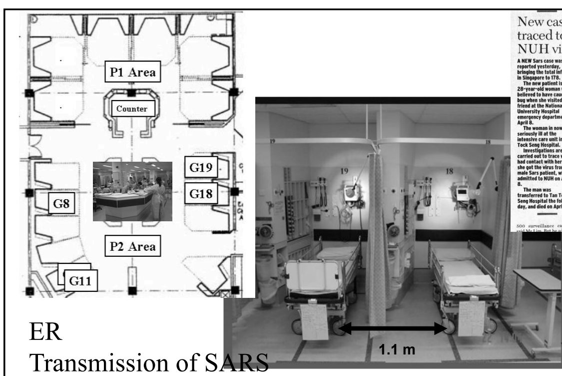
THE STRAITS TIMES
WAR ON SARS PARLIAMENT
Home quarantine orders
No more leniency: Tough penalties await those who break the rules
DO THE RIGHT THING
TAGGED IF YOU STILL LEAVE HOME
TAGGED IF YOU DON'T PICK UP THAT PHONE
DON'T TRY TO LEAVE THE COUNTRY
CALL-FORWARDING TRICKS ARE OUT
NAMING AND SHAMING IN PUBLIC

Table 2. Factors Shown to Be Important in the Transmission of Common Respiratory Agents.

Agent	Direct Contact	Large- or Medium-Droplet Aerosol	Tiny-Droplet Aerosol (Droplet Nuclei)
Bacteria			
Neisseria meningitidis	Yes	Yes	No
Streptococcus pyogenes	Yes	Yes	No
Streptococcus pneumoniae	Yes	Yes	No
Mycobacterium tuberculosis	No	No	Yes
Viruses			
Influenzavirus	Yes	Yes	Yes
Adenovirus	Yes	Yes*	Yes*
Respiratory syncytial virus	Yes†	Yes	No
Rhinovirus	Yes†	Yes	No

* Inhaling large or medium-size droplets that are trapped in the nose may cause upper respiratory tract infection, whereas inhaling tiny droplets (droplet nuclei) causes pneumonia.
† This virus may also be transmitted by inanimate vectors.

NEJM ***2003;348:1256-1266***



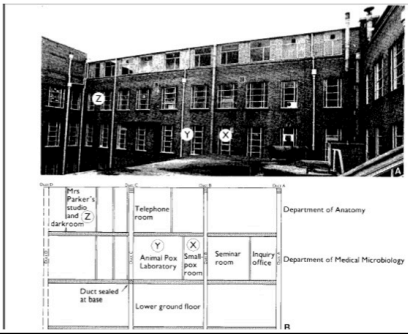
ER
Transmission of SARS

Emerging Infectious Disease in Southeast Asia

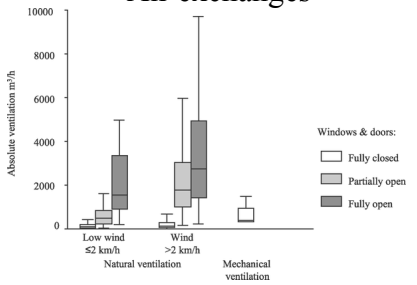
Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)

The last case of smallpox in the world

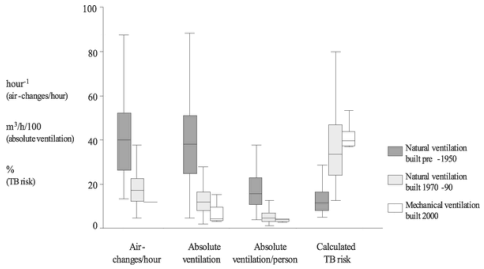


Air exchanges



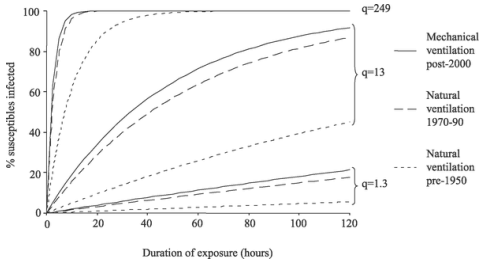
From: Natural Ventilation for the Prevention of Airborne Contagion Escombe AR, Oeser CC, Gilman RH, Navincopa M, Ticona E, et al.
PLoS Medicine Vol. 4, No. 2, e68 doi:10.1371/journal.pmed.0040068

Air exchanges



From: Natural Ventilation for the Prevention of Airborne Contagion Escombe AR, Oeser CC, Gilman RH, Navincopa M, Ticona E, et al.
PLoS Medicine Vol. 4, No. 2, e68 doi:10.1371/journal.pmed.0040068

Air exchanges & TB transmission



From: Natural Ventilation for the Prevention of Airborne Contagion Escombe AR, Oeser CC, Gilman RH, Navincopa M, Ticona E, et al.
PLoS Medicine Vol. 4, No. 2, e68 doi:10.1371/journal.pmed.0040068

So…is Influenza Airborne? Results of observational studies

A
A
A

	Number	Setting	Population	Case identification	
				Diagnostic criteria	Number (%) laboratory tested
Blumenfeld et al[9]	62	Hospital	Medical patients and staff	Viral isolation; serology	55 (89%)
McLean[10]	1116	Hospital housing tuberculosis patients	Medical patients and staff	Clinical; serology	1116 (100%)
Moser et al[11]	53	Aircraft	Healthy adults	Clinical; viral isolation; serology	Unclear
Klontz et al[12]	110	Naval base aircraft	Healthy adults	Clinical; viral isolation; serology	105 (95%)
Morens and Rash[13]	39	LTCF	Elderly residents	Clinical; viral isolation; serology	37 (95%)
Drinka et al[14]	690	LTCF	Elderly residents	Viral isolation	241 (35%)
Munoz et al[15]	15	NICU	Critical care neonates	Clinical; viral isolation; antigen detection	4 (27%)
Cunney et al[16]	54	NICU	Critical care neonates	Clinical; antigen detection	54 (100%)
Awofeso et al[17]	59	Correctional facility	Healthy adults	Clinical; viral isolation; antigen detection	21 (36%)

LTCF=Long-term care facility; NICU=neonatal intensive care unit.

Table 5: Summary of influenza epidemiological studies

Brankston et al Lancet Infectious Disease 2007;7:257-65

Staff are fully protected

PAPRs are available

PRIME NEWS

THE STRAITS TIMES : Wednesday, April 16, 2003

MASKED ROBBER STRIKES

Man who tried to rob Hong Leong Finance branch at Holland Drive yesterday could be the same one who held up a 4-D outlet and petrol stations in the west on Sunday and Monday

JOYCE FANG

Jobless suspect arrested near bank

N95 masks: Problems

Acta Neurol Scand 2006: 113: 199–202 DOI: 10.1111/j.1600-0404.2005.00560.x

ACTA NEUROLOGICA SCANDINAVICA

Headaches and the N95 face-mask amongst healthcare providers

Lim ECH, Seet RCS, Lee K-H, Wilder-Smith EPV, Chuah BYS, Ong BKC. Headaches and the N95 face-mask amongst healthcare providers. Acta Neurol Scand 2006: 113: 199–202

E. C. H. Lim[1], R. C. S. Seet[1], K.-H. Lee[1], E. P. V. Wilder-Smith[1], B. Y. S. Chuah[2], B. K. C. Ong[1]
...partment of Medicine and [2]Department of ...natology-Oncology, National University Hospital, ...gapore

Table 2 Comparison of demographic variables, duration of N95 face-mask use and pre-existing headache amongst healthcare workers with and without headache exacerbations following the use of the N95 face-mask

Demographic variables	With headache, $n = 79$ (%)	Without headache, $n = 132$ (%)	P-value[1]	Odds ratio (95% Confidence interval)
Gender				
Male	14 (17.7)	33 (25.0)	0.249	0.568 (0.216–1.488)
Female	65 (82.3)	99 (75.0)		1.0
Age (years) (mean ± SD)	30 ± 6	32 ± 8	0.153	0.966 (0.920–1.013)
Ethnicity				
Chinese	44 (55.7)	79 (59.8)	0.818	1.0
Malay	9 (11.4)	17 (12.9)		0.807 (0.313–2.081)
Indian	9 (11.4)	13 (9.8)		1.204 (0.460–3.148)
Caucasian	0	1 (0.8)		1.647 (0.665–4.075)
Filipino	13 (16.5)	17 (12.9)		1.795 (0.438–7.357)
Other	4 (5.1)	6 (3.8)		1.895 (0.318–4.537)
Occupation				
Doctor	21 (26.6)	35 (26.5)	0.394	1.805 (0.732–4.450)
Nurse	52 (65.8)	87 (65.9)		1.0
Paramedical personnel	6 (7.6)	10 (7.6)		1.568 (0.484–5.084)
Duration of N95 wear exceeding 4 h	44 (55.7)	58 (43.9)	0.053	1.85 (0.99–3.43)
Pre-existing headaches	27 (37.3)	28 (21.2)	0.041**	1.97 (1.03–3.77)

[1]Multiple logistic regression (statistically significant if $P < 0.05$).
**Statistically significant

...words: headaches; N95; frequency; risk factors; ...erity

...Chuen-Hian Lim, Division of Neurology, Department ...Medicine, National University Hospital, 5 Lower Kent ...ge Road, Singapore 119074
...: 65-67724353
...: 65-67794112
...ail: mdcelch@nus.edu.sg

...epted for publication November 11, 2005

What types of masks are available

There is a variety of masks/respirators that could be used during a pandemic depending on the circumstances. They are:

- Surgical masks—reduces chances of inhaling virus that is in respiratory droplets. This protection is most useful in lower risk situations, particularly when the infected patient is able to wear a mask.
- P2 masks (P2 respirator)—reduces chances of inhaling virus that is in the form of fine respiratory particles. This is only recommended for use when undertaking medical procedures that lead to the generation of aerosols, or if the patient is infectious and cannot wear a surgical mask. They are used in high-risk situations where the patient is known to be infectious and distancing is not possible.
- Powered Air Purifying Respirators (PAPR)—may also be used when aerosol-generating procedures are undertaken. Note PAPRs are specialised devices that will be in short supply.
- Other masks. Advice will be provided at the time regarding appropriate alternatives (either homemade or commercially available).

Testing is required so that P2 masks fit properly. A P2 mask fit testing and checking program is needed in hospitals and general practice. Ongoing training (via mask fitting accreditation) will ensure knowledge can be built and sustained. Further details around fit testing will be provided in the Clinical and Infection Control Annex.

PPE needs to be used in combination with other control measures

The following control measures will reduce the risk of transmission:

- regular hand cleaning with either soap or alcohol based hand rub, especially after removal of PPE

http://www.flupandemic.gov.au/internet/panflu/publishing.nsf/Content/ahmppi~ahmppi-appendixg

Surgical Mask vs N95 Respira... for Preventing Influenza Among Health Care Workers
A Randomized Trial

Mark Loeb, MD, MSc
Nancy Dafoe, RN
James Mahony, PhD
Michael John, MD
Alicia Sarabia, MD
Verne Glavin, MD
Richard Webby, PhD
Marek Smieja, MD
David J. D. Earn, PhD
Sylvia Chong, BSc
Ashley Webb, BS
Stephen D. Walter, PhD

INFLUENZA CAUSES ANNUAL EPIDEMics of respiratory illness worldwide and is the most important cause of medically attended acute respiratory illness.[1,2] Moreover, there is increasing concern about the recently declared influenza pandemic due to 2009 influenza A(H1N1) in humans.[3-5]

Transmission of influenza can occur by coughing or sneezing where infectious particles of variable size, ranging from approximately 0.1 to 100 µm, may be inhaled.[6] This range of particles has a yet undefined but possibly important role in transmission. Al-

Context Data about the effectiveness ... respirator for protecting health care wo... likelihood that N95 respirators will be in ... able in many countries, knowing the ef... health importance.

Objective To compare the surgical ma... care workers against influenza.

Design, Setting, and Participants ... 446 nurses in emergency departments, ... care Ontario hospitals.

Intervention Assignment to either a fit... providing care to patients with febrile re... enza season.

Main Outcome Measures The prim... enza measured by polymerase chain rea... Effectiveness of the surgical mask was a... compared with the N95 respirator. The c... limit of the 95% confidence interval (CI... tor minus surgical group) was greater th...

Results Between September 23, 2008, ... sessed for eligibility and 446 nurses were enrolled and randomly assigned the intervention; 225 were allocated to receive surgical masks and 221 to N95 respirators. Influenza infection occurred in 50 nurses (23.6%) in the surgical mask group and in 48 (22.9%) in the N95 respirator group (absolute risk difference, −0.73%; 95% CI, −8.8% to 7.3%; $P = .86$), the lower confidence limit being inside the noninferiority limit of −9%.

Conclusion Among nurses in Ontario tertiary care hospitals, use of a surgical mask compared with an N95 respirator resulted in noninferior rates of laboratory-confirmed influenza.

Trial Registration clinicaltrials.gov Identifier: NCT00756574

JAMA. 2009;302(17):(doi:10.1001/jama.2009.1466) www.jama.com

Table 2. Comparison of Laboratory-Confirmed Influenza Between the Surgical Mask and N95 Respirator Groups

	No. (%) Surgical Mask (n = 212)	No. (%) N95 Respirator (n = 210)	Absolute Risk Difference, % (95% CI)	P Value
Laboratory-confirmed influenza[a]	50 (23.6)	48 (22.9)	−0.73 (−8.8 to 7.3)	.86
RT-PCR influenza A	5 (2.4)	1 (0.5)	−1.88 (−4.13 to 0.36)	.22
RT-PCR influenza B	1 (0.5)	3 (1.4)	0.96 (−0.89 to 2.81)	.37
≥4-Fold rise in serum titers A/Brisbane/59/2007 (H1N1)[b]	25 (11.8)	21 (10)	−1.79 (−7.73 to 4.15)	.55
≥4-Fold rise in serum titers A/Brisbane/10/2007 (H3N2)[b]	42 (19.8)	49 (23.3)	3.52 (−4.32 to 11.36)	.38
≥4-Fold rise in serum titers B/Florida/4/2006[b]	15 (7.1)	19 (9.0)	2.0 (−3.0 to 7.17)	.46
≥4-Fold rise in serum titers A/TN/1560/09 (H1N1)[b]	17 (8.0)	25 (11.9)	3.89 (−1.82 to 9.59)	.18

Abbreviations: CI, confidence interval; RT-PCR, reverse-transcriptase polymerase chain reaction.
[a]Influenza detected by 1 or more of the following: RT-PCR A, RT-PCR B, and ≥4-fold rise in serum titers to A/Brisbane/59/2007(H1N1), A/Brisbane/10/2007(H3N2), and B/Florida/4/2006. Serology includes only nonvaccinated nurses.
[b]Includes both vaccinated and nonvaccinated nurses. Two hundred ninety-four nurses were not vaccinated (147 in each group).

Table 3. Comparison of RT-PCR Results for Other Respiratory Viruses Between the Surgical Mask and N95 Respirator Groups

	No. (%) Surgical Mask (n = 212)	No. (%) N95 Respirator (n = 210)	Absolute Risk Difference, % (95% CI)	P Value
Respiratory syncytial virus[a]	2 (0.9)	1 (0.5)	−0.47 (−2.07 to 1.13)	>.99
Metapneumovirus	4 (1.9)	3 (1.4)	−0.46 (−1.98 to 2.89)	>.99
Parainfluenza virus[b]	1 (0.5)	2 (1.0)	0.48 (−1.12 to 2.09)	.62
Rhinovirus-enterovirus	8 (3.8)	10 (4.8)	0.99 (−2.87 to 4.85)	.62
Coronavirus[c]	9 (4.3)	12 (5.7)	1.47 (−2.68 to 5.62)	.49
Total[d]	20 (9.4)	22 (10.5)	1.04 (−4.67 to 6.76)	.72

Abbreviations: CI, confidence interval; RT-PCR, reverse-transcriptase polymerase chain reaction.
[a]Refers to respiratory syncytial virus type B only because no type A was detected.
[b]Refers to parainfluenza 3 only because no parainfluenza 1, 2, or 4 was detected.
[c]Refers to coronaviruses OC43, 229E, NL63, and HKU1.
[d]Totals are less than sums because more than 1 virus was detected in some participants.

SHEA The Society for Healthcare Epidemiology of America — IDSA — APIC Spreading knowledge. Preventing infection.™

November 5, 2009

President Barack Obama
The White House
1600 Pennsylvania Avenue, NW
Washington D.C. 20500

Dear President Obama:

During this state of national emergency due to the 2009 H1N1 influenza pandemic, it i... imperative that healthcare professionals and facilities receive clear, practical, and evide... federal guidance to ensure patient and healthcare worker safety. With this in mind, the... for Healthcare Epidemiology of America (SHEA), Infectious Diseases Society of Ame... (IDSA), and Association of Professionals in Infection Control and Epidemiology (API... express significant concern with the federal guidance, developed by your Administratio... cooperation with several agencies and recently issued by the Centers for Disease Contr... Prevention (CDC), and Occupational Safety and Health Administration (OSHA) requi... concerning the use of personal protective equipment (PPE) by healthcare workers in tr... suspected or confirmed cases of H1N1 influenza.

In October, two separate studies were presented that reinforce our viewpoint on the use of surgical masks versus respirators. In the first study (Loeb, et al. JAMA, 2009), no significant difference in influenza acquisition was observed in nurses in Toronto assigned to wear N95 respirators or surgical masks. Last week, at the IDSA Annual Meeting, investigators from Australia presented a re-evaluation of a study performed in China (MacIntyre, et al). Again, no significant difference was observed between healthcare workers wearing surgical masks or N95 respirators. Of note, the MacIntyre study was initially reported to show a significant benefit associated with use of the N95 respirators and this preliminary report was both presented to the Institute of Medicine's Committee on Respiratory Protection for Healthcare Workers in the

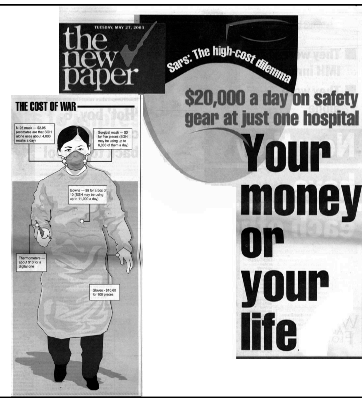
Thank you in advance for your careful consideration and expeditious implementation of these recommendations. Our leaders stand ready to continue to work with you in responding to the 2009 H1N1 pandemic. Should you have any questions, please contact Jennifer Bright, SHEA's executive director at 703-684-1007, Robert Guidos, IDSA's vice president for public policy and government relations at 703-299-0202 or Lisa Tomlinson, Director of Government Affairs for APIC at 202-454-2606.

Respectfully,

Mark E. Rupp, MD, SHEA President
Richard Whitley, MD, FIDSA, IDSA President
Christine Nutty, RN, MSN, CIC, APIC President

CC: Kathleen Sebelius, MPA, Secretary, DHHS
Tom Frieden, MD, Director, CDC
Francis Collins, MD, Director, NIH
Anthony Fauci, MD, Director, NIAID
Hilda Solis, Secretary, DOL
Jordan Barab, Acting Assistant Secretary, OSHA
Rosemary Sokas, MD, MOH Director, Office of Occupational Medicine, OSHA
Melody Barnes, JD, Director, Domestic Policy Council, The White House

Hospitals in Asia are alert against nosocomial influenza



Cost-effectiveness Analysis of Hospital Infection Control Response to an Epidemic Respiratory Virus Threat

Yock Young Dan, Paul A. Tambyah, Joe Sim, Jeremy Lim, Li Yang Hsu, Wai Leng Chow, Dale A. Fisher, Yue Sie Wong, and Khek Yu Ho

The outbreak of influenza A pandemic (H1N1) 2009 prompted many countries in Asia, previously strongly affected by severe acute respiratory syndrome (SARS), to respond with stringent measures, particularly in preventing outbreaks in hospitals. We studied actual direct costs and cost-effectiveness of different response measures from a hospital perspective in tertiary hospitals in Singapore by simulating outbreaks of SARS, pandemic (H1N1) 2009, and 1918 Spanish influenza. Protection measures targeting only infected patients yielded lowest incremental cost/death averted of $23,000 (US$) for pandemic (H1N1) 2009. Enforced protection in high-risk areas (Yellow Alert) and full protection throughout the hospital (Orange Alert) averted deaths but came at an incremental cost of up to $2.5 million/death averted. SARS and Spanish influenza favored more stringent measures. High case-fatality rates, virulence, and high proportion of atypical manifestations impacted cost-effectiveness the most. A calibrated approach in accordance with viral characteristics and community risks may help refine responses to future epidemics.

Pandemic influenza A (H1N1) 2009 virus is a new influenza virus of swine origin that was first detected in April 2009. Within 4 months of its appearance in Mexico, it had spread to >100 countries, with >200,000 confirmed cases globally, including >2,000 deaths (1). When the

Author affiliations: National University Health System, Singapore (Y.Y. Dan, P.A. Tambyah, J. Sim, L.Y. Hsu, D.A. Fisher, K.Y. Ho); and Singapore General Hospital, Singapore (J. Lim, W.L. Chow, Y.S. Wong)

DOI: 10.3201/eid1512.090902

Table 2. Variables used in Markov mode (base case and sensitivity analysis) to compare outbreak estimates, Singapore*

Variable	Description	Base case	Sensitivity analysis
Exposure	No. persons exposed in 1 day in hospital per index case (nonlinear)	15 (average for 2 days) 6 (average for 5 days)	2–30
Secondary attack rate	No. persons exposed/infected	30% Spanish influenza 10% SARS 30% pandemic (H1N1) 2009	10–100%
Incubation period	Time to symptoms	Spanish influenza: 2 days SARS: 4 day Pandemic (H1N1) 2009: 3 days	1–7
Infectious period preclinical	Incubation–latent	Spanish influenza: 1 day SARS: 0 day Pandemic (H1N1) 2009: 1 day	1–3
% Clinical versus asymptomatic		Spanish influenza: 95% SARS: 100% Pandemic (H1N1) 2009: 95%	70–100%
% Atypical (missed)		Spanish influenza: 5% SARS: 20% Pandemic (H1N1) 2009: 5%	0–50%
% Complication		10× mortality rate	
Infective atypical	Infective	4 days	1–7
Case-fatality rate	% death	Spanish influenza: 5% SARS: 10% Pandemic (H1N1) 2009: 4%	
Isolation failure	Transmission despite PPE/isolation	5%	0–10%
Exposure reduction	% reduction in exposure rate	Alert Green 50% Alert Yellow 80% Alert Orange 90%	0–100%
Cost based on alert policy, direct and indirect	Once Daily recurring	Activation: US$110,000 Green: US$4,000 Yellow: US$76,000 Orange: US$100,000	
Cost by type of treatment, based on actual financial charges	Isolation Treatment antiviral/day Uncomplicated influenza Complicated influenza Respiratory failure with mechanical ventilation	US$230 US$25 Mean: US$600, Median: US$420 Mean: US$1800, Median: US$220 Mean: US$5,500, Median:US$4,660	

*SARS, severe acute respiratory syndrome; PPE, personal protective equipment.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 12, December 2009 1909

Cost-effectiveness Analysis of Hospital Infection Control Response to an Epidemic Respiratory Virus Threat

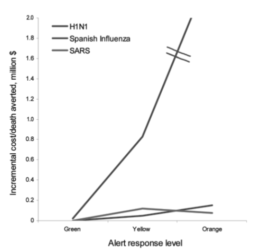
Yock Young Dan, Paul A. Tambyah, Joe Sim, Jeremy Lim, Li Yang Hsu, Wai Leng Chow, Dale A. Fisher, Yue Sie Wong, and Khek Yu Ho

Table 3. Results of cost-effectiveness analysis of potential outbreaks and responses, Singapore*

Alert level and disease	No. infected	No. deaths	Additional cost	Cost/case prevented†	Cost/death prevented†	Incremental cost/case‡	Incremental cost/death‡
None							
Pandemic (H1N1) 2009	2,580	10	25,200				
Spanish influenza	3,210	161	80,000				
SARS	825	83	99,200				
Green							
Pandemic (H1N1) 2009	316	1	326,430	95	23,644		
Spanish influenza	624	31	468,000	107	2,140		
SARS	105	11	220,500	120	1,195		
Yellow							
Pandemic (H1N1) 2009	59	0.2	1,485,500	414	103,274	3,221	827,907
Spanish influenza	120	6	2,212,000	493	9,857	2,472	49,829
SARS	43	4	1,188,000	995	9,945	11,146	121,241
Orange							
Pandemic (H1N1) 2009	24	0.1	1,836,000	506	126,807	7,153	2,503,600
Spanish influenza	59	2.95	2,856,000	629	12,590	7,541	153,333
SARS	12	1.2	1,537,000	1,263	12,601	8,041	7,541

*SARS, severe acute respiratory syndrome. All costs given in US$.
†Compared with no policy.
‡Compared with 1 alert level down.

Bottom line: Depends on the virus



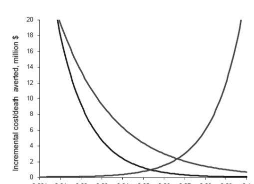


Figure 4. Sensitivity analysis for case-fatality rate (black line), % exposure reduction (red line), and secondary attack rate (blue line). Exponential graphs show poor cost-effectiveness at extremes of low case-fatality rate and low transmissibility (high % exposure reduction and low secondary attack rate).

Emerging Infectious Diseases: The bottomline…

- Emerging Infectious Diseases will occur
- We can be prepared
- Do good surveillance
- Protect staff
- Have good data
- Have friends – especially internationally!

Emerging Infectious Disease in Southeast Asia

Prof. PaulAnanth Tambyah, National University of Singapore

Broadcast from the 2010 conference of the Australian Infection Control Association (www.aica.org.au)