Infectious Diseases Research at NUS - A Personal Perspective

Paul Ananth Tambyah

FIFTY YEARS OF MEDICAL EDUCATION IN MALAYA 1905 - 1955

Department of Bacteriology.

Before the building of the new General Hospital and College of Medicine, all laboratory services for the Government Hospitals and Dispensaries were run by the Government Pathologist and Government Analyst, Singapore, under what judged by modern standards were very inadequate conditions. With the building of the new General Hospital a Department of Pathology with a separate Mortuary building was constructed.

In 1925 a donation was received from the Rockefeller Foundation for the institution of a Chair of Bacteriology and Dr. A. Neave Kingsbury became its first holder. When the present College building was opened in 1926, the laboratory services were reorganised and the bacteriological work put under the charge of the

RESEARCH IN THE MEDICAL SCHOOL

By D. W. G. Faris, *C.B.E.*, M.B., B.S., M.R.C.S., D.P.H.

icine. For
r Medical
nd holder
or Young
the staff
istant and
one laboratory servant. The present excellent staffing enjoyed by the department is the fruit of his labours. The department was reorganised into suitable small laboratories and as funds allowed equipment was obtained. Realising that experimental animals were essential for bacteriological work, Professor Young organised on a large scale the breeding of laboratory animals and it was this sure foundation that has enabled the department to breed the large number of animals required for its present work. In addition to teaching, routine bacteriological diagnosis and vaccine production, Professor Young carried out research work in leprosy, etc. Perhaps because of his hypercritical mind he did not publish any papers.

Before the foundation of the University in 1949, most of the research was of the applied type which has proved to be of great value in its local applications

Biology, Dentistry, Pathology, Physiology and Clinical Medicine in general. Applied research is still necessary and many local problems remain to be elucidated. Examples of pure or academic research before World War II are the anthropological

The view that the field of pure research should ordinarily be left to the laboratorie of Europe, America and elsewhere is no longer tenable for since the establishmen of the University, the appointment of a larger number of well qualified an experienced persons as teachers has tended to increase this type of research. Ther is room for effective collaboration between the biochemist, parasitologist, bacteriologist, physiologist and the clinician.

Early clinical research at NUS

THE PROBLEM OF DIABETES IN THE SINGAPORE POPULATION AND THE IMPACT OF ORAL ANTIDIABETICS ON ITS MANAGEMENT

Ann N Y Acad Sci. 1959;74:918-30

Ho Yuen

Singapore General Hospital, Singapore

posed by diabetes mellitus are difficult to obtain. However, there is little doubt that diabetes constitutes a large part of the problem of the care of the health of the population.

Problem in Management

It is generally known that the Chinese culture emphasizes good food and, in Singapore, this attitude toward food is shared by the other communities. Hence, it is extremely difficult, if not impossible, to expect our patients to adhere to a strict diabetic diet for long. It is chiefly for this reason that

Method of trial. The 67 trial cases were divided into three groups: Group *A*, those who did not have any previous treatment; Group *B*, those who were treated with tolbutamide; and Group *C*, those treated with insulin prior to chlorpropamide therapy.

the patients is related to the degree
).9 per cent of male and 60 per cent
It would seem that chlorpropamide
n in female diabetics, but a definite
be made without further investiga-
tion in a larger series of cases.

In relating the ethnic groups of patients to the number of cases with good control of glycosuria, it is obvious that chlorpropamide is equally effective in Chinese, Indians, and Malays.

Nearly 60 years of DM clinical trials

Proceedings of the Alumni Association,
Malaya
Vol. 10, No. 4, December, 1957

A CLINICAL TRIAL OF TOLBUTAMIDE IN 220 DIABETICS

By Tan Bock Yam, M.B., B.S., and Ronald Wells, M.R.C.P.
(From the Department of Medicine, University of Malaya)

Since Janbon and his co-workers (1942) observed the occurrence of hypoglycaemic reactions with a new sulphonamide I.P.T.D. (p-amino-benzene sulphonamido-isopropyl thiodiazole), later confirmed in a series of animal experiments by Loubatieres (1942-46), the oral treatment of diabetes mellitus with this and

Proceedings of the Alumni Association,
Malaya
Vol. 10, No. 2, June, 1957

A CLINICAL TRIAL OF SULPHONILYL-BUTYLCARBAMIDE IN 51 DIABETICS

By Ronald Wells, M.B., M.R.C.P. and Tan Bock Yam, M.B., B.S.

Until very recently the only successful methods of treating diabetes mellitus were insulin administration and dietary restriction. The use of insulin involves at least one injection every day, in most cases for life, and is associated with unavoidable discomfort to the patient. The difficulties in evolving and teaching

First research mentor From internship

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Weiss Memorial Internal Medicine Categorical and Preliminary Residents circa 1994
Our chief resident is in the middle with the tie and I am somewhere in the back!

Chicago Hopeful

By Assoc Prof Paul Ananth Tambyah

A/Prof Tambyah recalls fondly his training days as an Internal Medicine resident in cosmopolitan inner-city Chicago, and how being a trainee meant being given "ownership" of patient care, learning how to present and justify your own patient management plans, and being able to sit through teaching conferences without being paged away.

I will never forget what one Singaporean returning from overseas training said, which helped me decide to go to Chicago, "The only thing worse than being a MO in XYZ hospital is being a registrar. In the US, a trainee is a trainee. Your job is to learn. Here in XYZ hospital, your job is to take the subsidised workload off the consultants." Of course, that was more than 15 years ago, and I am sure

UW… thanks to Siok

who was terribly ill had very low oxygen levels. It appeared to be a powerful pneumonia.

"After I had concluded that it was an overwhelming viral pneumonia and we needed to add high-dose steroids, a very good medical student pointed out objects on the gram stain that he couldn't identify," says Maki.

When Maki double-checked the gram stain, he discovered budding yeasts. The patient had overwhelming pulmonary blastomycosis, the first case seen at University Hospital. Maki and his teams devised a very aggressive treatment plan based on the new information. A month later, the patient walked out of the hospital. Maki still takes care of him today.

The doctor leans forward in his chair when asked if he's all right with being wrong.

"I very much want my assumptions challenged," he says. "Nothing gives me more fulfillment than a very smart medical student or resident saying, 'Are you sure that's what is going on with the patient?' It's especially satisfying if they show me where I'm wrong and we can do better."

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and Public Heal
UNIVERSITY OF WISCONSIN

EDUCATION RESEARCH COMMUNITY & PUBLIC HEALTH PATIENT CARE

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Alumni Profile: Dennis Maki Deeply Connected to Infectious Diseases

Dennis Maki, MD, the University of Wisconsin School of Medicine and Public Health (SMPH) infectious disease researcher, physician and professor who just won the Wisconsin Medical Alumni Association's top award, has a very personal and emotional connection to a deadly infectious disease.

Maki's aunts died in their mother's arms of diphtheria at ages 3 and 4, years before the disease was virtually wiped out by an effective vaccine.

Related Information

Wisconsin Medical Alumni Association

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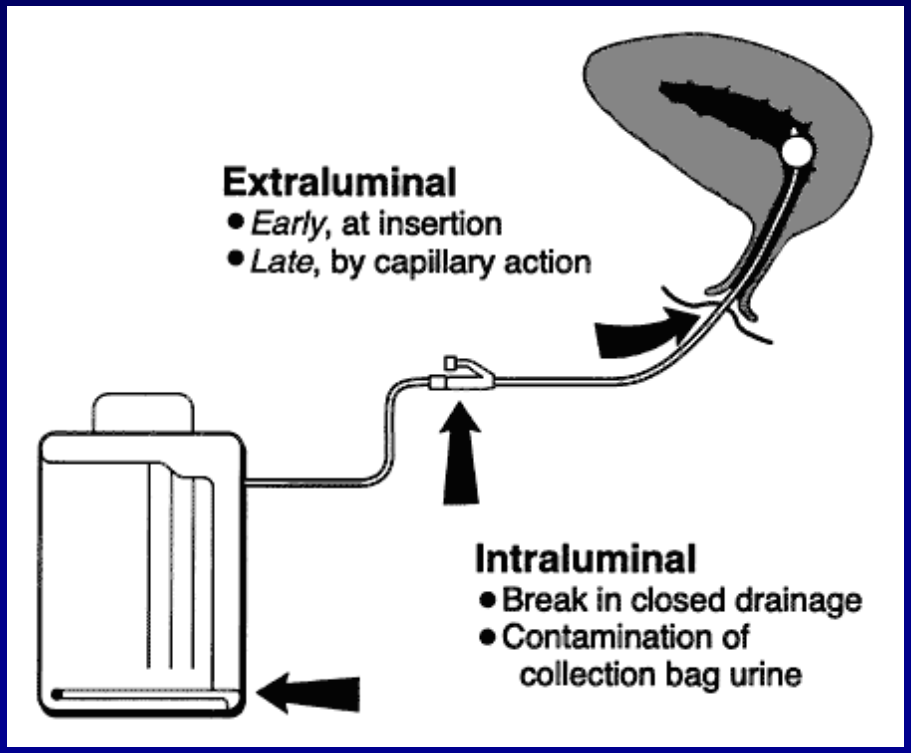
An NMRC fellowship and two large industry funded clinical trials…



Maki & Tambyah Emerg Infect Dis. 2001 Mar-Apr;7(2):342-7

Siver hydrogel catheters:

- 852 newly catheterised patients studied daily
  - CAUTI in controls: 21.2%
  - CAUTI in coated catheters: 15.4%
    - RR 0.72, 95% CI 0.68-0.84, P=0.03
  - Most effective for yeasts, staphylococci/enterococci
  - Little effect for gram-negative bacilli
    - *Maki, Knasinski, Halvorson, Tambyah SHEA 1998*

Nitrofurazone coated catheters:

- 344 newly catheterised patients studied daily
  - RR 0.672, P=0.30 overall
  - OR 0.22, P=0.02 for GNRs
  - Not effective for yeasts
  - Little effect beyond 7 days
    - *Maki, Knasinski, Tambyah SHEA 1997*

CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting

Teresa C. Horan, MPH, Mary Andrus, RN, BA, CIC, and Margaret A. Dudeck, MPH
Atlanta, Georgia

BACKGROUND

Since 1988, the Centers for Disease Control and Prevention (CDC) has published 2 articles in which nosocomial infection and criteria for specific types of nosocomial infection for surveillance purposes for use in acute care settings have been defined.[1,2] This document replaces those articles, which are now considered obsolete, and uses the generic term "health care–associated infection" or "HAI" instead of "nosocomial." This document reflects the elimination of criterion 1 of clinical sepsis (effective in National Healthcare Safety Network [NHSN] facilities since January 2005) and criteria for laboratory–confirmed bloodstream infection (LCBI). Specifically for LCBI, criterion 2c and 3c, and 2b and 3b, were removed effective in NHSN facilities since January 2005 and January 2008, respectively. The definition of "implant," which is part of the surgical site infection (SSI) criteria, has been slightly modified. No other infection criteria have been added, removed, or changed. There are also notes throughout this document that reflect changes in the use of surveillance criteria since the implementation of NHSN. For example, the

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Am J Infect Control 2008;36:309-32.

0196-6553/$34.00

doi:10.1016/j.ajic.2008.03.002

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following:

- Clinical evidence may be derived from direct observation of the infection site (eg, a wound) or

ASB-Asymptomatic bacteriuria

An asymptomatic bacteriuria must meet at least *1* of the following criteria:

1. Patient has had an indwelling urinary catheter within 7 days before the culture
   and
   patient has a positive urine culture, that is, $\geq 10^5$ microorganisms per cc of urine with no more than 2 species of microorganisms
   and
   patient has no fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness.
2. Patient has *not* had an indwelling urinary catheter within 7 days before the first positive culture
   and
   patient has had at least 2 positive urine cultures, that is, $\geq 10^5$ microorganisms per cc of urine with repeated isolation of the same microorganism and no more than 2 species of microorganisms
   and
   patient has no fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness.

SUTI-Symptomatic urinary tract infection

A symptomatic urinary tract infection must meet at least *1* of the following criteria:

1. Patient has at least *1* of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness
   and
   patient has a positive urine culture, that is, $\geq 10^5$ microorganisms per cc of urine with no more than 2 species of microorganisms.
2. Patient has at least *2* of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness
   and
   at least *1* of the following
   a. positive dipstick for leukocyte esterase and/or nitrate
   b. pyuria (urine specimen with ≥10 white blood cell [WBC]/mm^3 or ≥3 WBC/high-power field of unspun urine)
   c. organisms seen on Gram's stain of unspun urine
   d. at least *2* urine cultures with repeated isolation of the same uropathogen (gram-negative bacteria or *Staphylococcus saprophyticus*) with $\geq 10^2$ colonies/mL in non-voided specimens
   e. $\leq 10^5$ colonies/mL of a single uropathogen (gram-negative bacteria or *S saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection
   f. physician diagnosis of a urinary tract infection
   g. physician institutes appropriate therapy for a urinary tract infection.
3. Patient ≤1 year of age has at least *1* of the following signs or symptoms with no other recognized cause: fever (>38°C rectal), hypothermia

Symptoms and Catheter UTI??

Table 1. Epidemiological Characteristics of 1273 Patients Without CAUTI and 224 Patients With 235 Nosocomial CAUTIs Identified in a Prospective Study of Catheterized Patients*

Characteristic	Without CAUTI	With CAUTI	*P*
Age, mean ± SD, y	55.0 ± 17.3	56.0 ± 18.3	.47
Sex, No. (%)			
Male	787 (62)	77 (34)	<.001
Female	486 (38)	147 (66)	
Service, No. (%)			
Surgical	1024 (80)	138 (62)	<.001
Medical	249 (20)	86 (38)	
Antibiotics per catheter-day, mean ± SD	2.4 ± 1.9†	1.6 ± 1.7‡	<.001
APACHE II score, mean ± SD	16.2 ± 6.3	16.4 ± 6.5	.58
Days catheterized before onset of infection, mean ± SD	4.4 ± 3.8†	6.4 ± 6.1	<.001

**CAUTI indicates catheter-associated urinary tract infection; APACHE II, Acute Physiology and Chronic Health Evaluation II.[21]*
†Total days catheterized.
‡Days preceding CAUTI.

8 research nurses questioned catheterized patients daily

Tambyah, Maki
Arch Intern Med. 2000 Mar 13;160(5):678-82.

Symptoms and Catheter UTI??

Table 2. Symptoms Referable to the Urinary Tract, Fever, Leukocytosis, and Quantitative Pyuria in a Subset of 1034 Hospitalized Patients With Urinary Catheters*

	Without CAUTI (n = 945)	With CAUTI (n = 89)	*P*
Proportion with symptoms, %			
Pain	5.9	4.8	.81
Urgency	7.6	6.0	.68
Dysuria	8.0	6.0	.66
Temperate >38.5°C	19.8	17.7	.77
Highest temperature, mean ± SD, °C	38.1 ± 0.7	37.8 ± 0.5	<.01
Peripheral white blood cell count, mean ± SD, $\times 10^3$/L	11.3 ± 4.1	10.7 ± 3.6	.14
Highest urine white blood cell count, mean ± SD, /μL†	11 ± 100	309 ± 1065	.009

**Other than catheter-associated urinary tract infection (CAUTI), which was detected in 89 patients, no infections were identified. The proportion of patients with and without CAUTI who could respond to daily questions regarding symptoms was identical in the 2 groups: 94%.*

†Excludes kidney transplant patients, whom we have found show a burst of sterile pyuria following transplantation.

Symptoms are uncommon with catheter UTI

Tambyah, Maki
Arch Intern Med. 2000 Mar 13;160(5):678-82.

ORIGINAL INVESTIGATION

Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic

A Prospective Study of 1497 Catheterized Patients

Paul A. Tambyah, MBBS; Dennis G. Maki, MD

[HTML] Catheter-associated urinary tract infection is rarely symptomatic: a prospective study of 1497 catheterized patients
PA Tambyah, DG Maki - Archives of internal medicine, 2000 - jamanetwork.com
... Stamm WE Measurement of pyuria and its relation to bacteriuria. Am J Med. 1983;75(suppl 1B)53- 58Article. 25. Garner JSJarvis WREmori TGHoran TCHughes JM CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16128- 140Article. 26. **Tambyah** PAMaki
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Background: Catheter-associated urinary tract
tion (CAUTI) is the most common nosocomial
tion, accounting for more than 1 million cases eac
in US hospitals and nursing homes.

Objective: To define the clinical features of CA

Setting and Patients: A university hospital; 1497 newly catheterized patients.

Design: Every day that the catheter was in place, a quan-

cant differences between patients with and without CAUTI in signs or symptoms commonly associated with urinary tract infection—fever, dysuria, urgency, or flank pain—or in leukocytosis. Only 1 of the 235 episodes of CAUTI that were prospectively studied was unequivocally associated with secondary bloodstream infection.

Conclusions: Whereas CAUTIs are a major reservoir of antibiotic-resistant organisms in the hospital, they are rarely symptomatic and infrequently cause bloodstream infection. Symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CAUTI.

Accepted for publication December 16, 1999.

This study was supported by research grants from Bard International, Covington, Ga, and Rochester Medical Inc, Rochester, Minn, and by an unrestricted gift for research in infection control from the Oscar Rennebohm Foundation, Madison, Wis. Dr Tambyah is the recipient of a Singapore National Medical Research Council Fellowship and the Academy of Medicine Singapore Travel Fellowship.

Presented in part at the Eighth Annual Meeting of the

ORIGINAL INVESTIGATION

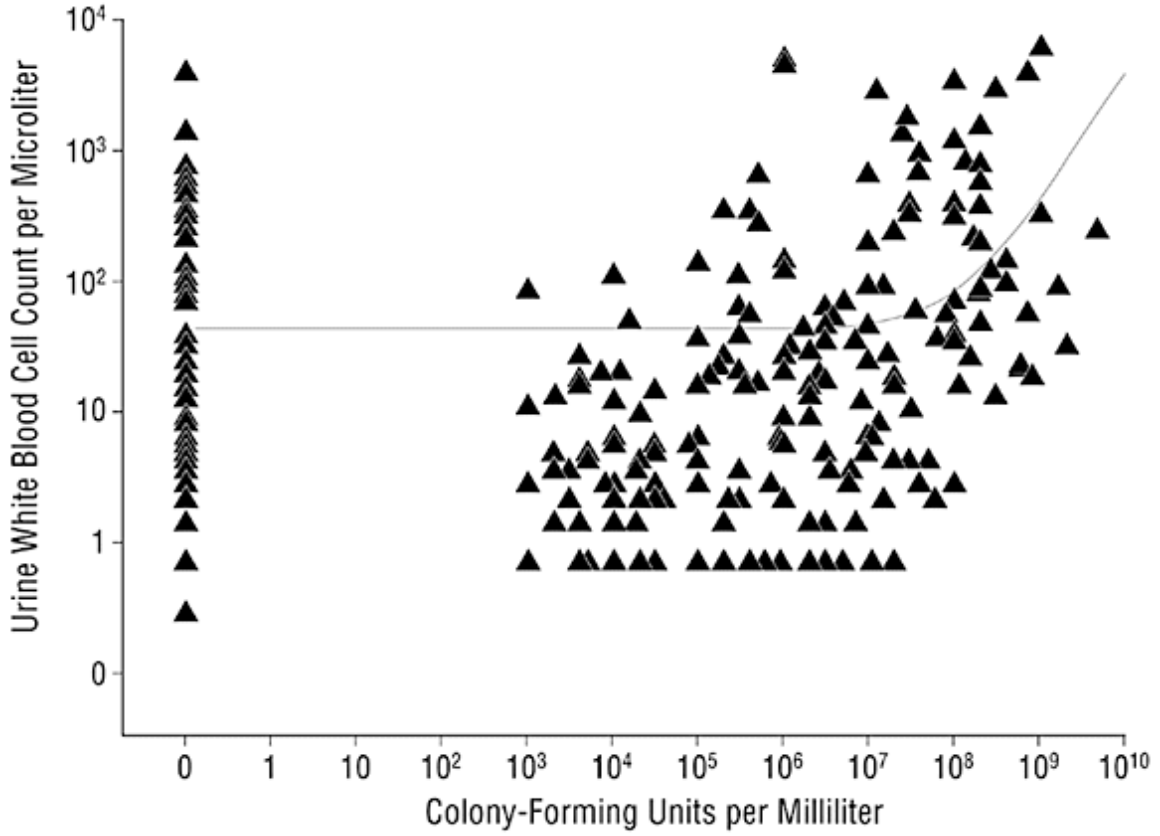
The Relationship Between Pyuria and Infection in Patients With Indwelling Urinary Catheters

A Prospective Study of 761 Patients

Paul A. Tambyah, MBBS; Dennis G. Maki, MD

Background: Pyuria is universally considered as esser
tial for identifying urinary tract infections in noncath
eterized patients. The utility of pyuria in the catheter
ized patient, to identify catheter-associated urinary trac
infection (CAUTI), has not been adequately defined.

Methods: We prospectively studied 761 newly cath
eterized patients in a university hospital; 82 (10.8%) de



Accepted for publication May 6, 1999.

This study was supported by research grants from Bard International, Covington, Ga; and Rochester Medial Inc, Rochester, Minn. Dr Tambyah is the recipient of a Singapore National Medical Research Council Fellowship.

Presented in part at the 38th Interscience Conference

More Importantly

finally, in 2009

Table 1. ***Urinary Tract Infection Criteria***

Criterion	Urinary Tract Infection (UTI)
	Symptomatic UTI (SUTI) Must meet at least 1 of the following criteria:
1a	Patient had an indwelling urinary catheter in place for >2 calendar days, with day of device placement being Day 1, and catheter was in place on the date of event *and* at least 1 of the following signs or symptoms: fever (>38°C); suprapubic tenderness*; costovertebral angle pain or tenderness* *and* a positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml and with no more than 2 species of microorganisms. Elements of the criterion must occur within a timeframe that does not exceed a gap of 1 calendar day between two adjacent elements. ----------OR---------- Patient had an indwelling urinary catheter in place for >2 calendar days and had it removed the day of or the day before the date of event *and* at least 1 of the following signs or symptoms: fever (>38°C); urgency*; frequency*; dysuria*; suprapubic tenderness*; costovertebral angle pain or tenderness*

The controversies continue

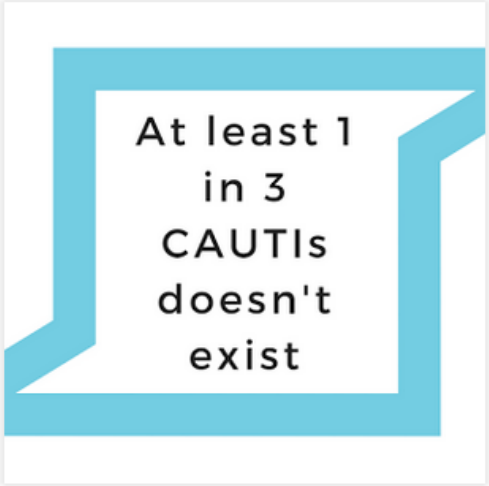
Controversies in Hospital Infection Prevention Pondering vexing issues in infection prevention and contro

Classic Flipcard Magazine Mosaic Sidebar Snapshot Timeslide

NOV
21

CAUTI SCHMAUTI ! (part 4)

A new paper in Infection Control and Hospital Epidemiology takes us another step closer to reclassifying CAUTI from a healthcare associated infection to a healthcare associated myth. Tom Fraser and colleagues at the Cleveland Clinic worked with their ICUs to reach consensus to limit urine cultures in patients with fever to kidney transplant recipients, neutropenic patients, patients with recent GU surgery, and patients with evidence of urinary tract obstruction. One year later, here's what they found:



- There was no significant change in urinary catheter utilization (approximately 70% of patient days were associated with catheter use 1 year before and after implementation of changes in ordering urine cultures).
- The number of urine cultures ordered fell by ~50%.
- The CAUTI rate fell from 3.0 to 1.9/1,000 catheter days, a significant reduction of 33%.
- There was no change in the rate of healthcare associated bloodstream infections, and no change in the subset due to Enterobacteriacae, which implies that there was no increase in bacteremic urinary tract infections. The potential for bacteremia is a major reason for treating CAUTI.

A similar study from Mayo Clinic showed similar findings (50% reduction in urine cultures ordered and a 30% reduction

http://haicontroversies.blogspot.sg/2016/11/cauti-schmauti-part-4.html

Avian influenza in Indonesia

Avian Flu

Sulianti Saroso Infectious Disease Hospital, Jan 06

1957 “Asian Flu”
Dr Lim Kok Ann

Most of the chronic sick are elderly, but unfortunately there is a small minority of young people among them. It is, as the Minister says, “ wholly unsatisfactory ” for them to be nursed for, “ perhaps, the greater part of a life-time in the company of older patients in all stages of terminal illness or of much greater ages.” He asked regional hospital boards to consider how far these patients could be grouped together without losing touch with their own families.

The Minister reminded the local authorities that there were still many people—it had been estimated at 4500—who were occupying hospital beds but who could be in residential homes if they were available. A smaller number of people living in homes would probably benefit by being moved to hospital. These ill-used beds showed the need for closer coöperation between hospitals and the local services, which should cover not only the patients on the hospitals' waiting-lists but also the patients who had returned to their homes. Both of these groups stood in special need of the help of the domiciliary health services. These, the Minister thought, though generally adequate, were too thinly spread in some areas and he urged their continued expansion.

The advice which the Minister has offered the hospital and the local authorities was based on Dr. C. A. Boucher's report[3] on the survey of services for the chronic sick and elderly. This survey was carried out during 1955 in each hospital region by teams headed by a prin regional officer of the Ministry. The teams colle opinions as well as facts, and not the least intere part of the report is the chapter on the views on geria as a specialty. At one extreme it was held that an el patient should be treated in the general wards of hospital, and geriatricians were regarded as “ me practitioners of a clinical calibre who could not alv claim equality with other consultants.” There was siderable prejudice against geriatric appointments some ignorance of the possibility of reablement. On other hand those who supported these appointments sure that, thanks to them, the pressure on beds relieved, and the turnover improved. Many geri units had been remarkably successful; some less perhaps because the geriatrician's responsibilities limited to the daily treatment of patients and bec there was lack of junior medical staff and an insuffici of almoning, physiotherapy, and occupational-ther help. Though geriatrics offers clinical opportunitie unlimited interest and wide opportunities of resea the survey found that the recruitment of junior remained difficult and senior staff with suitable experi were not always forthcoming. New units would entail appointment of more physicians with a clear underst ing of the social and medical problems of the eld patient, yet the number of registrar appointment existing units did not seem to meet the demand for se appointments.

3. *Rep. publ. Hlth med. Subj., Lond.* no. 98, 1957. H.M. Stationery Office. Pp. 60. 3s.

Public Health

INFLUENZA OUTBREAK IN SINGAPORE

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SURGEON COMMANDER, R.N.; PRINCIPAL MEDICAL OFFICER, H.M. DOCKYARD, SINGAPORE

An outbreak of influenza, which seems to have begun in North China, reached Singapore in May, 1957. Influenza is not notifiable in the island and no reliable figures for overall incidence could be obtained. Moreover, a large proportion of the population does not seek Western-type medical care. Mainly for these reasons, our detailed study of the outbreak has been confined to the civilian population in the Singapore Naval Base, consisting of Naval Base workers and their dependants. The main advantages of this include fairly complete ascertainment of cases from the working population at least, reasonable

data, with certain other observations made in the Singa Civilian General Hospital in the city.

Clinical Findings

For present purposes, the clinical observations re to 298 patients with influenza admitted to the A hospital in the Base. Criteria of admission were diffi to specify since they depended on many factors (ag the patient, general state of health, availability of b &c.). Doctors were asked to assess their cases clinic in three categories—mild, moderate, and severe—bu became evident that such classification was difficult unreliable and it was accordingly dropped.

Table 1 shows the distribution of the 298 admit cases by age and sex. At the younger ages little differe is seen between the numbers of males and females, as age increases female cases are fewer. This is proba due to a difference in the numbers seeking treatm rather than in the numbers affected. Table 1 also sh the duration of hospital stay by age. It is clear t hospital stay was longest in the very young and the Young adults had the shortest stay.

Pyrexia

All patients had pyrexia, and they were not dischar until their temperatures had returned to normal. The m duration of pyrexia over all ages was 2·4±0·87 days an varied little with age.

The mean temperature on admission was 102·9°F and mean highest record was 103·1°F. In 41 of the 298 cases highest record was higher than the record on admission. the patients with temperatures below 100°F on admiss the temperature rose in 63% during their hospital st

No MTAs/ RCAs

3:14 Flu Fighter.

On the first Monday that I returned to the laboratory I got a call from Dr. Huang who had attended the course we had been giving for Diploma in Public Health students. He asked me if I would like to visit Pulau Bukom with him to see some patients suspected of having got influenza from the Hong Kong outbreak. "What outbreak?" I asked, "Hong Kong?". It had been in the papers, I was told, but I had not caught up with the news yet. Hale confirmed that an outbreak of influenza had been reported in Hong Kong and very likely the patients in Pulau Bukom, where Shell Oil Company had a large installation and where some port workers lived, had caught influenza from passengers off ships they had visited. It was an opportunity to perform our duties as a WHO Influenza Observer, appointed by WHO in various parts of the world to detect new variants of influenza as early as possible.

I went over to Pulau Bukom with the Public Health doctor and found typical cases of influenza - the patients had fever, running noses, red eyes, some cough,, and were miserable. I took throat swabs and blood specimens and returned to the laboratory. I got some 8-day-old and some 14 day-old chick embryos from Crawford Street where there were a number of hatcheries (who thought I was making some kind of medicine with the un-hatched chicks) and inoculated them with extracts of the throat swabs to which a mixture of penicillin and streptomycin was added. Before the days of these antibiotics, inoculation of bacteria from the throat would assuredly kill the chicks. Then I waited. On the second day - Wednesday - I opened a couple of the 14-day eggs that had been inoculated amniotically, removed the lungs from the baby chick and ground them up to make a suspension. I mixed the clarified suspension with some chick red blood cells and was elated to find that the red blood cells had clumped together as they would be by an influenza virus. I took the precaution of mixing the red blood cells with a suspension made from lungs of un-inoculated chicks to show that

International Influenza Centre with instructions for the dry ice to be renewed every 24 hours. Identical packages were sent to the American International Influenza Centre in Washington and other influenza virus laboratories including the Hall Institute in Melbourne. I cabled Dr. Eric French to tell him that I thought I had isolated an influenza virus but I could not type it with the serum he had given me; could he help? It was Friday morning.

The specimens arrived in London on Saturday afternoon and sat in the Airport icebox until the following Monday. French personally went to Melbourne Airport on Friday night to retrieve the specimens that I had sent him and immediately inoculated some chicks amniotically the way that he had taught me. On Sunday morning French went to his laboratory and opened up some inoculated eggs and found that there was, indeed, a red blood cell clumping agent present. He repeated the tests that I had done using the same influenza antisera that he had given me and confirmed my negative results. He then tested the chick embryo extract by another test called the complement-fixation test (CIFT) which proved that our virus isolate belonged to the Influenza A virus group (there were two other Influenza virus groups, B and C Influenza groups that behaved differently by the CFT) but was sufficiently different from other Influenza A viruses as not be neutralized by their antisera in HI tests. his implied also that a person who had experienced the old Influenza A viruses would not be protected against the new variant. French called Sir Mac who came to the laboratory to review his results then called the newspapers. On Monday morning the Singapore Straits Times reported my coup with front page headlines: "Brilliant Singapore scientist discovers new influenza virus". In following write-ups they called me Flu-fighter. I did not think that they knew my Grand Uncle by marriage, Dr.Wu Lien-Teh, had published his memoirs under the title Plague Fighter.

The aftermath of my discovery of the new Influenza virus, subsequently

http://limkokann.blogspot.sg/

Scientists say the flu bug is new type

HIGH PRAISE FOR COLONY DOCTOR

MELBOURNE, Thursday.

SIR MacFarlane Burnet, director of the Walter and Eliza Hall Institute for Medical Research, said today that a new type of influenza virus was responsible for the epidemic now sweeping the Far East.

Scientists at the institute had established that the virus was a new type of influenza virus A, he said.

"This means that the virus formerly known as

DR. LIM

Type A has undergone a sharp change in character," Sir MacFarlane said. He added that serums developed to combat the previously known virus would now be "useless."

'Great credit'

Sir MacFarlane said great credit must be given to Dr. Lim Kok Ann, lecturer in the University of Malaya, for isolating specimens which were examined at the institute.

Sir MacFarlane will confer tomorrow with the head of the Commonwealth Serum Laboratory on plans to produce a new serum.

Commenting on reports

FLU VICTIMS BARRED ON MADRAS BOAT

PENANG, Thurs.—Five suspected influenza victims were not allowed to sail from here aboard the State of Madras today.

A family of four were also barred, after the ship's doctor, Dr. A. Rahman, found that the youngest child had measles.

These nine disappointed passengers will leave instead on May 28 for Madras by the same boat.

The 'flu epidemic is still declining throughout Malaya.

'Bomb' protest

TOKYO, Thurs.—Students and Buddhists today began indefinite picket outside United States and British bases in protest against clear tests.—Reuter.

OUS AGAIN

ur General Hospital, hospital spokesman said day she was "progressing satisfactorily."

police spokesman told e Straits Times that Evarett would be

Dr. Lim, the flu fighter, says: It was a case of teamwork really

DR. LIM KOK ANN, the University of Malaya virologist who isolated the virus which is causing the flu epidemic, yesterday modestly disclaimed the praise heaped on him by Australian specialists.

In his laboratory—littered with some of the 400 eggs he has used so far in his researches—Dr. Lim said:

"It's really a matter of teamwork—modern research always is."

He added that first credit was due to Dr. W. K. Ng, the rural health officer, who drew his attention to the infection when it first broke out on Pulau Brani.

Dr. Lim has been working 0 hours a day since the nd of April on analysing the pidemic.

He expects to continue oing so for the next two or ree months.

He is trying now to classify e manner in which the sease spread through the fferent age, social and cial groups.

A graduate of Edinburgh iversity, Dr. Lim is a ss fanatic in his spare e. He is champion of the gapore Chess Club and itor of its magazine

Vaccine on way

n Thursday, Dr Lim was ed by Sir MacFarlane net, Director of the Walnd Eliza Hall Institute Medical Research in ourne.

MacFarlane said the specimens isolated by Lim had enabled scien- at the Institute to lish that the epidemic sweeping the Far East caused by a new type

tralia is now develop-

Fish poisoned—

PENANG, Fri.—The Director of Fisheries, Mr. D. W. Le Mare, said today that poisoning of fishing waters was a "royal prerogative."

He was commenting on a report that a fish drive

will be held in t River next wee brate the Sultan jubilee.

Plans for this c vide for the cons of the river wit tuba roots wh paralyse the fish They will then be

HE WILL ADVISE RUBBER MISSION

SCHO 'HE

New rules

PARENTS here hours which se Monday.

Under a new Federa gulation requiring a m number of hours for subjects, particularly schools will work a five hours a week.

To cope with this, so nang schools will sta early as 7.30 a.m. and at 2 p.m.

Afternoon sessions

Wise advice

http://limkokann.blogspot.sg/

3.7 My first invention

Professor Wilson Smith, head of the Department of Bacteriology of UCHMS was an international authority on influenza viruses. To get a traineeship in his laboratory was not an easy thing and was made possible for me because of Hale's influence. In the academic world, andespecially in England, much is achieved through "old boys networks". One goes through the formalities of applying for a position, but the appointment comes because someone influential knew someone with the authority to say yes. "Kwansi" we say nowadays, though this term connotes some kind of nepotism or corruption which was not always the case.

When I had just joined the Medical College staff, my Uncle Robert passed through Singapore on his way to the United States and he gave mc some advice. The first was: "To be successful in research choose a topic ignored by others and make it your own specialty." The second was: "Find the best man in your field of study; go to work for him for a while and suck his brains dry. Then, go and work for his greatest rival and suck his brains dry. You will then be ready to work on your own." I was not in the position to do quite what Uncle Robert recommended, but being with Wilson Smith was a little step in the right direction.

Professor Wilson Smith put me to work with Dr. Margaret Edney, a staff member of the Walter and Eliza Hall Institute of Medical Research in Melbourne, who was on a staff-exchange appointment for post-doctoral experience. Wilson Smith had this to say before he passed me on to her: "Don't publish anything on what you do here without letting me see it, and don't mention my name without my permission." Besides Marge Edney, other people I got to know well were Dr. George Belyavin, Senior Lecturer, who was Professor Hale's junior before Hale went to Singapore, and Dr.

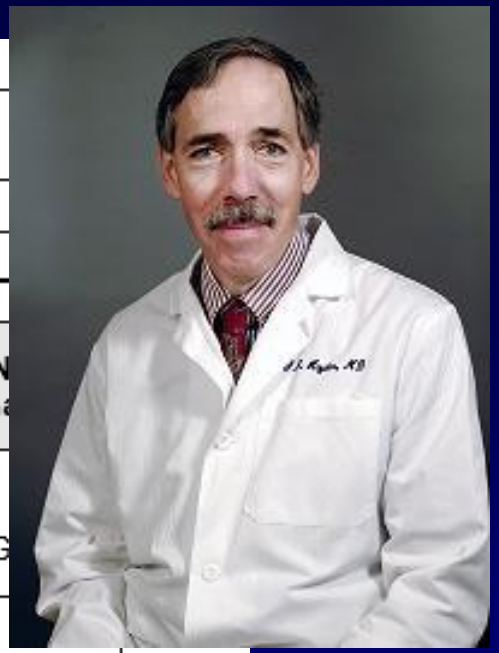
3:9 Down Under

In the summer of 1956 I took two months leave to visit the Walter and Eliza Hall Institute in Melbourne. The University then allowed a staff member to be absent from his department during the university vacation so long as he occupied his time usefully and caused the University no expense. Hale was impressed, perhaps, that I had the entree to the laboratory of MacFarlane Burnet, a Nobel Prize winner, and made no objections. On the way to Melbourne I stopped in Sydney to call on C.J.S. Purdy, the leading Australian chess player and author. The strong rivalry between Sydney (even before the Opera House was built) and Melbourne was illustrated by the following experience I had: when I tol
I was on the way to Melbourne, they cried
told Melbourne people that I had been i
luck!"

Two months was too short a time in wh
asked me to work with Dr. Eric French (a
out-break of influenza. He was also using
Edney had been doing in London and I w
chart which Dr. French had not yet adopt
number of serum samples that he collecte
testing them for influenza antibodies. H
throat swabs from patients from which
viruses by a method that I had not seen
involved the inoculation of patients' materi

ANNEX 1 – PROGRAMME

HMDP Visiting Expert in:	**Infectious Diseases**			
Name of Expert:	**Professor Fred Hayden**			
Programme Dates:	**From:**	**1 Dec 06**	**To:**	**6 Dec 06**



Date and Day	Time	Activities	Venue	Name and Designation of Coordinator	Contact N Coordina
1 Dec Friday	*10:30-12:00*	*Seminar on Influenza Vaccine Development + case presentation*	**NUS Dept of Microbiology Seminar Room**	Paul Ananth Tambyah/ Mary Ng ML	98126960/ 65163275(G
	12:00-13:00	*Lunch with ID trainees*	**NUH Level 5 Conf Rm**	Paul Ananth Tambyah	98126960
	13:00-14:00	*Dept of Medicine Rounds:* *Update on antivirals and Vaccines for Pandemic Influenza*	**NUH Level 5 Seminar Room**	Paul Ananth Tambyah	98126960
	14:00-15:00	*NUH Influenza research seminar*	**NUH OPAT conf room**	Paul Ananth Tambyah	98126960 *Dr Hayden will be attending but not speaking here
2 Dec Saturday	*08:00-10:00*	*Meeting with NUS ID Division on research agenda*	**Grand Copthorne**	Paul A Tambyah **closed meeting	98126960
					Dr Hayden will be

OPEN ACCESS Freely available online

PLoS MEDICINE

The PLoS Medicine Debate

What Is the Optimal Therapy for Patients with H5N1 Influenza?

Nicholas J. White[1]*, Robert G. Webster[2]*, Elena A. Govorkova[2], Timothy M. Uyeki[3¶]*

1 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, **2** Department of Infectious Diseases, Division of Virology, St. Jude Children's Research Hospital, Memphis, Tennessee, United States of America, **3** Epidemiology and Prevention Branch, Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America

Background to the debate: In a 2007 article in *PLoS Medicine* [10], Holger J. Schünemann and colleagues described a new process used by the World Health Organization for rapidly developing ment guidelines in emergency situati tions include outbreaks of emerging in

tions has serious consequences. Therefore, common sense argues for recommending higher doses for such infections, at the expense of increased toxicity, to avoid any possibility of under dosing those

Citation: White NJ, Webster RG, Govorkova EA, Uyeki TM (2009) What Is the Optimal Therapy for Patients with H5N1 Influenza? PLoS Med 6(6): e1000091. doi:10.1371/journal.pmed.1000091

BMJ

BMJ 2013;346:f3039 doi: 10.1136/bmj.f3039 (Published 30 May 2013)

RESEARCH

Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial

OPEN ACCESS

South East Asia Infectious Disease Clinical Research Network

Abstract

Objective To investigate the validity of recommendations in treatment guidelines to use higher than approved doses of oseltamivir in patients with severe influenza.

Design Double blind randomised trial.

Setting Thirteen hospitals in Indonesia, Singapore, Thailand, and Vietnam.

Participants Patients aged ≥1 year admitted to hospital with confirmed severe influenza.

Interventions Oral oseltamivir at double dose (150 mg twice a day/paediatric equivalent) versus standard dose (75 mg twice a day/paediatric equivalent).

Main outcome measure Viral status according to reverse transcriptase polymerase chain reaction (RT-PCR) for influenza RNA in nasal and throat swabs on day five.

Results Of 326 patients (including 246 (75.5%) children aged <15), 165 and 161 were randomised to double or standard dose oseltamivir, respectively. Of these, 260 (79.8%) were infected with influenza virus A (133 (40.8%) with A/H3N2, 72 (22.1%) with A/H1N1-pdm09, 38 (11.7%) with seasonal A/H1N1, 17 (5.2%) with A/H5N1) and 53 (16.2%) with influenza virus B. A further 3.9% (13) were false positive by rapid antigen test (negative by RT-PCR and no rise in convalescent haemagglutination inhibition titers). Similar proportions of patients were negative for RT-PCR on day five of treatment: 115/159 (72.3%, 95% confidence interval 64.9% to 78.7%) double dose recipients versus 105/154 (68.2%, 60.5% to 75.0%) standard dose recipients; difference 4.2% (−5.9 to 14.2); P=0.42. No differences were found in clearance of virus in subgroup analyses by virus type/subtype, age, and duration of illness before randomisation. Mortality was similar: 12/165 (7.3%, 4.2% to 12.3%) in double dose recipients versus 9/161 (5.6%, 3.0% to 10.3%) in standard dose recipients. No differences were found between double and standard dose arms in median days on supplemental oxygen (3 (interquartile range 2-5) *v* 3.5 (2-7)), in intensive care (4.5 (3-6) *v* 5 (2-11), and on mechanical ventilation differences in tolerabili

Conclusions There w double dose oseltamiv severe influenza admit

Registration Clinical T

Introduction

Human influenza is febrile illness. Occa respiratory complica Clinical trials have clinical and virologi influenza when it is symptoms.[4-7] Randor are lacking, but obse hospital indicate tha given early, is assoc length of stay, altho H1N1-pdm09 (pand influenza.[8-12] Timely H5N1 influenza redu treatment.

Higher oseltamivir uncomplicated influ or virological outcor dose.[4 5 13 14] Despite suggested use of dou The use of higher d management, public

The sudden emergence of pandemic H1N1 virus in 2009, the persistent circulation of highly pathogenic avian H5N1 viruses across large regions of the world since 1997, and the recent emergence and spread of avian H7N9 influenza virus in China[18]

Table 4| **Risk factors identified by conditional multiple logistic regression for being viral RNA negative by RT-PCR on day five. Important non-significant factors are also included. Patients with no detected influenza were excluded from analysis**

Factor	No of patients*	No of events*	OR (95% CI)	P value
Nose viral load†	304	213	0.73 (0.62 to 0.86)	<0.01
Karnofsky score <50‡	35	15	0.24 (0.08 to 0.78)	0.02
Child	236	49	0.62 (0.17 to 2.22)	0.46
Double dose oseltamivir	156	112	1.27 (0.73 to 2.20)	0.39
Virus type:				
B	51	36	0.88 (0.32 to 2.41)	0.80
H3N2	132	91	0.72 (0.30 to 1.70)	0.45
H5N1	15	2	0.03 (0.00 to 0.64)	0.03
H12009	68	57	1.01 (0.34 to 2.97)	0.99
H1N1-pdm	38	27	Reference	—

RT-PCR=reverse transcriptase polymerase chain reaction.
*Total number of patients in group and total number negati
†After $\log_{10}$ (x+1) transformation, odds ratio corresponds to
‡Patients with score <50 require frequent medical attention

Funding and sponsorship: The study was conducted by the South East Asia Infectious Diseases Clinical Research Network (www.seaicrn.org/) and supported by the National Institute of Allergy and Infectious Diseases and the Wellcome Trust of Great Britain. The Singapore site was supported by the Singapore National Medical Research Council.

No difference

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2008;358:2573-84.

ORIGINAL ARTICLE

A Clinical Trial of a Whole-Virus H5N1 Vaccine Derived from Cell Culture

Hartmut J. Ehrlich, M.D., Markus Müller, M.D., Helen M.L. Oh, M.D., Paul A. Tambyah, M.B., B.S., Christian Joukhadar, M.D., Emanuele Montomoli, Ph.D., Dale Fisher, F.R.A.C.P., Greg Berezuk, M.S., Sandor Fritsch, Ph.D., Alexandra Löw-Baselli, Ph.D., Nina Vartian, Ph.D., Roman Bobrovsky, Ph.D., Borislava G. Pavlova, Ph.D., Eva Maria Pöllabauer, M.D., Otfried Kistner, Ph.D., and P. Noel Barrett, Ph.D., for the Baxter H5N1 Pandemic Influenza Vaccine Clinical Study Team

vic, R. Sauermann, R. Schaberl, G. Sodeck, C. Thallinger, F. Traunmueller, C. Wagner, M. Zeitlinger; **Singapore:** *Changi General Hospital (Study Center Management):* S.K. Chua, S. Chuin, R. Fong, A.S. Foo, A.G. Koh, P.K. Lim, S.Y. Yap, L.H. Yew; *National University Hospital (Study Center Management):* J.W.L. Goh, L.Y. Hsu, C.W.P. Loke, J.Y.C. Ng, E.L. Toh, P. Weatherill, Y.P. Zhou.

It turned out to be swine flu not bird flu that came…

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SINGAPORE NEWS

E-mail Print

Singapore reports 12th H1N1-related death

By Rekha | Posted: 21 August 2009 2004 hrs

SINGAPORE: A 41-year-old male foreigner is Singapore's latest H1N1-related fatality, and the 12th so far.

The Health Ministry said the man had a history of diabetes. The cause of his death at Tan Tock Seng Hospital was certified as pneumonia due to H1N1 flu infection.

The ministry added that the number of patients seeking help at polyclinics for acute respiratory infection has decreased.

The ministry, which tracks the cases on a weekly basis, said the number had dropped from some 20,435 for the week starting August 2, to 15,486 for the week starting August 9.

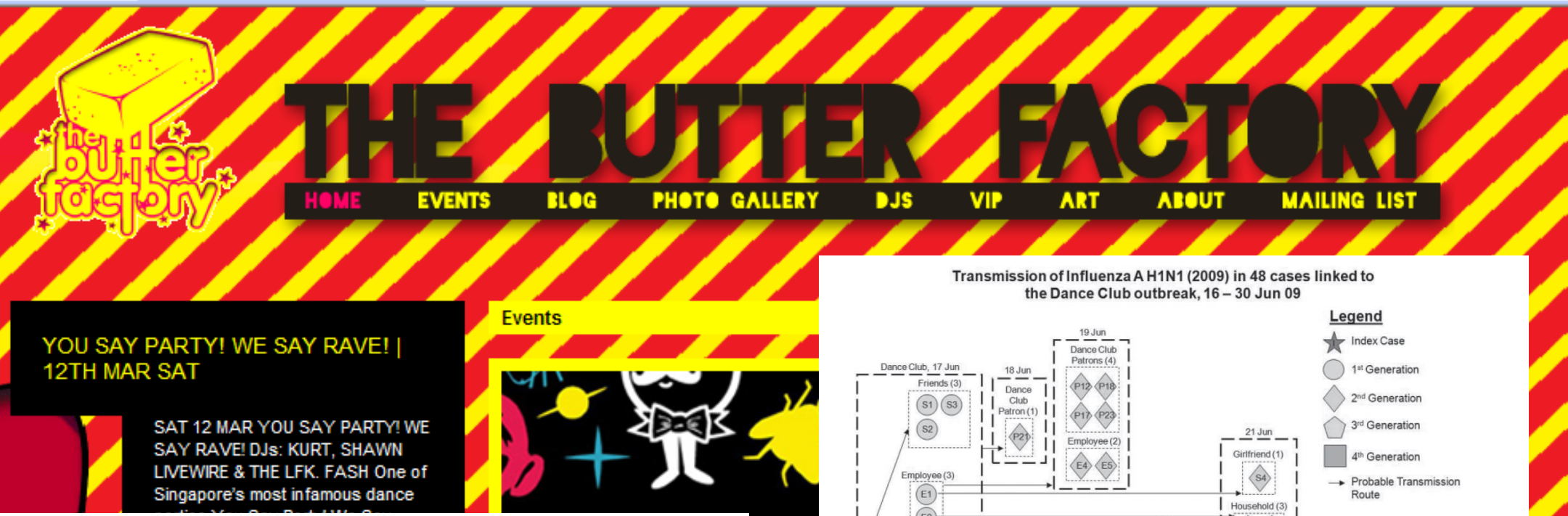
It added that the data from the influenza bio-surveillance programme showed that the proportion of H1N1 flu cases detected among patients with influenza-like illness seen at polyclinics, GP clinics and hospitals in the week of August 2 continued to remain above 50 per cent.

- CNA/yt

Photos 1 of 1

Special Report

- Flu Outbreak



Original Article

Outbreak of Novel Influenza A (H1N1-2009) Linked to a Dance Club

Pei Pei Chan,[1] *BSc (Hons)*, Hariharan Subramony,[1] *MBBS*, Florence YL Lai,[1] *MPhil*, Wee Siong Tien,[1] *BSc (Life Sciences) (Hons)*, Boon Hian Tan,[1] *BSc (Life Sci) (Hons)*, Suhana Solhan,[1] *BSc (Phar) (Hons)*, Hwi Kwang Han,[1] *BEOHS*, Bok Huay Foong,[1] *BA*, Lyn James,[1] *MBBS, MMed (PH), FAMS*, Peng Lim Ooi,[1] *MSc, MPH, FAMS*

Abstract

Introduction: This paper describes the epidemiology and control of a community outbreak of novel influenza A (H1N1-2009) originating from a dance club in Singapore between June and July 2009. Materials and Methods: Cases of novel influenza A (H1N1-2009) were confirmed using in-house probe-based real-time polymerase chain reaction (PCR). Contact tracing teams from the Singapore Ministry of Health obtained epidemiological information from all cases via telephone. Results: A total of 48 cases were identified in this outbreak, of which 36 (75%) cases were patrons and dance club staff, and 12 (25%) cases were household members and social contacts. Mathematical modelling showed that this outbreak had a reproductive number of 1.9 to 2.1, which was similar to values calculated from outbreaks in naïve populations in other countries. Conclusion: This transmission risk occurred within an enclosed space with patrons engaged in intimate social activities, suggesting that dance clubs are places conducive for the spread of the virus.

Ann Acad Med Singapore 2010;39:299-302

Key words: Contact tracing, Control, Epidemiology, Mathematical modelling

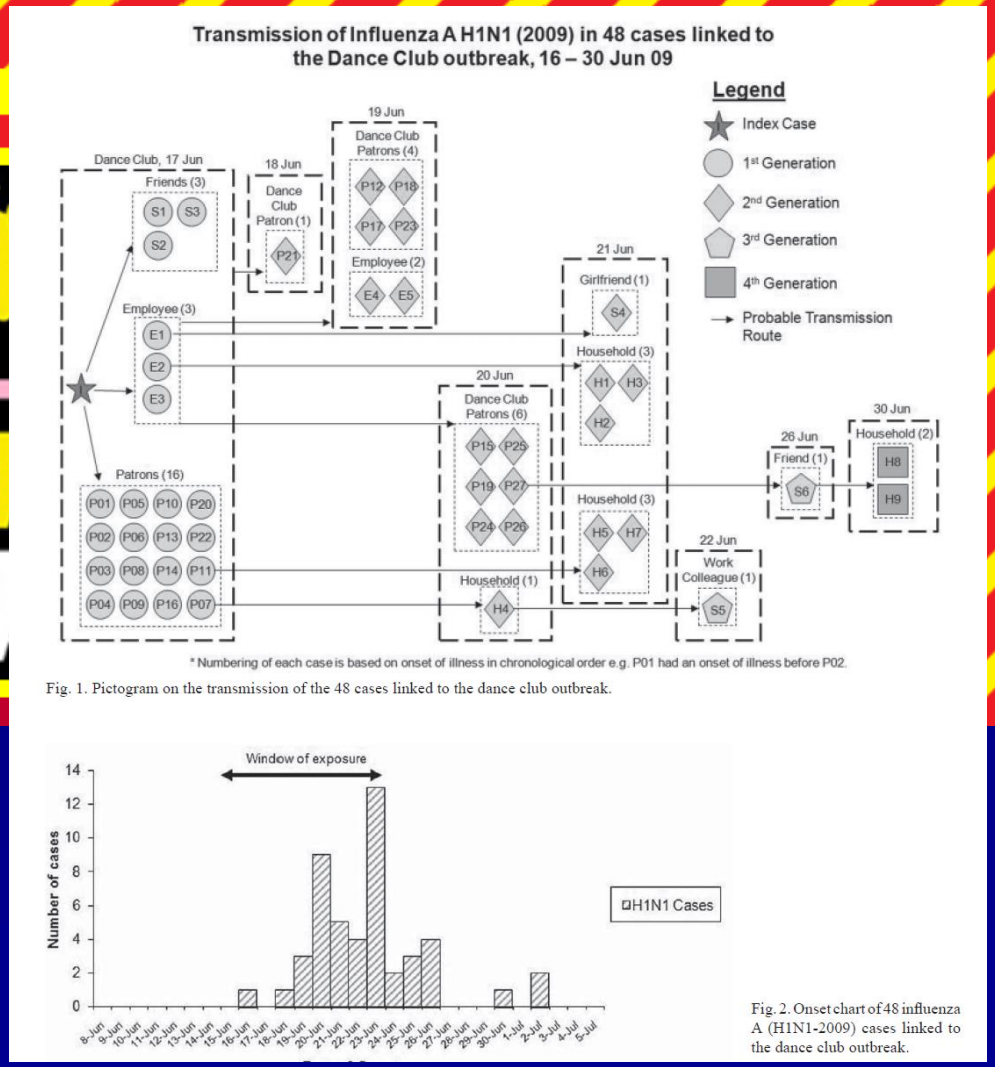


Fig. 1. Pictogram on the transmission of the 48 cases linked to the dance club outbreak.

Fig. 2. Onset chart of 48 influenza A (H1N1-2009) cases linked to the dance club outbreak.

News

Press Releases

91 new confirmed cases of Influenza A (H1N1-2009)

03 Jul 2009

Situational Report

Singapore has confirmed 91 new cases (879th – 969th case) of Influenza A (H1N1-2009) today, bringing the total tally to 969 confirmed cases. Investigation are on-going for the remaining 97 cases. Of the 89 cases investigated yesterday there were 61 local cases and 28 imported cases.

Coping with Influenza A (H1N1- 2009)

2. H1N1 is now a global pandemic. It is widely circulating in all countries and communities. The virus is here to stay, just like other influenza strains. Fortunately, the current strain remains mild, except for high-risk individuals with underlying medical conditions where complications and even deaths may occur. Our focus is on caring for those with more severe illness.

3. Many countries no longer track the number of infected cases or report them. The listing of countries with reported confirmed cases is therefore becoming misleading.

4. Likewise, travel advisory is also becoming less useful as the risk of picking up the virus at home or in any other country has evened. That is why the WHO does not recommend any travel advisory.

5. Instead, the approach in managing this virus should be largely based on personal responsibility. All Singaporeans should observe good personal hygiene at all times. If they are unwell with flu-like symptoms (fever, cough, sore throat,

Breakdown of Total Confirmed Cases

DETAILS OF NEWLY INVESTIGATED CASES

Classification	New cases	Total
(1) LOCAL	61	504
A) **Community clusters**		
RiverlifeChurch	0	10
Butter Factory	0	44
Workplace	0	3
Republic Polytechnic	4	95
Fishermen of Christ Church	0	13
Maju Camp	0	23
NUS Orientation Camp	0	6
Pulau Tekong Camp	1	10
Clementi Camp	1	58
Police Coast Guard (Brani Base)	1	8
Social (Party)	0	4
Social (Tour Group)	10	16
Raffles Institution Boarding	0	4
Jurong Camp	1	7
NUH Cluster	4	5
B) **Local transmission from imported case.**	1	17
C) **Unlinked**	38	181
(2) IMPORTED	28	368
TOTAL	**89**	**872**

Press Releases

Print This Page

SAF STEPS UP MEASURES AGAINST H1N1 VIRUS

MINDEF SINGAPORE

1. In view of the community spread of the H1N1 virus in Singapore and confirmed cases among Singapore Armed Forces (SAF) personnel, the SAF is putting in place additional measures which have been planned for against the H1N1 virus. These measures will ensure that the SAF maintains its operational readiness, our servicemen will be protected against the H1N1 virus, and the training of our servicemen will continue.

2. Measures that will be taken SAF-wide to detect cases early include active surveillance for flu-like illness as well as implementing daily temperature monitoring regime and self declaration by SAF personnel if they feel unwell. All SAF medical centres are H1N1-ready based on the criteria established by the Ministry of Health (MOH). The SAF medical centres are also stocked with the Tamiflu prophylaxis to treat infected personnel. In addition, these centres are equipped with rapid test kits to diagnose H1N1 cases.

3. Servicemen who are confirmed to be infected with the H1N1 virus will be referred to public hospitals for treatment. Personnel who have been in close contact with infected servicemen will be issued with a Home Quarantine Order in accordance to MOH policies. They will monitor their temperature twice daily and provide daily updates on their condition to their units. This is in line with existing MOH guidelines.

4. To prevent the further spread of the virus, units with infected servicemen will be physically separated from the other units in the same camp. The premises of the infected units will also be disinfected. Additional measures which will be taken include systematically screening for the H1N1 virus in all personnel exposed and nasal swabs for virus-testing, and prescription of the Tamiflu prophylaxis.

5. The SAF will continue to monitor the situation and emphasise the importance of social responsibility, vigilance and personal hygiene to all its personnel.

WAR ON SARS PARLIAMENT

Home quarantine orders

No more leniency: Tough penalties await those who break the rules

Clearly in no mood to tolerate socially irresponsible behaviour, the Government yesterday spelt out what it expects of those served with home quarantine orders — and showed just how tough it is prepared to get from now. **M. NIRMALA** *explains:*

DO THE RIGHT THING

TAGGED IF YOU STILL LEAVE HOME

ANY individual who breaches a home quarantine order will no longer just be issued with a warning. He will be electronically tagged immediately. At last count, 14 people broke quarantine orders by venturing outside their homes.

TAGGED IF YOU DON'T PICK UP THAT PHONE

INDIVIDUALS are checked via electronic cameras installed in their homes.

They need to turn on the cameras when Cisco officers make their telephone checks. But some refuse to answer.

As of now, a quarantined person who does not pick up the telephone after a third call is made by Cisco officers will be electronically tagged.

Nine people have already been tagged as they could not be contacted after three calls.

After amendments are made to the Infectious Diseases Act, those who break the rules can also be given composition fines of up to $5,000 instead of being charged in court.

The general penalty for committing an offence under the Act will also be doubled, to a maximum of $10,000 or six months' imprisonment for a first offence, and $20,000 or 12 months' imprisonment for a repeat offence.

CALL-FORWARDING TRICKS ARE OUT

SMART alecs who think they can use a telephone's call-forwarding facility and be somewhere else can think again.

Anyone on a home quarantine order and who has this service will have it cut for the duration of their quarantine.

"Let me tell you: Don't try," Home Affairs Minister Wong Kan Seng warned.

Deputy Prime Minister Lee Hsien Loong had said that someone had alerted him to deal with the call-forwarding facility in case individuals tried to outsmart the authorities.

Mr Lee said the quarantine system had to be watertight: "It takes only one undeclared contact, one irresponsible breach of a home quarantine order, to start a whole new cluster of infections.

"It is therefore absolutely essential that those served with HQOs obey the orders and stay at home, and not put many others at risk."

DON'T TRY TO LEAVE THE COUNTRY

INDIVIDUALS on home quarantine orders cannot leave the country.

Once they are quarantined, their details will be flagged with the immigration authorities, and any such person attempting to leave Singapore will be detained.

"We recognise the emotional anxiety and fear that some of these persons on home quarantine orders may be facing," said the Home Affairs Minister.

"But, to win this battle against Sars, we cannot afford any kinks in our armour," he added.

"Otherwise, we put the whole community at risk, and the consequential impact will be disastrous."

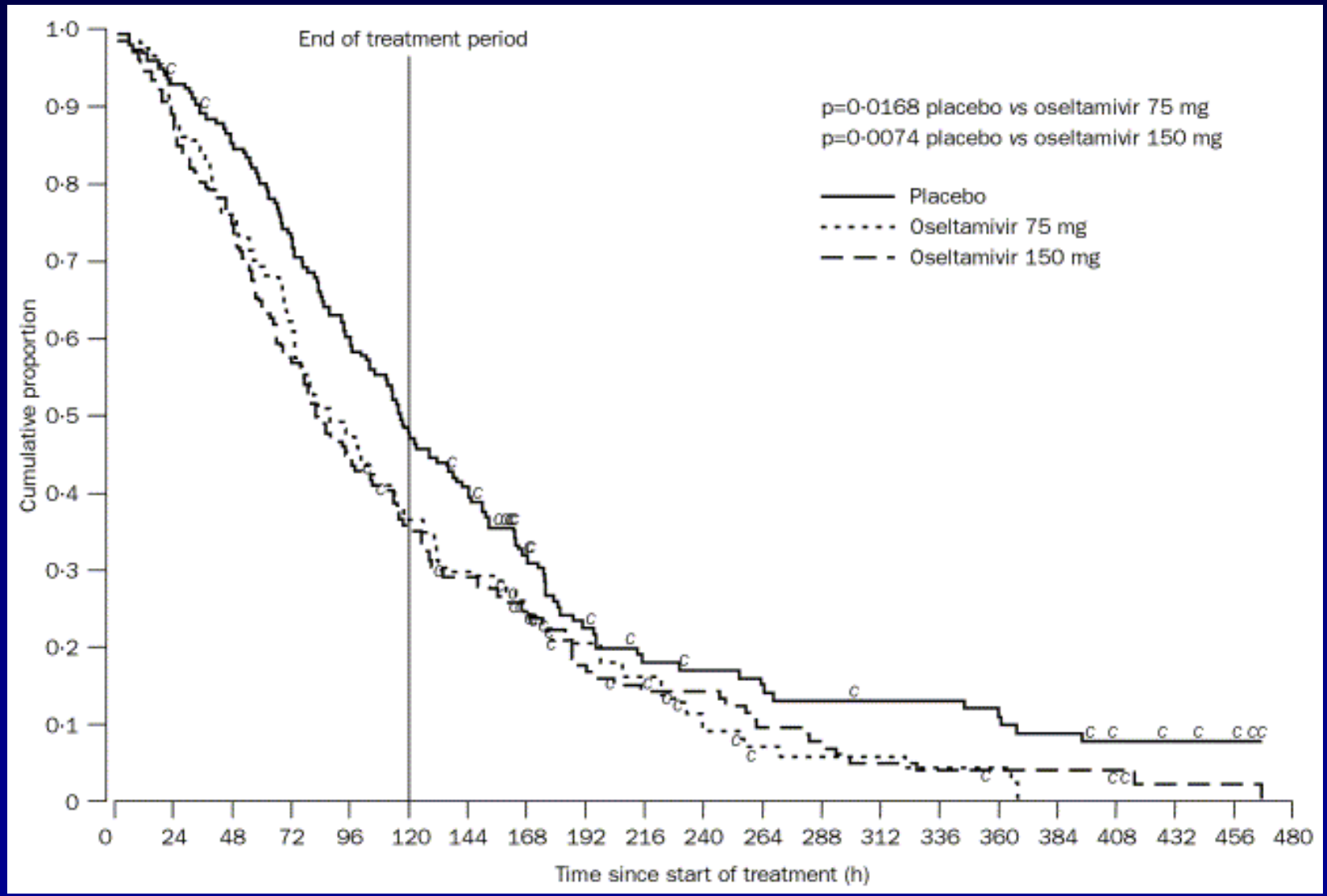
NAMING AND SHAMING IN PUBLIC

RECALCITRANTS and defaulters should definitely be named and shamed, said Health Minister Lim Hng Kiang. "I think we should publish these names and shame them, because otherwise such Singaporeans will continue not to do what is necessary of them," he said, echoing a sentiment expressed by many Singaporeans who felt this was the only way to get irresponsible Sars-affected individuals to behave.

WANG HUI FEN

Those under home quarantine will be under watchful eyes to make sure they stay at home — with the help of electronic cameras.

Oseltamivir vs Influenza



Nicholson et al. Lancet 2000;355:1845-50

Neurotoxicity especially in adolescents

HSA

Adverse Drug Reactio

n e w

Published by the Centre for Drug Administration, HSA and the HSA Pharmacovigilance Advisory Co

Oseltamivir and neuropsychiatric events

Monitor patients on oseltamivir for signs of unusual behaviour

Oseltamivir (Tamiflu®, Roche) is an antiviral agent licensed by HSA in October 2000 for the treatment of uncomplicated acute illness due to influenza infection (influenza A & B) in adults and children ≥ 1 year old who have been symptomatic for no more than two days and for the prophylaxis of influenza in adults and children ≥ 13 years old.

Recent post-marketing reports of CNS disorders[1,2]

The Health Sciences Authority (HSA) has reviewed the data from the 103 post-marketing reports of neuropsychiatric adverse events suspected to be associated with oseltamivir received between August 2005 to July 2006. These include events such as delirium with prominent behavioural disturbances (n=60) and suicidal events (n=6) including self-injury and suicidal ideation.

The majority of the cases were reported from Japan (92%) and were predominantly for the treatment of influenza (97%). These were primarily among paediatric patients (67%) with an age range of 1.5 to 17 years old. There were three deaths: a 14 year-old boy and two adults who fell to their deaths. The patients who died were healthy before contracting influenza

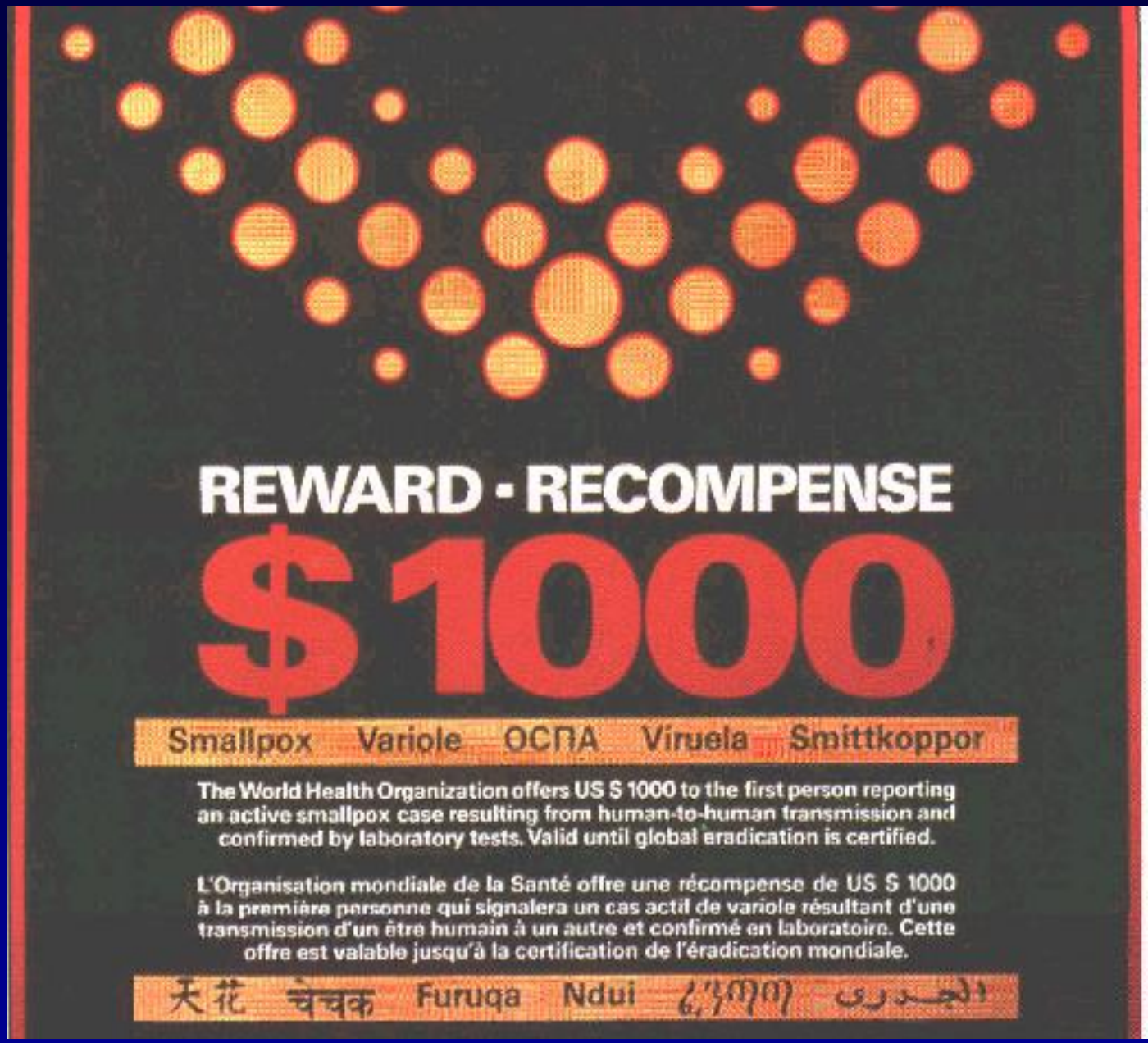
coincident period of intensive monitoring of adverse e
Japan or a combination of any of these possible
Additionally, many events such as convulsions, deliri
depressed levels of consciousness are complications
encephalitis secondary to influenza making a direct caus
to Tamiflu® administration very difficult.

Nonetheless, considering the rapid temporal relationship of adverse event to the use of oseltamivir, and cases which reported positive de-challenge (n=65) where there was rapid and full recovery from neuropsychiatric adverse effects once oseltamivir was discontinued and/or lack of positive neuro-imaging findings in the reviewed reports (n=25), the local prescribing information of Tamiflu® will be updated to warn of the potential for the occurrence of neuropsychiatric adverse events. In addition, it also advised that patients with flu, particularly children may be at an increased risk of self-injury and confusion shortly after taking Tamiflu® and should be closely monitored for signs of unusual behaviour.

Local situation

HSA has received three adverse drug reactions suspected with use of oseltamivir. They are one report of hepatitis, and another of nausea and urticaria. There is also one report of a middle-aged male who committed suicide by falling to his death. He was prescribed oseltamivir at 75mg twice a day for flu and the adverse event was reported to have occurred on the 7th day. The causality however could not be established as it was reported that the patient was also taking other medications.

Ring prophylaxis worked for smallpox



Original Article

Oseltamivir Ring Prophylaxis for Containment of 2009 H1N1 Influenza Outbreaks

Vernon J. Lee, M.B., B.S., M.P.H., Jonathan Yap, M.B., B.S., Alex R. Cook, Ph.D., Mark I. Chen, M.B., B.S., Ph.D., Joshua K. Tay, M.B., B.S., Boon Huan Tan, Ph.D., Jin Phang Loh, M.Sc., Seok Wei Chew, B.Sc., Wee Hong Koh, B.Sc., Raymond Lin, M.B., B.S., Lin Cui, Ph.D., Charlie W.H. Lee, M.Sc., Wing-Kin Sung, Ph.D., Christopher W. Wong, Ph.D., Martin L. Hibberd, Ph.D., Wee Lee Kang, M.B., B.S., M.Med., Benjamin Seet, M.B., B.S., M.P.H., and Paul A. Tambyah, M.D.

N Engl J Med
Volume 362(23):2166-2174
June 10, 2010

The NEW ENGLAND JOURNAL of MEDICINE

Summary of the Four Outbreaks of 2009 H1N1 Influenza and Efficacy of Oseltamivir Prophylaxis and Other Interventions

Table 1. Summary of the Four Outbreaks of 2009 H1N1 Influenza and Efficacy of Oseltamivir Prophylaxis and Other Interventions.*

Variable	Total	Outbreak 1	Outbreak 2	Outbreak 3	Outbreak 4
Total no. of personnel	1175	216	47	219	693
Confirmed cases — no. (%)	82 (7.0)	11 (5.1)	6 (12.8)	2 (0.9)	63 (9.1)
Before intervention — no. (%)	75 (6.4)	8 (3.7)	6 (12.8)	2 (0.9)	59 (8.5)
After intervention — no. (%)	7 (0.6)	3 (1.4)	0	0	4 (0.6)
Posterior hypothesis probability	<0.001	0.11	<0.001	<0.001	<0.001
Symptomatic personnel (excluding confirmed cases)					
Tested and negative — no. (%)	23 (2.0)	11 (5.1)	0	1 (0.5)	11 (1.6)
Not tested — no. (%)	47 (4.0)	3 (1.4)	0	4 (1.8)	40 (5.8)
Mild respiratory symptoms only	40 (3.4)	1 (0.5)	0	4 (1.8)	35 (5.1)
Reported fever with respiratory symptoms	7 (0.6)	2 (0.9)	0	0	5 (0.7)
Completion of oseltamivir prophylaxis — no./total no. (%)†	929/974 (95.4)	185/205 (90.2)	41/41 (100)	186/193 (96.4)	517/535 (96.6)
Confirmed cases and symptomatic personnel who were not tested‡					
Total — no./total no.	115/1161	14/216	6/47	5/218	90/680
Before intervention — no./total no. (%)	85/1161 (7.3)	10/216 (4.6)	6/47 (12.8)	3/218 (1.4)	66/680 (9.7)
After intervention — no./total no. (%)	30/1076 (2.8)	4/206 (1.9)	0	2/215 (0.9)	24/614 (3.9)
Posterior hypothesis probability	<0.001	0.02	<0.001	0.09	<0.001

* The posterior hypothesis probabilities were calculated for the comparison of the incidence of infection before intervention and after intervention, as described in the Supplementary Appendix.

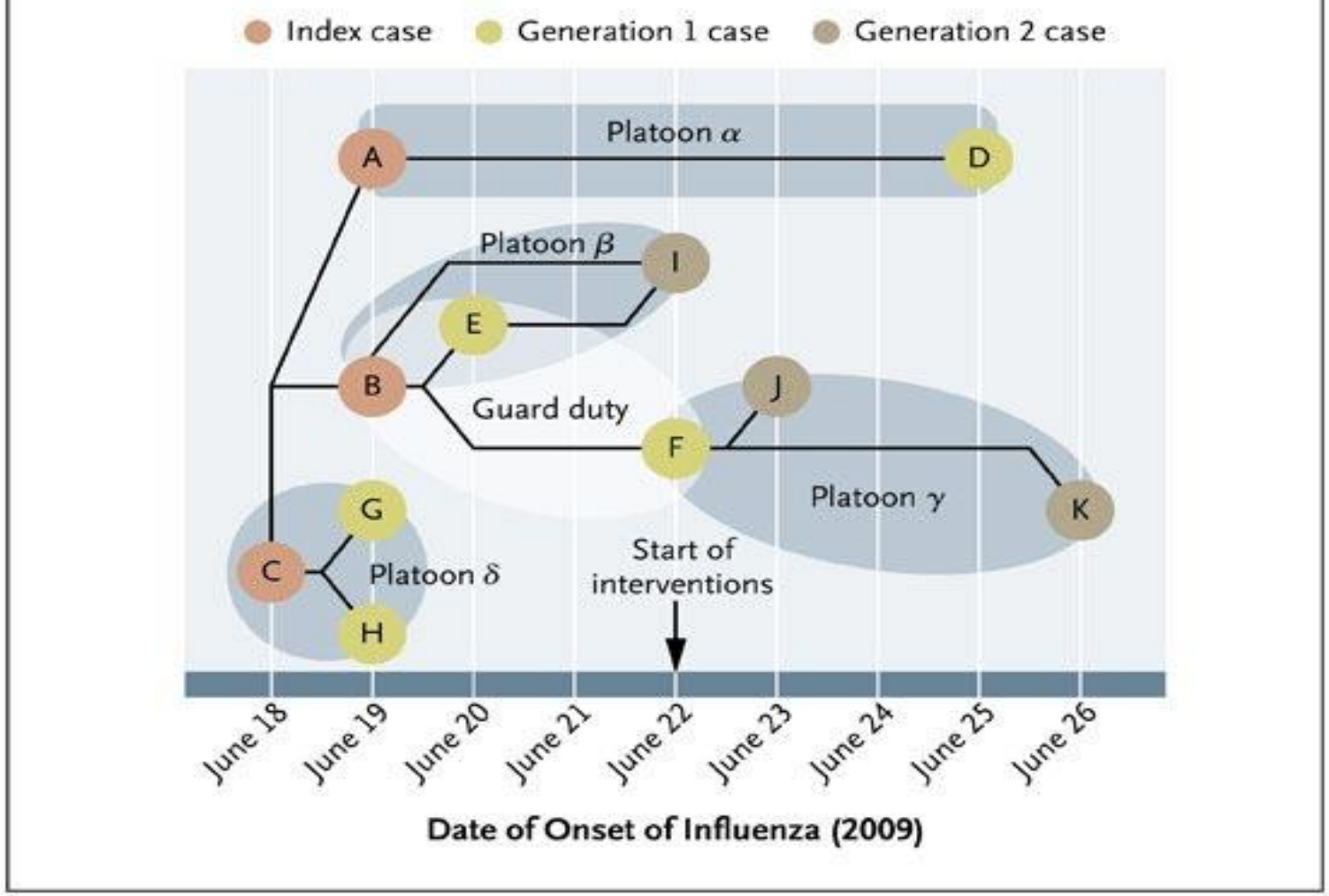
† The number of subjects who completed the oseltamivir prophylaxis regimen excludes those with confirmed infections and those who could not be contacted.

‡ The number of confirmed cases and symptomatic personnel who were not tested excludes 14 symptomatic personnel who could not remember the date of onset of their illness. The percentage of confirmed cases and symptomatic personnel who were not tested before intervention is based on the total number with data; the percentage after intervention is based on the total number with data minus the number identified before intervention.

Lee VJ et al. N Engl J Med 2010;362:2166-2174

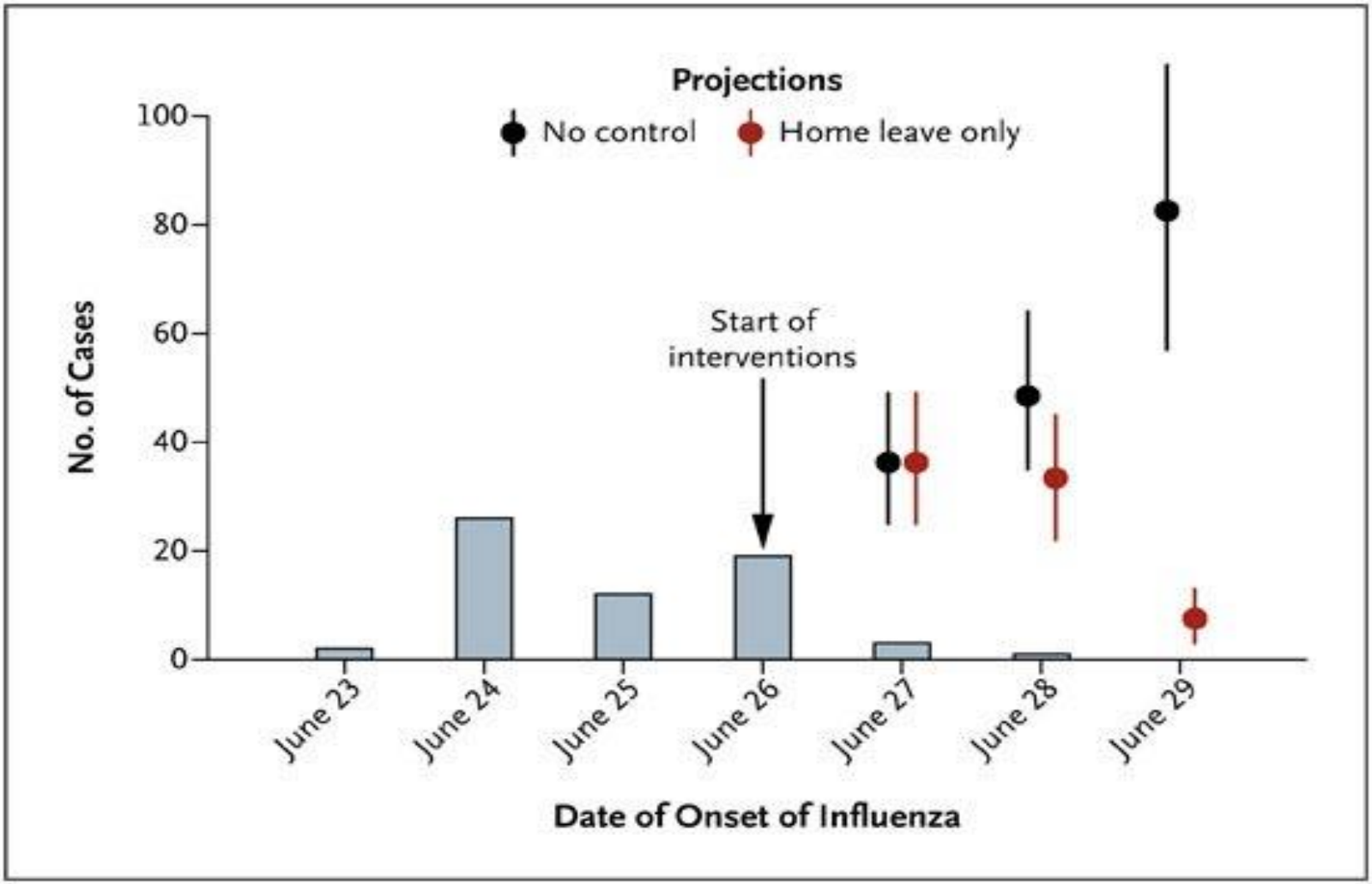
The NEW ENGLAND JOURNAL of MEDICINE

Timing of Events and Cases during Outbreak 1, According to Date of Onset of Influenza



Lee VJ et al. N Engl J Med 2010;362:2166-2174

Epidemiologic Data and Model Projections for Outbreak 4, According to Date of Onset of Influenza



Lee VJ et al. N Engl J Med 2010;362:2166-2174

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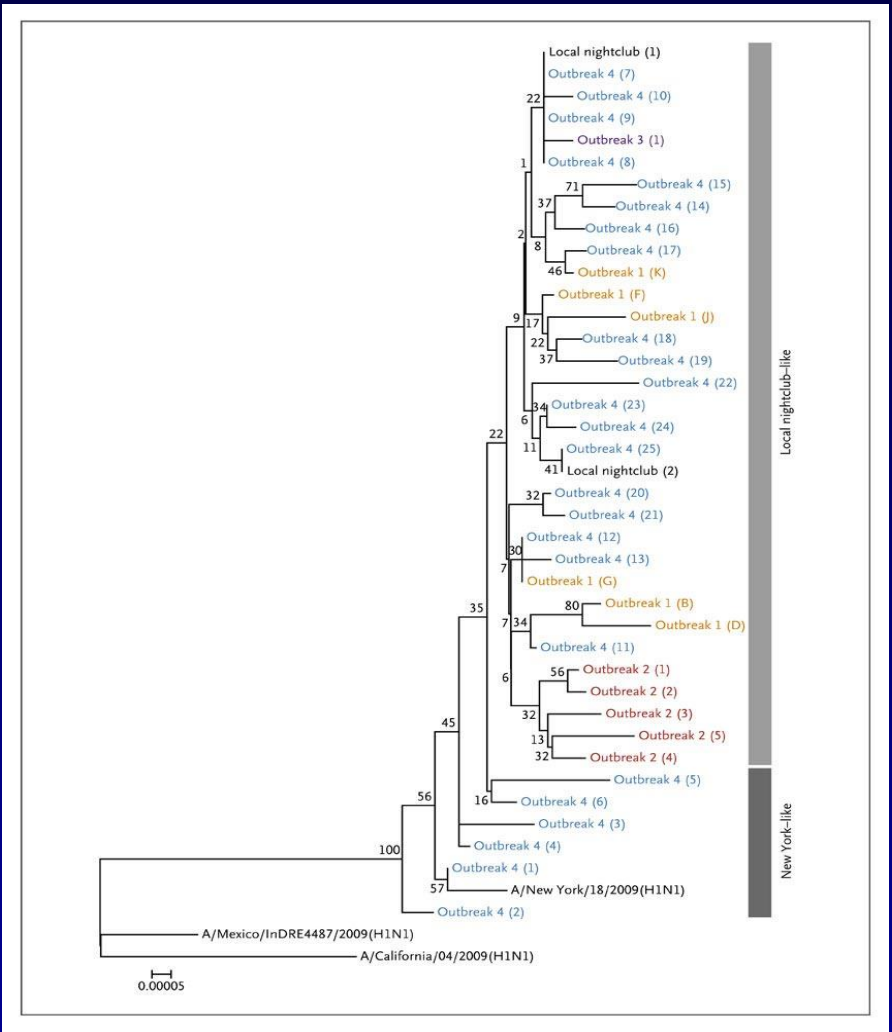
Phylogenetic Relationships among the Viruses Identified during the Four Outbreaks with the Use of Whole-Genome Sequencing



Lee VJ et al. N Engl J Med 2010;362:2166-2174

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Side Effects of Oseltamivir Prophylaxis

Table 2. Side Effects of Oseltamivir Prophylaxis.

Side Effect	Personnel (N=816)
	no. (%)
Diarrhea	14 (1.7)
Headache	9 (1.1)
Nausea or vomiting	22 (2.7)
Dizziness	5 (0.6)
Epigastric pain	4 (0.5)
Drowsiness	8 (1.0)
Mild allergic reaction (rash)	6 (0.7)

Lee VJ et al. N Engl J Med 2010;362:2166-2174

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Conclusion

- Oseltamivir ring chemoprophylaxis, together with prompt identification and isolation of infected personnel, was effective in reducing the impact of outbreaks of 2009 H1N1 influenza in semiclosed settings

The NEW ENGLAND JOURNAL of MEDICINE

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PLOS | ON

microRNAs in Circulation Are Altered in Response to Influenza A Virus Infection in Humans

Paul A. Tambyah[1], Sugunavathi Sepramaniam[2], Jaminah Mohamed Ali[1], Siaw Ching Chai[2], Priyadharshini Swaminathan[2], Arunmozhiarasi Armugam[2], Kandiah Jeyaseelan[2,3*]

1 Department of Medicine, Centre for Translational Medicine, Yong Loo Lin School of Medicine, National University Health System, National University Singapore, Singapore, Singapore, **2** Department of Biochemistry, Centre for Translational Medicine, Yong Loo Lin School of Medicine, National University Health System, National University of Singapore, Singapore, Singapore, **3** Department of Anatomy and Developmental Biology, School of Biomedical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Victoria, Australia

Abstract

Changes in microRNA expression have been detected *in vitro* in influenza infected cells, yet little is known about them in patients. microRNA profiling was performed on whole blood of H1N1 patients to identify signature microRNAs to better understand the gene regulation involved and possibly improve diagnosis. Total RNA extracted from blood samples of influenza infected patients and healthy controls were subjected to microRNA microarray. Expression profiles of circulating microRNAs were altered and distinctly different in influenza patients. Expression of highly dysregulated microRNAs were validated using quantitative PCR. Fourteen highly dysregulated miRNAs, identified from the blood of influenza infected patients, provided a clear distinction between infected and healthy individuals. Of these, expression of miR-1260, -26a, -335*, -576-3p, -628-3p and -664 were consistently dysregulated in both whole blood and H1N1 infected cells. Potential host and viral gene targets were identified and the impact of microRNA dysregulation on the host proteome was studied. Consequences of their altered expression were extrapolated to changes in the host proteome expression. These highly dysregulated microRNAs may have crucial roles in influenza pathogenesis and are potential biomarkers of influenza.

Citation: Tambyah PA, Sepramaniam S, Mohamed Ali J, Chai SC, Swaminathan P, et al. (2013) microRNAs in Circulation Are Altered in Response to Influenza A Virus Infection in Humans. PLoS ONE 8(10): e76811. doi:10.1371/journal.pone.0076811

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Clinical work continues: Antibodies

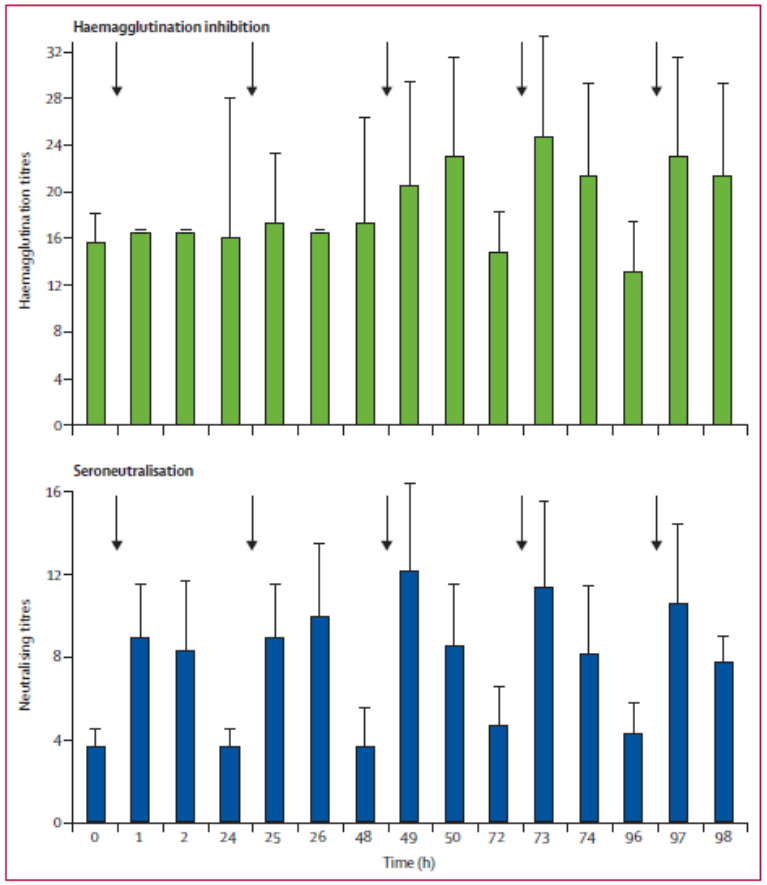

Figure 4: **Haemagglutination inhibition and neutralising titres after five infusions of FBF001**
Data are means (bars show SD). Titres measured in patients after five doses of FBF001 at 0 h, 24 h, 48 h, 72 h, and 96 h (arrows) in study phase 2.

Safety, potential efficacy, and pharmacokinetics of polyclonal immunoglobulin F(ab')$_2$ fragments agai influenza A (H5N1) in healthy volunteers: a single-c randomised, double-blind, placebo-controlled, phase 1 study

Céline Bal, Cécile H Herbreteau, Philippe Buchy, Sareth Rith, Masliza Zaid, William Kristanto, Velda Han, Charlotte Reynaud, Patrick Granjard, Bertrand Lépine, Caroline Durand, Paul A Tambyah**

Lancet Infect Dis 2015; 15: 285–92
Published Online February 5, 2015
http://dx.doi.org/10.1016/S1473-3099(14)71072-2

Summary

Background Human infection with the avian influenza A H5N1 virus results in disease with a high fatality rate, against which antiviral treatments have limited efficacy. We aimed to investigate the safety, pharmacokinetics, and therapeutic potential of specific polyclonal immunoglobulin equine F(ab')$_2$ fragments raised against influenza A/Vietnam/1194/2004 virus (H5N1 subtype) in healthy volunteers.

Methods We did a randomised, double-blind, placebo-controlled, single-centre phase 1 study. In stage 1 (one

Ann Clin Biochem. 2016 Jul;53(Pt 4):466-76. doi: 10.1177/0004563215604001. Epub 2015 Aug 19.

microRNA expression in blood of dengue patients.

Tambyah PA[1], Ching CS[2], Sepramaniam S[2], Ali JM[1], Armugam A[2], Jeyaseelan K[3].

Author information

Abstract

BACKGROUND: Dengue is the most common arboviral illness worldwide. While most infected patients recover, a proportion of them develop severe complications or fatality. Nevertheless, the pathophysiological mechanisms which distinguish the disease severity and associated complications are not clearly understood. We studied blood profiles of dengue patients in order to identify microRNAs that could play a role in these pathophysiological mechanisms.

METHODS: Blood samples from 26 dengue-infected patients were collected within 0-14 days of infection. Together with samples obtained from six healthy individuals, microRNA profiles were generated to identify significantly altered microRNAs upon dengue infection. Profiles of patients with influenza were also used to determine the disease specificity of these altered microRNAs. Their discriminative power to distinguish dengue from influenza was then tested statistically.

RESULTS: Several significantly altered microRNAs were identified in patients with dengue. Twelve microRNAs were specifically altered upon acute dengue whereas 14 microRNAs exhibited similar expression between dengue and influenza. Seventeen microRNAs which could potentially distinguish dengue-related complications were also identified. Expression of miR-24-1-5p, miR-512-5p and miR-4640-3p distinguished mild dengue from those exhibiting liver complications whereas miR-383 was significantly upregulated in mild dengue compared to those diagnosed as severe dengue with fluid accumulation.

CONCLUSIONS: We identified two panels of microRNAs - one specific for dengue and the other common to dengue and influenza. We also report on the differentially expressed microRNAs in patients with mild versus severe dengue, which could be the basis for the complications seen in them.

KEYWORDS: DNA and RNA techniques; Genetics; clinical studies; laboratory methods

Dengue Hemorrhagic Fever Transmitted by Blood Transfusion

TO THE EDITOR: Dengue, the most common vectorborne viral infection worldwide,[1] is predominantly transmitted by the *Aedes aegypti* mosquito. We describe a well-documented cluster of blood transfusion–associated dengue infections in Singapore, a country in which the disease is endemic.

A 52-year-old, asymptomatic, repeat blood donor gave blood on July 15, 2007. An investigation of all recipients of his blood products was initiated after he informed the blood bank that he had had a fever the day after donation. The stored serum sample was positive for dengue virus type 2, as ascertained by means of a polymerase-chain-reaction (PCR) assay.[2]

The recipient of the donor's red cells had fever and myalgia 2 days after transfusion. The recip-

Table 1. Characteristics of the Donor and Recipients.

Patient	Age	Sex	Coexisting Conditions	Symptoms of Dengue Fever	Signs of Capillary Leak	Results of Serologic Testing	Findings on PCR Assay*	Outcome
	yr							
Donor	52	M	None	Fever and myalgia after donation (not hospitalized)	None	Not done	Dengue virus type 2	Full recovery
Recipient of fresh-frozen plasma	64	M	Diabetes mellitus, hypertension, ischemic heart disease, recent coronary-artery bypass graft, chronic renal impairment	Day 2 after transfusion (hospital day 12): fever, jaundice, malaise, and worsening thrombocytopenia	Worsening of bilateral pleural effusions	Seroconversion (on July 19, negative for IgG and IgM; on July 31, positive for both)	Dengue virus type 2	Discharged in good health
Recipient of packed red cells	72	M	Diabetes mellitus, hypertension, ischemic heart disease, peptic ulcer disease	Day 2 after transfusion (hospital day 6): fever, myalgia, malaise	Small right pleural effusion	IgG-positive on follow-up	Dengue virus type 2	Discharged in good health
Recipient of platelets	74	M	Hepatocellular carcinoma	None	None	Positive for both IgG and IgM on follow-up	Not done	Discharged in good health

* PCR denotes polymerase chain reaction.

Failure of Routine HIV-1 Tests in a Case Involving Transmission With Preseroconversion Blood Components During the Infectious Window Period

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Teresa M. Brown, BS
Valerie Dunmire, MS
Su Yun Se Thoe, MSc
Sin-Yew Wong, MD
Yee Sin Leo, MD
Diana Teo, MD
James Gallarda, PhD
Bruce Phelps, PhD
Mary E. Chamberland, MD
Michael P. Busch, MD, PhD
Thomas M. Folks, PhD
Marcia L. Kalish, PhD

Context Current screening prac... reducing human immunodeficienc... taminated blood products. Howe... seroconversion and before high l... using both serologic antigen and a... cation (NAT) is being implemente... this period, yet the issue of single ...

Objectives To determine HIV-1 ... recipients of blood components an... tibody negative at the time of don... NAT assays, including those curren...

Design and Setting Case study ... municable Disease Centre, Singapo... fusion Service, Singapore.

Subjects The blood donor and t...

Main Outcome Measures Ge... *gag* and the C2V5 region of *env* ... the donor and recipients; reactivity ... ity in donor screening HIV NAT ... contexts.

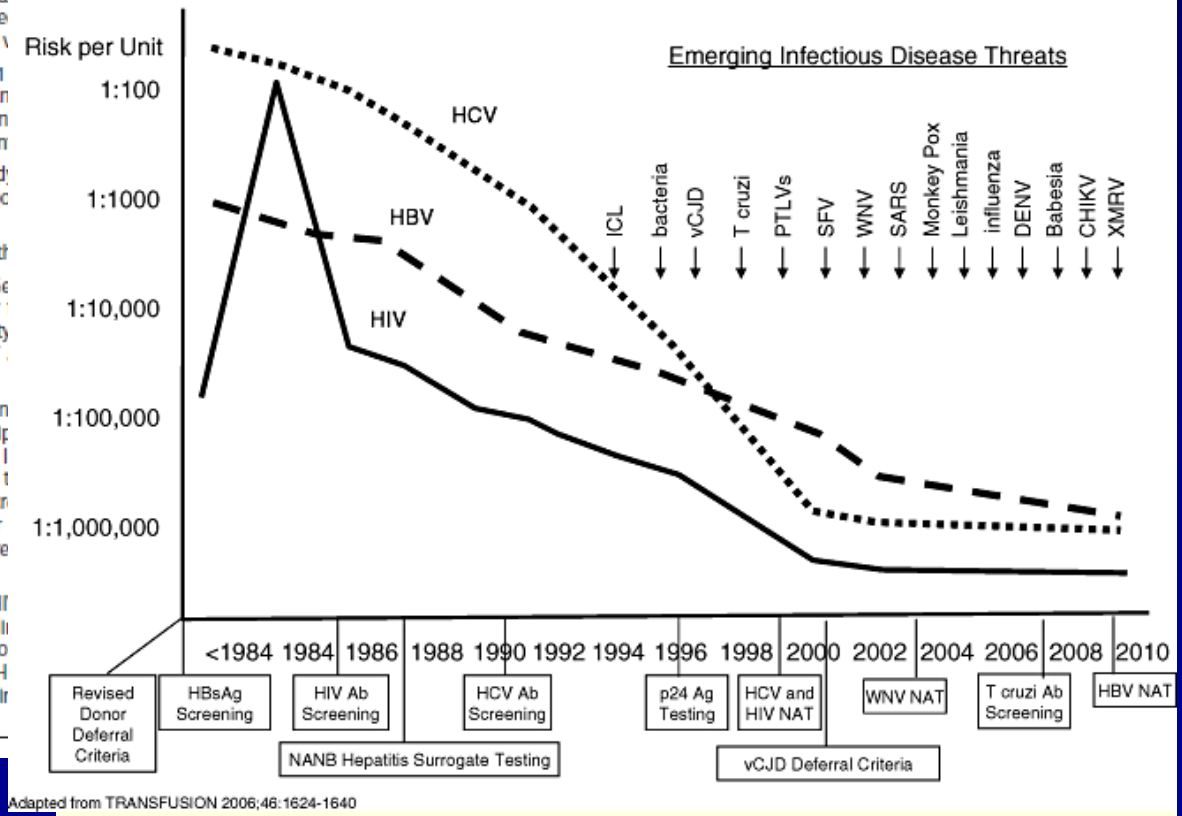
Results Direct DNA sequencin... sequences in the donor and recip... quantitative assay for HIV-1 RNA l... in plasma) was estimated to be in t... Additional testing using donor-scr... HIV RNA in the undiluted donor ... 1:16 and 1:24 dilution levels curre... in the United States.

Conclusions Transmission of HI... red blood cell recipient occurred i... The viral load in the implicated do... of plasma. Current US minipool H... sensitive to detect all infectious wi...

JAMA. 2000;284:210-214

IN THE UNITED STATES, DONATED blood and plasma is tested for antibodies to human immunodeficiency virus types 1 (HIV-1) and 2 (HIV-2) by screening with an enzyme immunoassay (EIA), as well as an HIV-1 p24 antigen EIA.[1] Despite a dramatic reduction in risk due to the improved sensitivity of these tests, it is estimated that from 1 in 450000 to 1 in 660000 US blood donations may transmit HIV,[2,3] with nearly all cases of transfusion-associated HIV infection being caused by donations made during the infectious window period, prior to seroconversion. Contemporary HIV EIAs have

Risks of major TTVs linked to interventions, and accelerating rate of EIDs of concern to blood safety



Adapted from TRANSFUSION 2006;46:1624-1640

Transfusion
Volume 50, Issue 10, pages 2080-2099, 24 AUG 2010 DOI: 10.1111/j.1537-2995.2010.02851.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1537-2995.2010.02851.x/full#f4

THELANCET-D-16-07584R1
S0140-6736(17)30269-6
Embargo: [add date when known]

Embargoed!!!

David C Lye, Sophia Archuleta, Sharifah F Syed-Omar, Jenny G Low, Helen M Oh, Yuan Wei, Dale Fisher, Sasheela S L Ponnampalavanar, Limin Wijaya, Linda K Lee, Eng-Eong Ooi, Adeeba Kamarulzaman, Lucy C Lum, Paul A Tambyah, Yee-Sin Leo

From: "Lau, Esther (ELS-GBR0070)" <esther.lau@lancet.com>
Date: 14 February 2017 at 11:45:03 PM GMT+7
To: "David Lye Chien Boon (TTSH)" <david_lye@ttsh.com.sg>
Subject: RE: THELANCET-D-16-07584R1: Your manuscript for The Lancet

Hi David,

I'm pleased to let you know that your paper is scheduled for publication on March 7, embargoed until 23:30 UK time.

Best wishes,
Esther

Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, Singapore (D C Lye FRACP, L K Lee MPH, Prof Y-S Leo FRCP); **Yong Loo Lin School of Medicine** (D C Lye, S Archuleta MD, H M Oh FRCP, Prof D Fisher FRACP, Prof P A Tambyah MD, Prof Y-S Leo) **and Saw Swee Hock School of Public Health** (Prof Y-S Leo), **National University of Singapore, Singapore; Division of Infectious Diseases, National University Hospital, National University Health System, Singapore** (S Archuleta, Prof D Fisher, Prof P A Tambyah); **University Malaya Medical Centre, Kuala Lumpur, Malaysia** (S F Syed-Omar MMed, S S L Ponnampalavanar MMed, Prof A Kamarulzaman FRACP, Prof L C Lum MRCP); **Singapore General Hospital, Singapore** (J G Low MRCP, L Wijaya MRCP); **Duke-NUS Medical School, Singapore** (J G Low, Prof E-E Ooi PhD); **Changi General Hospital, Singapore** (H M Oh); **Singapore Clinical Research Institute, Singapore** (Y Wei MS); **and Lee Kong Chian School of Medicine, Singapore** (Prof Y-S Leo)

Correspondence to:
Dr David C Lye, Institute of

Funding National Medical Research Council, Singapore.

Prof Chan YC - *arboviruses*

Dengue Type 2 Virus in Naturally Infected Aedes albopictus Mosquitoes in Singapore

Abstract. *A strain of dengue type 2 virus has been isolated from* Aedes albopictus *collected in Singapore. This is the first report of a natural isolation of dengue virus from this species, which has long been suspected as a vector in nature.*

Mosquito-borne hemorrhagic fever is a severe clinical syndrome etiologically associated with strains of dengue virus and newly recognized in southeastern Asia and India (*1–3*). During an in- circumstances.

In November 1960, following the peak of the epidemic in Singapore, and while cases were still occurring, a mosquito survey was initiated. Adult mosquitoes were taken routinely on a weekly basis from urban and rural houses, in diurnal and nocturnal biting collections, and from animal bait. A total of 12,505 mosquitoes, representing more than 40 species of eight genera, was collected in a 3-month period. Of these, more than 6000 female mosquitoes were processed for virus isolation.

Collected mosquitoes were held alive for a minimum of 24 hours before be- tions of all mosquito suspension mouse brain suspensions were sto −70°C. Part of the laboratory was done in Singapore, where the were held in a mosquito-proof The remainder of the work was in San Francisco, a dengue-free a

Five strains of dengue virus isolated from *A. aegypti* pools ar strain was isolated from a pool *albopictus*. The *A. albopictus* (SM-18) was from a pool of males that were collected in Nov 1960 in urban Singapore, while were attempting to feed on huma The dengue virus infection rates 0.8 per 1000 for *A. albopictus* pared to 18.6 per 1000 for *A.* (*12*).

Strain SM-18 caused illness in mice 10 days after inoculation w mosquito suspension, but it adapted to mice with difficulty. Ten serial brain passages in infant mice were required before the incubation period was reduced to 7 days and a regular pattern of illness and death appeared. Of the

Table 1. Neutralization of dengue strain SM-18 virus from *Aedes albopictus* by dengue types 1, 2, 3, and 4 hyperimmune serums prepared in mice and rabbits.

Serums	Neutralizing antibody as represented by the $\log_{10}$ neutralization index with hyperimmune serums to:				
	D1 (Hawaiian)	D2 (New Guinea "C")	D3 (H-87)	D4 (H-241)	SM-18
Mouse	<1.2	2.2	<1.2	1.4	2.7
Rabbit	1.3	3.9	1.2	2.6	

The significance of the single isolation of dengue virus from *A. albopictus* cannot be evaluated without further investigation, although epidemiological evidence suggests that this species is an important vector of endemic dengue in southeastern Asia (*8*).

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Department of Bacteriology, University of Singapore, Singapore 3, Malaysia

References and Notes

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6 AUGUST 1965

Cellulose acetate electrophoresis of a urinary concentrate may prove of value in elucidating the nature of abnormal levels of serum amylases.

I thank Prof. I. D. P. Wootton and Dr. J. R. Hobbs of the Postgraduate Medical School, London, for their advice.

S. E. Aw*

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* On an overseas training scholarship from the University of Singapore.

[1] McGeachin, R. L., and Lewis, P., *J. Biol. Chem.*, **234**, 795 (1959).

and in this respect they resembl
sheep[9]. Considerably more gly
foetal liver than in the placenta.
tion of the foetal blood and i
foetal fluids is high. It was, ho
resulting colour after heating
atypical and indicated the pr
substance. It thus became im
presence of fructose by other m
spectrum of the acid-resorcin
amniotic fluid was similar to tha
having peaks at 410 and 480 m
SP 600 spectrophotometer. T

a 'slow-moving' component seen in cord blood hæmoglobin collected in Singapore. Usually this pigment is present in very small amounts and cannot be detected with the naked eye, but has to be made visible by drying the paper after electrophoresis and staining it with a protein dye or with benzidine (pseudo-peroxidase reaction). Amounts visible without staining have, however, been found in several Chinese, three Malays, one European (English) and one Eurasian. One sample (Chinese cord blood 675), in which the proportion of this 'slow' component amounted to about 15 per cent of the total hæmoglobin, was suitable for further investigation. The infant had been delivered normally and its weight at birth was 7 lb. 13 oz. Both parents are healthy
pore and neither of them
the hæmoglobin on electro-

sis at *p*H 8·6, one fraction
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e similar to that of hæmo-

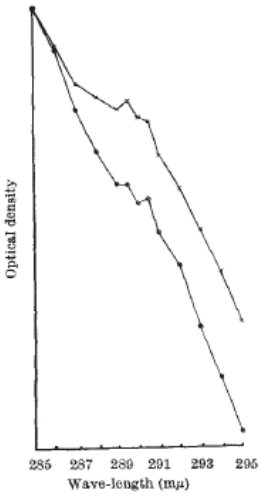

Fig. 3. Ultra-violet spectrum of the slow component isolated from Chinese cord blood *CF*-675 and of purified hæmoglobin from human cord blood containing 80 per cent F and 20 per cent A. ×—×, Cord blood control; ○—○, Chinese cord blood *CF*-675 slow component

globin A_1. The two fractions were eluted, and on paper electrophoresis at *p*H 8·6 it was seen that the major fraction was composed of hæmoglobin F and the new hæmoglobin. Thus on paper electrophoresis at *p*H 8·6 the new hæmoglobin resembles hæmoglobin O, which by this technique migrates between S (or D) and E (or A_2), and on chromatography and agar electrophoresis at *p*H 6·2 it resembles hæmoglobin F and unlike O moves faster than A.

It was unfortunate that the hæmoglobin solution had to be transmitted in the carbonomonoxy form and the alkali-denaturation properties of the isolated pigment could therefore not be determined. The ultra-violet spectrum was determined after elution from paper after electrophoresis. It showed a tryptophan fine-structure band of the fœtal hæmoglobin type.

We reported the observation of a slow-moving fœtal component to Dr. Ph. Fessas, who kindly informed us that he had observed a similar or perhaps identical abnormal fœtal hæmoglobin at the Alexandra Hospital in Athens which he proposed to call hæmoglobin 'Alexandra'. As it is very likely that the slow-moving hæmoglobins from cord blood seen in Athens and in Singapore are the same, we have thought it preferable for the time being to refrain from naming the new hæmoglobin described here.

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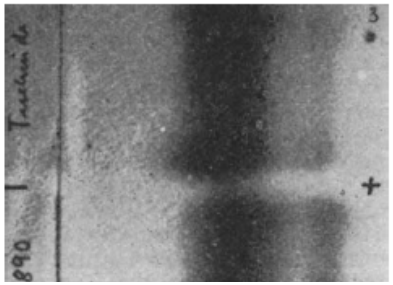
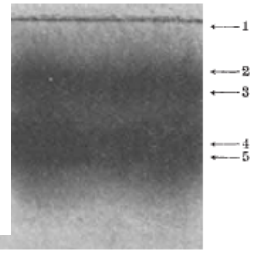


in this work and for help in identifying the sample *FC* 890 as 'Bart's' hæmoglobin. Mr. Stephen Pang rendered valuable technical assistance during this work.

F. Vella

Department of Biochemistry,
Faculty of Medicine,
University of Malaya in Singapore.

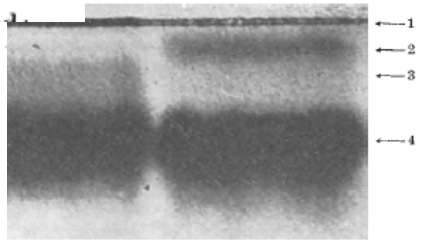
$A + S$



+

son of the hæmoglobin from Chinese cord blood
hæmoglobin $A + S$ control by paper electro-
8·6, hanging strip technique. The paper strip
otographed unstained. (1) Line of application;
component in *CF*-675; (3) hæmoglobin S;
bin $F + A$ in *CF*-675; (5) hæmoglobin A

5 Control containing increased amount of $A2$



+

LUENZA VIRUSES IN TISSUE CULTURE
D WITH SKIM MILK

	Titre of virus (log_{10})	
ly	Dried and stored at 4° C for 4 weeks	Dried and stored 2 weeks at 4° C and 2 weeks at room temperature
	4·9	4·4
	4·2	4·2
	6·2	6·2
	4·9	4·4

Rapid Typing of Dengue Viruses by the Micro-precipitin Agar-gel Diffusion Technique

The agar-gel precipitin technique has been used to differentiate members of the tick-borne encephalitis virus complex of group *B* arboviruses[1]. This report describes the application of this technique in the rapid typing of dengue virus types 1, 2, 3 and 4.

Y. C. Chan

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University of Singapore, Singapore, Malaysia.

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Today, contracts can take months ☹

PROJECT AGREEMENT

This Project Agreement ("**Project Agreement**") is made on the [_____] day of [_____] 2013

between

(1) **NATIONAL UNIVERSITY OF SINGAPORE**, (Company Registration Number: 200604346E), a company limited by guarantee incorporated in Singapore under the Companies Act (Cap. 50) and having its registered office at 21 Lower Kent Ridge Road, Singapore 119077 ("NUS") acting through its Department of Paediatrics of its Yong Loo Lin School of Medicine (hereinafter referred to as "**NUS**")

and

(2) **NATIONAL UNIVERSITY HOSPITAL (SINGAPORE) PTE LTD**, (Company Registration Number: 200604346E), a company incorporated in Singapore under the Companies Act (Cap. 50) and having its registered office at 5, Lower Kent Ridge Road, Singapore 119074 ("**NUH**")

(hereinafter referred to collectively as the "**Project Parties**" and individually as a "**Project Party**").

WHEREAS:

It wasn't just the ID/microbiologists who published regularly in *Science* and *Nature* then

Gene deletion as the cause of α thalassaemia

Two independent groups show that the absence of all or part of the globin α-chain gene is the origin of homozygous α thalassaemia.

The severe form of α thalassaemia is caused by a haemoglobin gene deletion

A complementary DNA copy (cDNA) was prepared to various human globin mRNAs with avian myeloblastosis virus reverse transcriptase[23] using labelled ^{3}H-dCTP only. cDNA was centrifuged on an alkaline sucrose gradient and the material larger than approximately 5S (300 nucleotides) was pooled and used for further hybridisation. cDNAs were prepared using mRNA from adult ($cDNA_{\alpha,\beta}$) or newborn ($cDNA_{\alpha,\gamma,\beta}$) reticulocytes as templates; in these cases, unlike that of foetal

A deletion of more than half of the α-globin gene at all

in its homozygous state, the Hb Bart's hydrops syndrome. Extrapolating from our results with α-thal 1, it seems likely that in many cases α-thal 2 results from the loss of a single α-gene locus. Since there is now strong evidence that the heterozygous state for Hb CS also mimics the clinical picture of α-thal 2, it is possible that some cases of α-thal 2 result from a molecular mechanism other than a deletion.

From a practical point of view, it is perhaps discouraging that a disorder such as this severe form of α thalassaemia, which causes a major public health problem in many parts of the

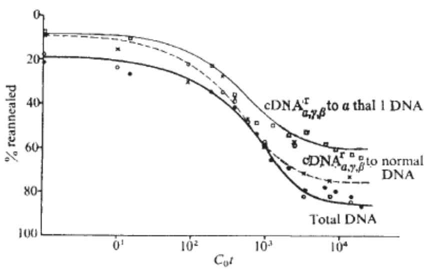

Fig. 2 Reassociation of $cDNA_{\alpha,\gamma,\beta}$ to excess normal or α-thalassaemic total DNA. DNA was prepared from nuclei of normal human spleen or of hydrops fetalis liver with hydroxylapatite[25], and sonicated in 0.1 NaOH to an average size of approximately 300 nucleotides. DNA fragments were neutralised, ethanol precipitated, redissolved in distilled water and dialysed three times against 20 volumes of water. $cDNA_{\alpha,\gamma,\beta}$ (0.5 ng) was mixed with excess (20 × 10^6 l^{-1}) normal or α-thalassaemic DNA at a concentration of 8.3 mg DNA ml^{-1} in 0.12 M sodium phosphate, pH 6.8. 120 µl aliquots of the solution were sealed in sterile silicone-treated capillaries; the mixtures were denatured for 10 min at 100° C, then annealed at 60° C. At the appropriate times

but sometimes the small amounts obtained precluded such an analysis.

hybridisation with *E. coli* DNA has been previously reported[22].

world, results from a gene deletion, since this precludes any possibility of correction at the post-transcriptional level.

We thank our clinical colleagues in Glasgow and Aberdeen for providing pathological and normal haematological specimens, and for discussions. Drs Paul Harrison and George Birnie advised on the use of reverse transcriptase in hybridisation reactions and Dr Bryan Young helped us with the mathematical analysis of our results. S.O. was on leave from the Institute of General Pathology, University of Milan, on a Royal Society exchange fellowship from the Accademia Nazionale dei Lincei when this work was carried out. The Beatson Institute for Cancer Research is supported by the Cancer Research Campaign and the Medical Research Council. D.J.W. and J.B.C. thank the Medical Research Council and Wellcome Trust for support.

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Received May 20; revised August 14, 1974.

$C_0t_{1/2}$ of approximately 700, slightly more rapid than the $C_0t_{1/2}$ of the total DNA which is 1,000. This might be predicted from

HÆMATOLOGY

Xg Blood Groups of Chinese

SAMPLES of blood from 64 normal unrelated Chinese people, mostly from Singapore, were tested for the X-linked blood group antigen Xg^a with the following results:

	Xg(a+)	Xg(a−)	total
Males	16	19	35
Females	20	9	29

The number is small because the supply of anti-Xg^a plasma is being used mainly for the investigation of X-linkage and of abnormalities of sex, but the results are sufficient to show that the antigen is less common in Chinese than in Europeans.

Chinese gene frequencies calculated from the male and

Chinese	64	0·46	0·54

We thank Dr. A. Cahan of Knickerbocker Biologics, New York, and Dr. J. D. Mann of Butterworth Hospital, Grand Rapids, for gifts of the anti-Xg^a plasma.

WONG HOCK BOON

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JUNE GAVIN
R. R. RACE

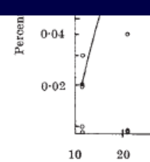

Fig. 1. Dose-response c human peripheral bloc indices at various conc

residue, for in the sequence

121 122 123 124 125 126
. . . Glu. Phe. Thr. Arg. Pro. Val . . .

Pro bond would probably be quite resistant to

Khartoum on starch gel electrophoresis, a basic variant was observed with an electrophoretic mobility similar to Hb-S, and slightly faster than Hb-O (Arabia), both of which have been found previously in the area. The variant, Hb-Khartoum, comprised about 30 per cent of the total haemoglobin. No intracellular inclusion bodies could be demonstrated and electrophoresis on starch gel revealed no free α-chains. The haemolysate containing Hb-Khartoum was, however, slightly less heat-stable than that of a normal control sample. The propositus and his family have not yet been available for further investigation.

Separation of the α and β-chains of globin prepared from the red cells of the heterozygote for Hb-Khartoum indicated an abnormal and more basic β-chain, and peptide maps of the aminoethylated $\beta^{Khartoum}$-chain showed that, like Hb-O (Arabia), the substitution had occurred in peptide βT13. Amino-acid analysis of this peptide, however, showed that both lysine and arginine were present, and that one of the two residues of proline was missing (Table 1), indicating replacement of either Pro 124 or Pro 125 by arginine.

The fact that a tryptic split had not occurred at the substituted arginine suggested that Pro 124 might be the

previously observed with haemoglobin variants g proline substitutions which, with the exception hiapas[2], have been shown to be unstable and ed with marked haematological abnormalities[1]. Singapore substitution of the terminal HC3 might not cause conformational changes in the , although the function of this residue is not yet r it is not visible on electron-density maps[6]. In rtoum the proline replacement evidently leads minor changes in the stability of the molecule. ither haemoglobin seems to be unstable *in vivo*. n the lack of clinical and haematological indications in the patients no gross functional abnormalities seem likely, although we have not yet been able to check this latter point.

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Received January 16, 1969.

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[7] Sanger, F., and Thompson, E. O. P., *Biochim. Biophys. Acta*, **71**, 468 (1963).


Pamphlet reference
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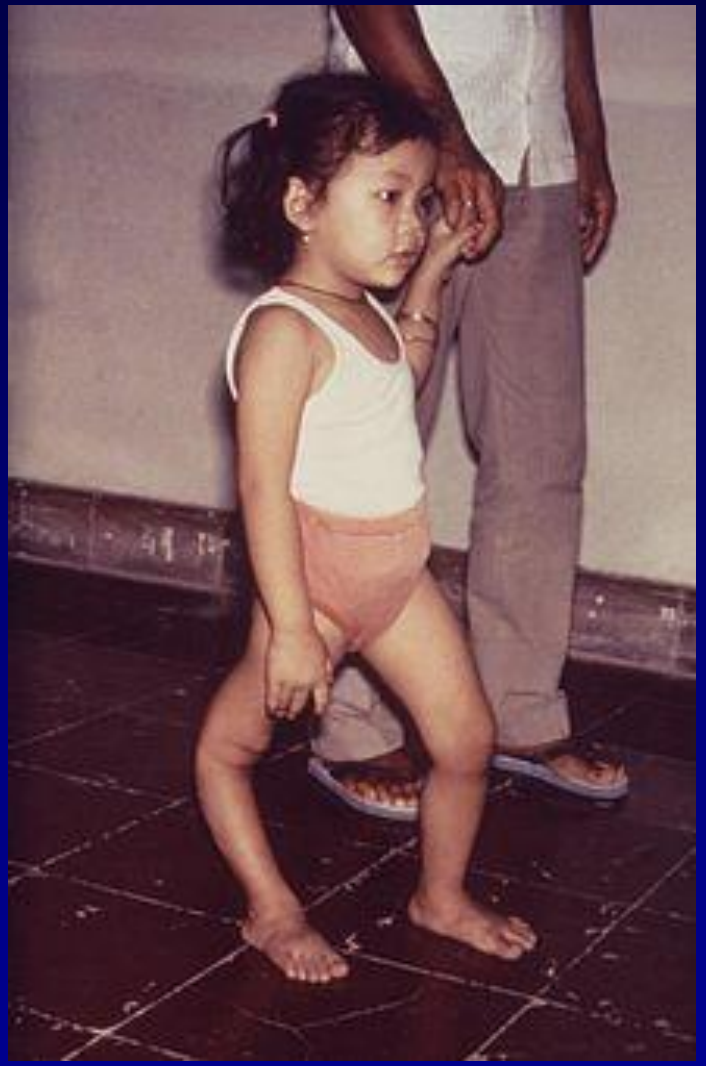

Clinical research that made a difference: What were these people waiting for?

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 20 1959

LARGE-SCALE USE OF SABIN TYPE 2 ATTENUATED POLIOVIRUS VACCINE IN SINGAPORE DURING A TYPE 1 POLIOMYELITIS EPIDEMIC

BY

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K. KANAGARATNAM, M.B., B.S., D.P.H. K. W. LEONG, M.B., B.S.

AND

E. S. MONTEIRO, C.B.E., M.D., F.R.C.P., F.R.F.P.S., D.C.H.

From the Department of Bacteriology, University of Malaya, the Medical Departments, Singapore Government and Singapore City Council

In the latter half of 1958 Singapore experienced an epidemic outbreak of poliomyelitis due to the type 1 virus. Eleven weeks after the first case was reported the Minister of Health in the Singapore Government decided, after consultation, to make available the attenuated type 2 vaccine elaborated by Sabin (1957a, 1957b) for children between the ages of 3 months and 10 years. Dr. Sabin agreed to the release of this vaccine on condition that adequate laboratory control could be assured. The following communication gives the reasons for the selection of the type 2 vaccine, the experimental details, and the results of the campaign.

TABLE I.—*Incidence of Poliomyelitis in Singapore Since 1946 up to Period of Epidemic*

of 1951. The majority of cases were in children under the age of 2, and the general picture was that of an area in which poliomyelitis was endemic, but with periodic increases in the number of cases.

Paul (1958) drew attention to the fact that this endemic state of poliomyelitis was associated with a high infantile mortality rate, and if the infantile mortality rate fell below 60–80 per 1,000 live births a rise in the number of cases of poliomyelitis could be expected. The infantile mortality rates for Singapore since 1946 are shown in Table II.

This fall in the infantile mortality rate could presage a shift to the direction of increased activity of poliomyelitis and the possible appearance of cases in older

Prevention of Poliomyelitis in Singapore by Live Vaccine

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Brit. med. J., 1964, **1**, 1077–1080

In recent years Singapore's population has grown rapidly, accompanied by great improvement in general health standards. These changes are reflected in the data in Table I. Three-quarters of the population are Chinese, about 14% Malay, 8% Indian and Pakistani, and the remaining 3% are roughly equally divided between three groups—Eurasians, Europeans, and others.

TABLE I.—*Trends in Some Vital Indices for Singapore*, 1940–62

	Population	Crude Death Rate per 1,000 Population	Infant Mortality Rate per 1,000 Live Births
1940	751,000	20·9	142·6
1950	1,022,000	12·0	82·2
1960	1,634,000	6·2	34·9
1962	1,733,000	5·9	31·2

In recent years, too, the epidemiological pattern of poliomyelitis in Singapore has tended to show some transition from the endemic behaviour characteristic of countries with low health standards towards the epidemic behaviour characteristic of countries with high sanitary standards. However, cases continue to be confined predominantly to very young children, and the pattern is that of an endemic disease periodically breaking out in epidemic form. Such epidemic waves were seen in 1946 and 1948, soon after the war, but they subsequently appeared to be decreasing in violence until 1958, when an outbreak of over 400 cases occurred (see Table II).

to the Ministry of Health, Singapore (1961). In 1962 a mass immunization campaign was inaugurated, during which about 60% of children from 1 to 5 years of age received two doses of trivalent attenuated virus vaccine. In 1963 a routine programme was inaugurated whereby attenuated vaccine was given to young infants and to children first entering school.

This paper reports the investigations undertaken in the course of the committee's deliberations and the results to date of poliomyelitis immunization in Singapore.

1960 Survey

This survey was designed to assess the immune status of children in Singapore and to study the results of the administration of type 2 vaccine in 1958–9.

Blood and stool specimens were taken from children below 5 years of age, this being the age-group principally effected by poliomyelitis in Singapore. The sample was drawn from healthy children attending at maternal and child health centres in both urban and rural areas. For the sake of homogeneity the survey was restricted to Chinese children. About 75% of the population at all ages are Chinese ; therefore if other ethnic groups had been included their numbers would have been insufficient for comparative purposes unless the total sample size were greatly increased.

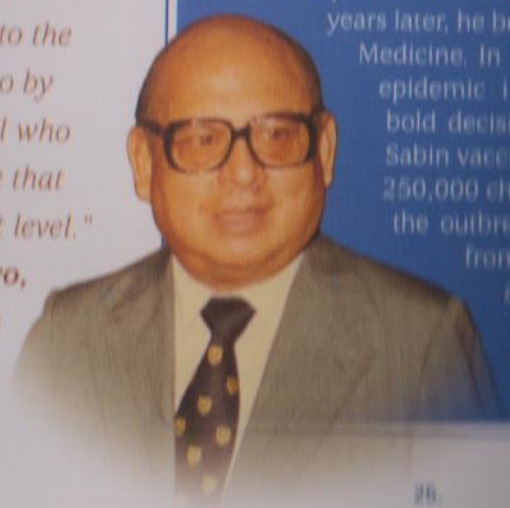
In the selection of subjects, those who had received Salk vaccine were excluded. Those who had documentary

"The Class of 1929 was unique as the first
undergo the six-year medical course of the
g Edward VII College of Medicine which was
ished on the recommendation of the General
dical Council of Great Britain. Medical
cation in Singapore was comparable to the
in the United Kingdom, as attested to by
pectors of the General Medical Council who
d regular visits to Singapore to ensure that
ndards were maintained at the highest level."

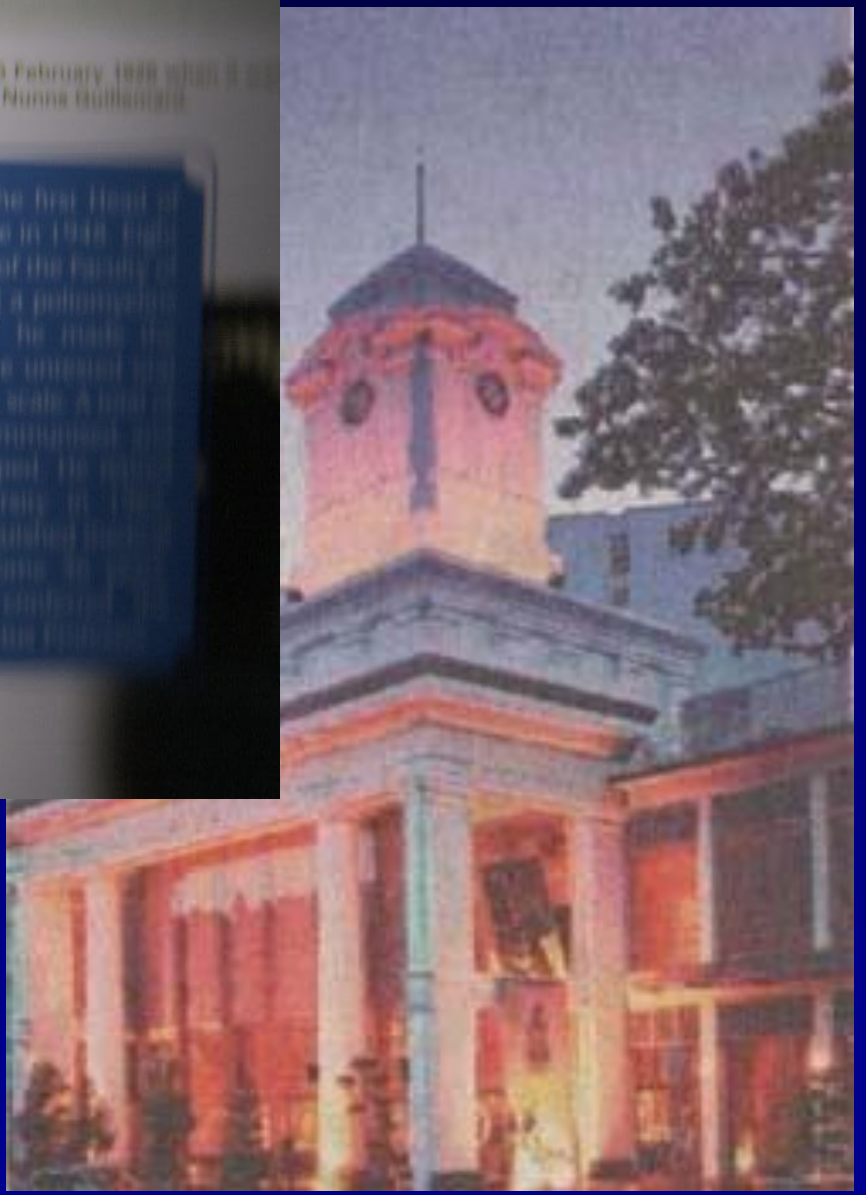
— Prof E S Monteiro,
class of 1929;
Dean of the Faculty
of Medicine, 1956-1960

The Past — the faculty building as it was on 16 February 1928 when it was officially opened by the Governor Sir Laurence Nunns Guillemard

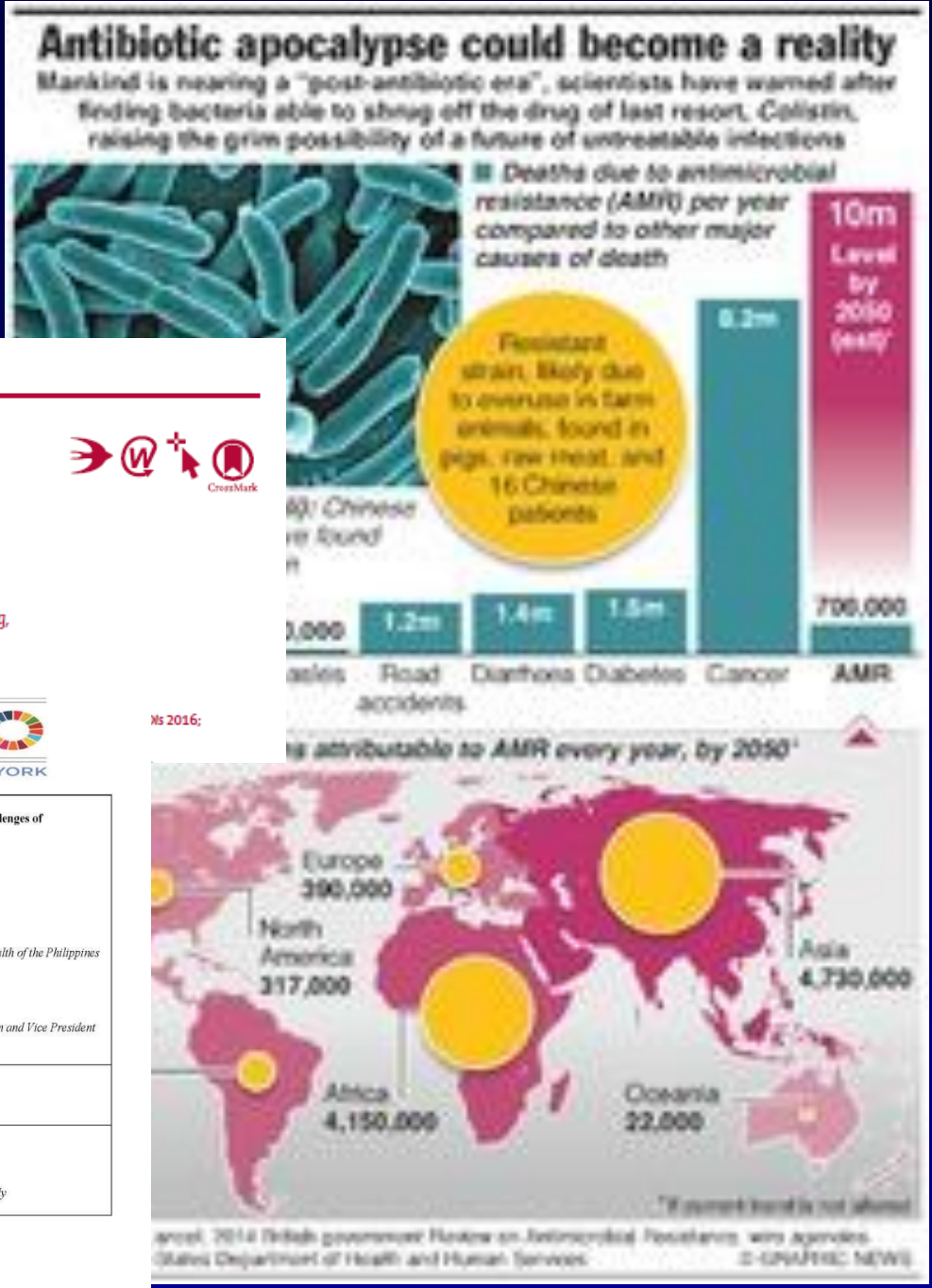
Prof E S Monteiro was appointed the first Head of the Department of Clinical Medicine in 1948. Eight years later, he became Dean of the Faculty of Medicine. In 1958, during a poliomyelitis epidemic in Singapore, he made the bold decision to use the unproved oral Sabin vaccine on a wide scale. A total of 250,000 children were immunised and the outbreak was stopped. He retired from the University in 1960 after a distinguished medical career of some 30 years and was conferred the title Emeritus Professor.



Prof E S Monteiro



Today's problem…



Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu*, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen

Summary

Background Until now, polymyxin… horizontal gene transfer. During …

HIGH-LEVEL MEETING ON ANTIMICROBIAL RESISTANCE

21 SEPTEMBER 2016, UN HEADQUARTERS, NEW YORK

11:45-13:00		**Panel 2: Addressing the multisectoral implications and implementation challenges of antimicrobial resistance in a comprehensive manner** (ECOSOC Council Chamber) *Panellists:* *Member States:* 1. ***H.E. Ms. Erna Solberg,*** *Prime Minister of Norway* 2. ***H.E. Dr. Jorge Lemus,*** *Minister of Health of Argentina* 3. ***H.E. Dr. Paulyn Jean B. Rosell-Ubial,*** *Secretary of the Department of Health of the Philippines* *Stakeholders:* 4. ***Dr. Jim Kim,*** *President, World Bank* 5. ***Ms. Martha L. Tellado,*** *President and CEO, Consumer Reports* 6. ***Mr. David George Velde,*** *Board Member of World Farmers Organisation and Vice President of United States National Farmers' Union*
15:00-17:30	**Plenary Segment** (Trusteeship Council Chamber)	
17:30-18:00	**Closing segment** (Trusteeship Council Chamber) *Closing statement by* ***H.E. Mr. Peter Thomson,*** *President of the 71st session of the United Nations General Assembly*	

AMR was clearly not just a hospital problem

ELSEVIER

International Journal of Antimicrobial Agents 18 (2001) 391–393

INTERNATIONAL JOURNAL OF Antimicrobial Agents

www.ischemo.org

Short communication

Widespread resistance to new antimicrobials in a university hospital before clinical use

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Received 26 March 2001; accepted 6 June 2001

Abstract

The activity of cefpirome, cefepime and piperacillin/tazobactam previously unused in the hospital was evaluated in parallel with five broad-spectrum antibiotics (ceftazidime, ceftriaxone, imipenem, ciprofloxacin and amikacin) currently being used to treat serious infections in the National University Hospital, Singapore. Two hundred and two clinically significant, organisms consecutively isolated during 1998 were included in the study. In vitro efficacy of cefepime, cefpirome and piperacillin/tazobactam was not superior to imipenem, ciprofloxacin and amikacin which are currently used. More than 40% of Enterobacteriaceae were

Increasing antibiotic resistance in *Streptococcus pneumoniae* colonizing children attending day-care centres in Singapore

SHAWN VASOO,[1] KAMALJIT SINGH,[1,2] LI YANG HSU,[3] YOKE FONG CHIEW,[5] CAROL CHOW,[4] RAYMOND T.P. LIN[4] AND PAUL A. TAMBYAH[3]

Table 3 Antibiotic susceptibilities of pneumococcal isolates—comparison between 1997 and 2007–2008

	No. (%) of isolates—1997 ($n = 102$)†			No. (%) of isolates—2007–2008 ($n = 59$)			
Antibiotic	Sensitive	Intermediate	Resistant	Sensitive	Intermediate	Resistant	P‡
PEN§	74 (72.6)	19 (18.6)	9 (8.8)	18 (30.5)	34 (57.6)	7 (11.9)	<0.001
CEF	84 (82.4)	18 (17.6)	0 (0)	55 (93.2)	4 (6.8)	0 (0)	0.053
ERY	67 (65.7)	2 (2.0)	32 (31.4)	13 (22.0)	0 (0)	46 (78.0)	<0.001
CLI	76(74.5)	2 (2.0)	23 (22.5)	32 (54.2)	0 (0)	27 (45.8)	0.006
SXT¶	—	—	—	20 (33.9)	6 (10.2)	33 (55.9)	—
TET	52 (51.0)	—	49 (48.0)	19 (32.2)	1 (1.7)	39 (66.1)	0.018
LEV¶	—	—	—	58 (98.3)	1 (1.7)	0 (0)	—

This study was presented in part at the 48th Annual ICAAC/IDSA 46th Annual Meeting, October 25–28, 2008 and was supported by grant from the National Medical Research Council, Singapore (NMRC/1083/2006).

Health Care-associated Methicillin-resistant *Staphylococcus aureus* Colonization in Children Attending Day Care Centers in Singapore

Presented in part at the 48th Annual ICAAC/IDSA 46th Annual Meeting, October 25–28, 2008, and was supported by grant from the National Medical Research Council, Singapore (NMRC/1083/2006).

The overall *S. aureus* colonization rate was 27.3%. Antibiotic resistance rates were as follows: penicillin 82.5%, oxacillin 1.8% (n = 2), erythromycin 16.7%, clindamycin 0%, trimethoprim-sulfamethoxazole 2%, gentamicin 1%, and levofloxacin 2%.

Vasoo S, Singh K, Chow C, Parthasarathy P, Lin RT, Hsu LY, **Tambyah** PA.
Pediatr Infect Dis J. 2012;31:213-4.

Pneumococcal carriage and resistance in children attending day care centers in Singapore in an early era of PCV-7 uptake

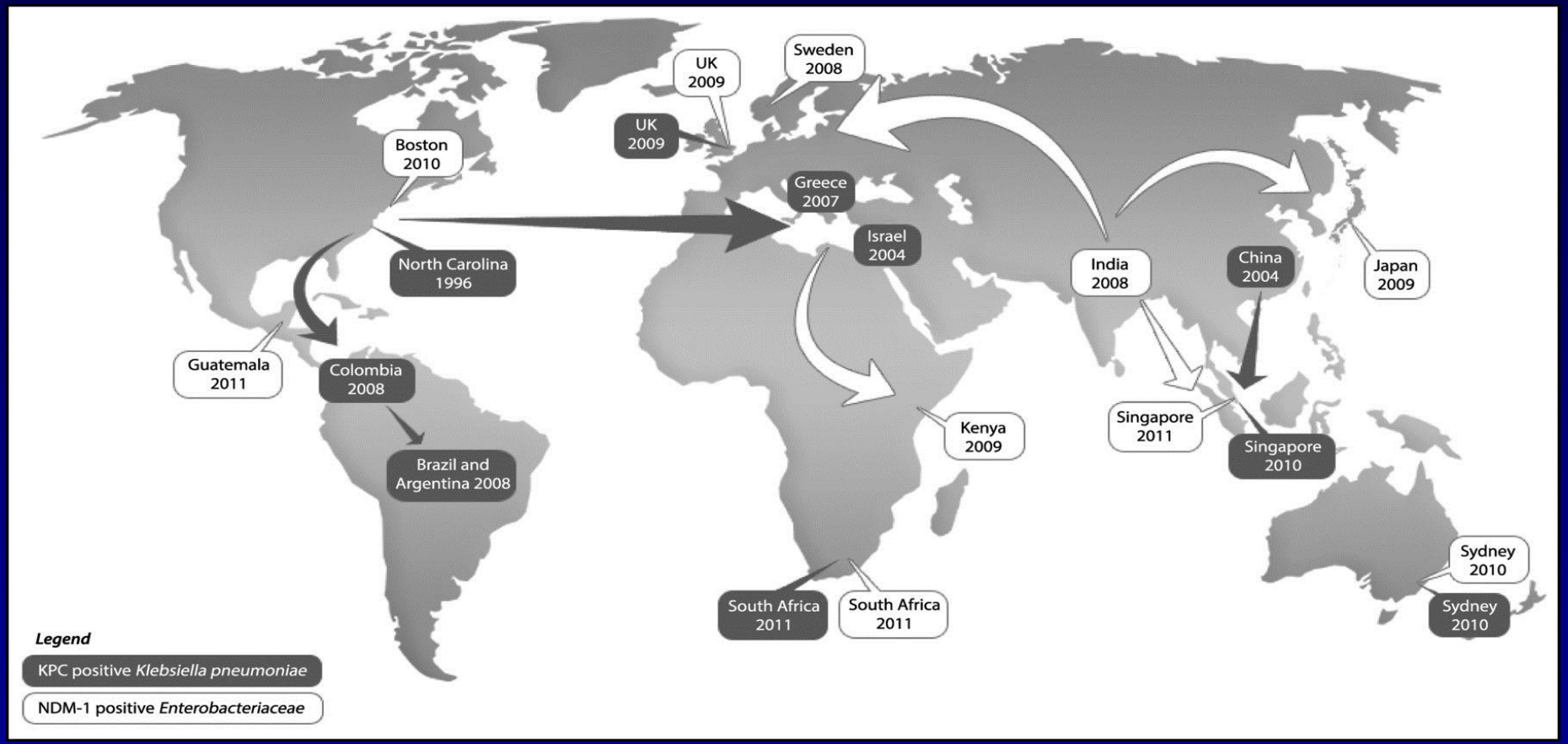
IDSA 46th Annual Meeting, October 25–28, 2008 and was supported by grant from the National Medical Research Council, Singapore (NMRC/1083/2006).

Vasoo S, Singh K, Chow C, Lin RT, Hsu LY, Tambyah PA.
J Infect. 2010;60:507

A young man with post-op complications….

	Update 1/8 at 11.40: Tigecycline 2mg/L is interpreted as intermediate susceptibility.	
Identification	.	
Organism 1	Klebsiella pneumoniae	
Comment	Isolated from both aerobic & anaerobic bottles	
Organism 2	Bacteroides fragilis group	
Comment	Isolated from anaerobic bottle only	
Sensitivity 1	.	
Organism 1	Klebsiella pneumoniae	
Ampicillin	Resistant	
Ampicillin	>=32 mg/L	
Tigecycline	Intermediate	
Tigecycline	2.000	mg/L
Amox/Clavulanic Acid	Resistant	
Amox/Clavulanic Acid	>=32 mg/L	
Ceftriaxone	Resistant	
Ceftazidime	Resistant	
Ceftazidime	>=64 mg/L	
Imipenem MIC	Intermediate	
Imipenem MIC	6.000	mg/L
Pip/Tazobactam	Resistant	
Pip/Tazobactam	>=128 mg/L	
Meropenem MIC	Resistant	
Meropenem MIC	> 32.000	mg/L
Gentamicin	Resistant	
Gentamicin	8.000	mg/L
Amikacin	Resistant	
Amikacin	>=64 mg/L	
Ciprofloxacin	Resistant	
Ciprofloxacin	>=4 mg/L	
Cotrimoxazole	Resistant	
Cotrimoxazole	>=320 mg/L	
Polymyxin B	Resistant	
Polymyxin B	3.000	mg/L
Ertapenem	Resistant	
Ertapenem	>=8 mg/L	

Global dissemination of Klebsiella pneumoniae carbapenemase–producing K. pneumoniae and New Delhi metallo-β-lactamase-1–producing Enterobacteriaceae.



Molton J S et al. Clin Infect Dis. 2013;56:1310-1318

Clinical Infectious Diseases

RCT Meropenem vs Piperacillin-Tazobactam for Definitive Treatment of BSI's Due to Ceftriaxone Non-susceptible Escherichia Coli and Klebsiella Spp. (MERINO)

This study is currently recruiting participants. (see Contacts and Locations)

Verified November 2016 by The University of Queensland

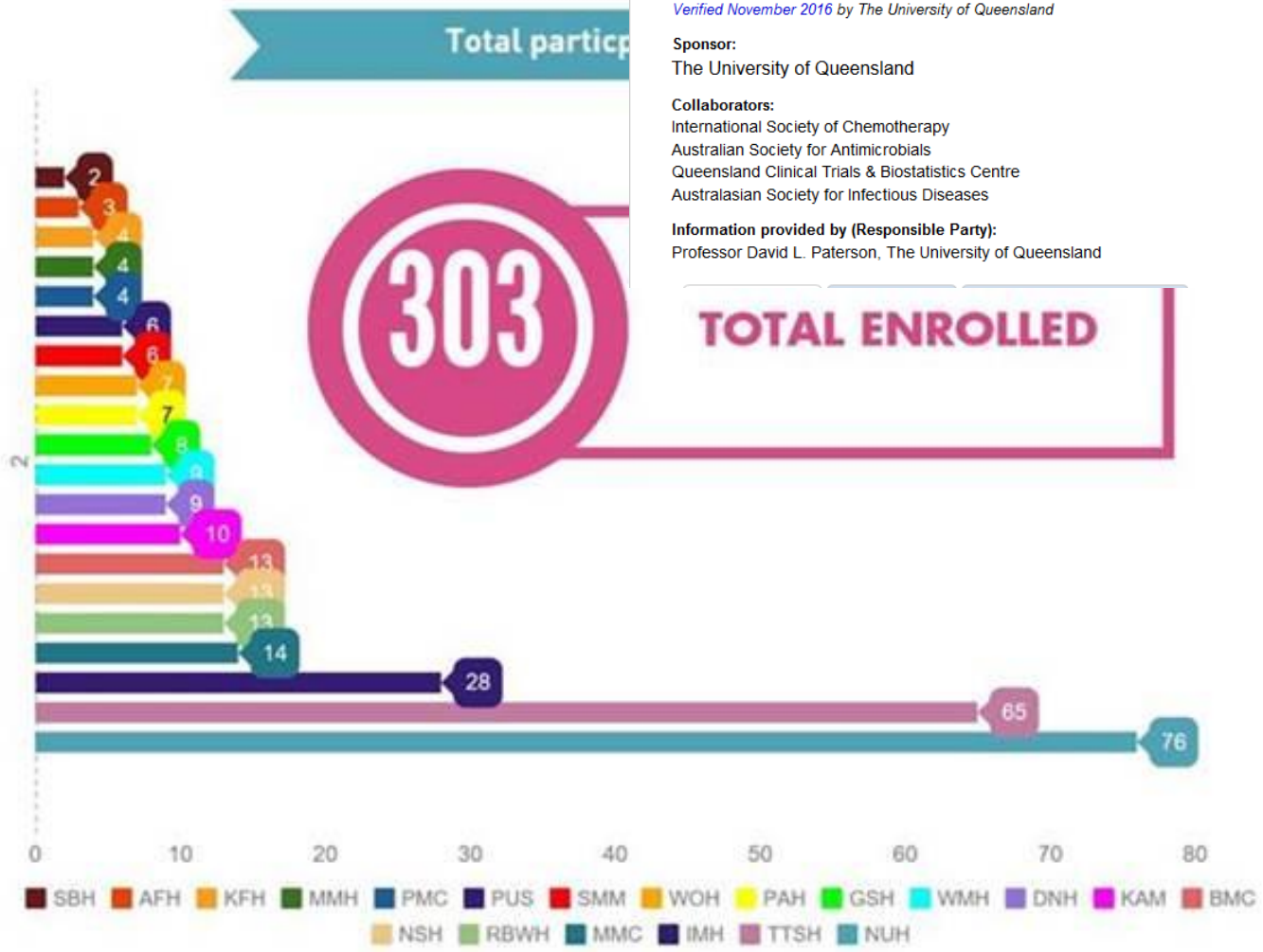
Sponsor:
The University of Queensland

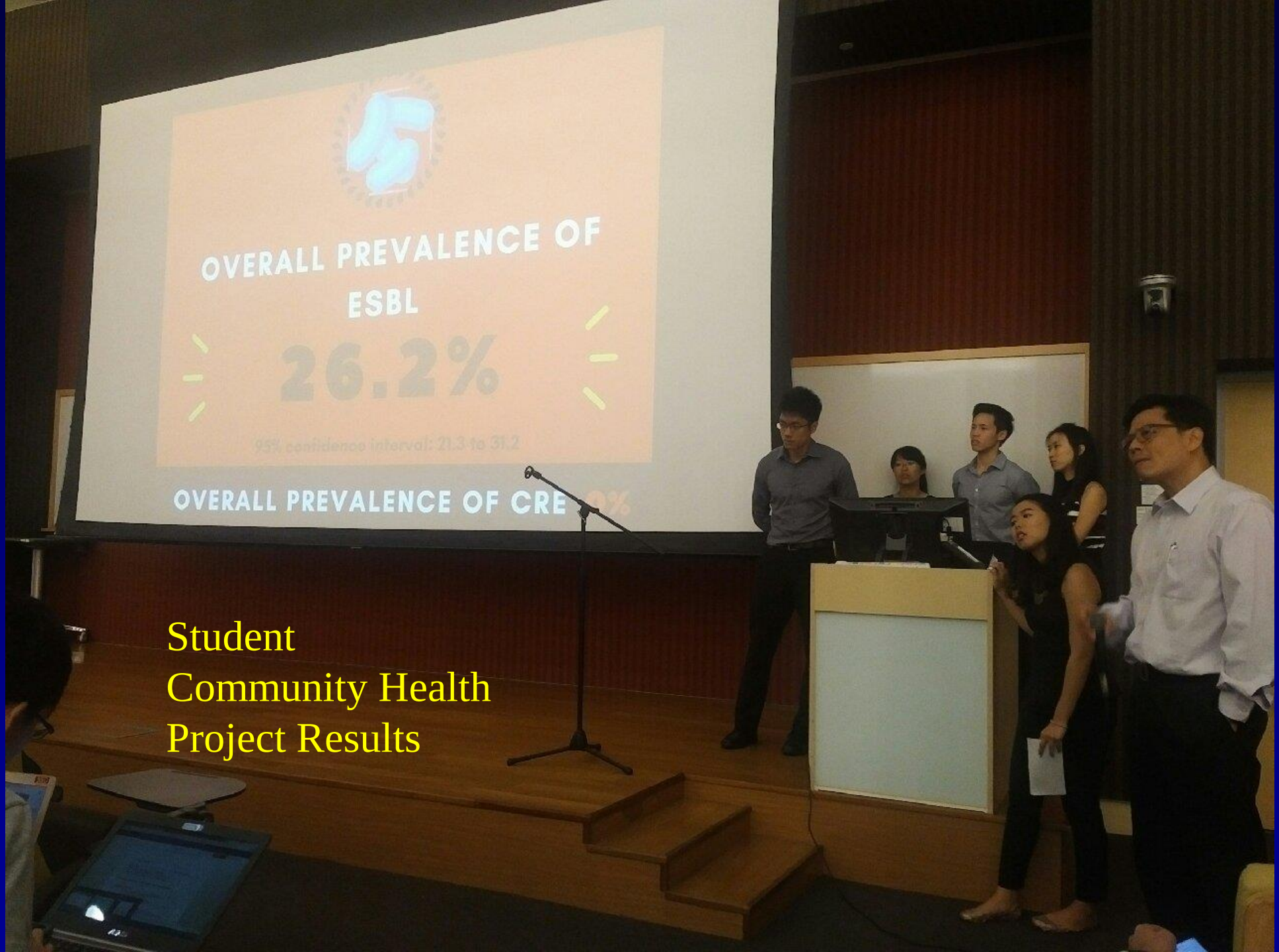
Collaborators:
International Society of Chemotherapy
Australian Society for Antimicrobials
Queensland Clinical Trials & Biostatistics Centre
Australasian Society for Infectious Diseases

Information provided by (Responsible Party):
Professor David L. Paterson, The University of Queensland

ClinicalTrials.gov Identifier:
NCT02176122

First received: June 24, 2014
Last updated: November 15, 2016
Last verified: November 2016
History of Changes





Student
Community Health
Project Results

CARCUTI Trial

14 months in IRB!

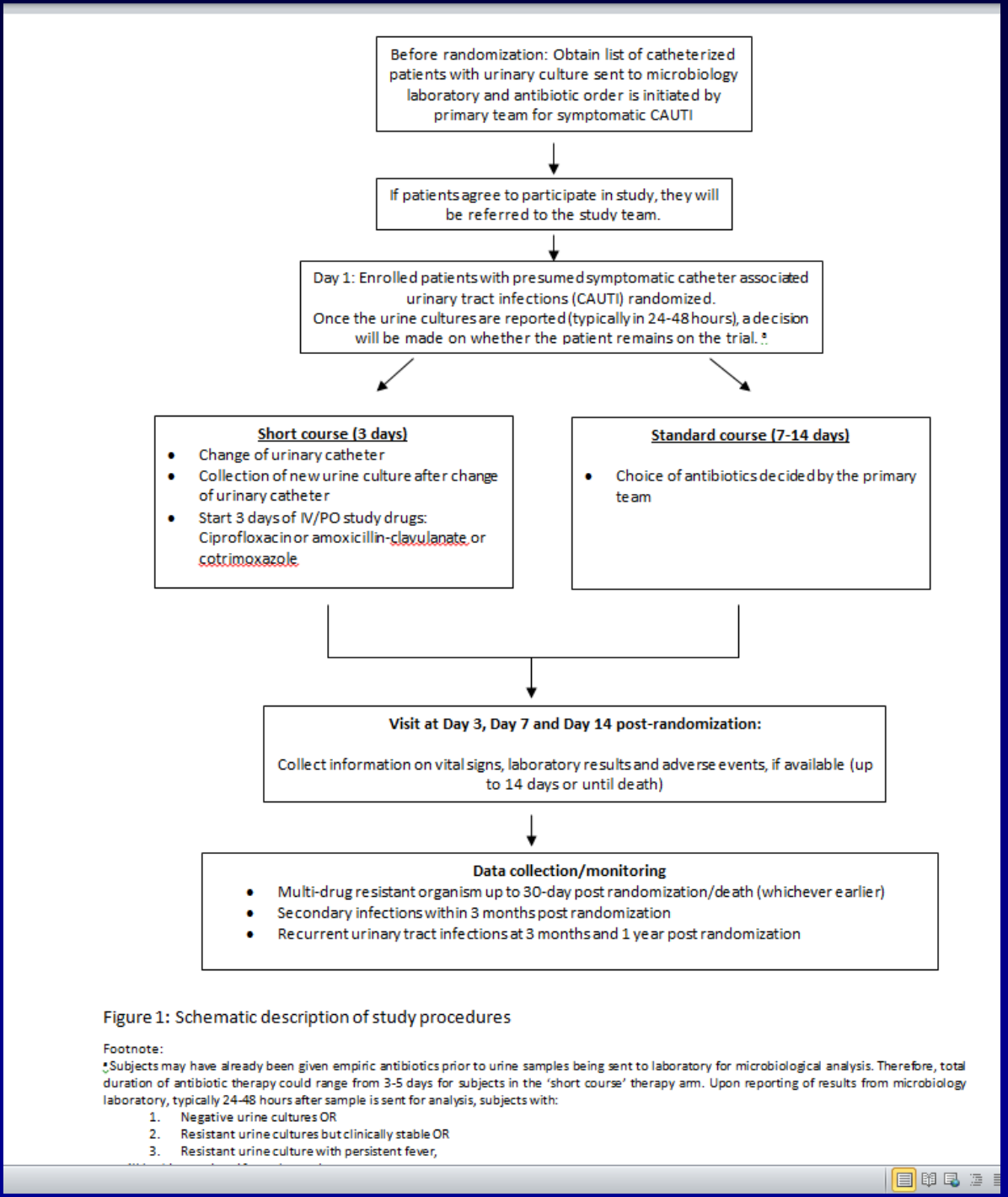


Figure 1: Schematic description of study procedures

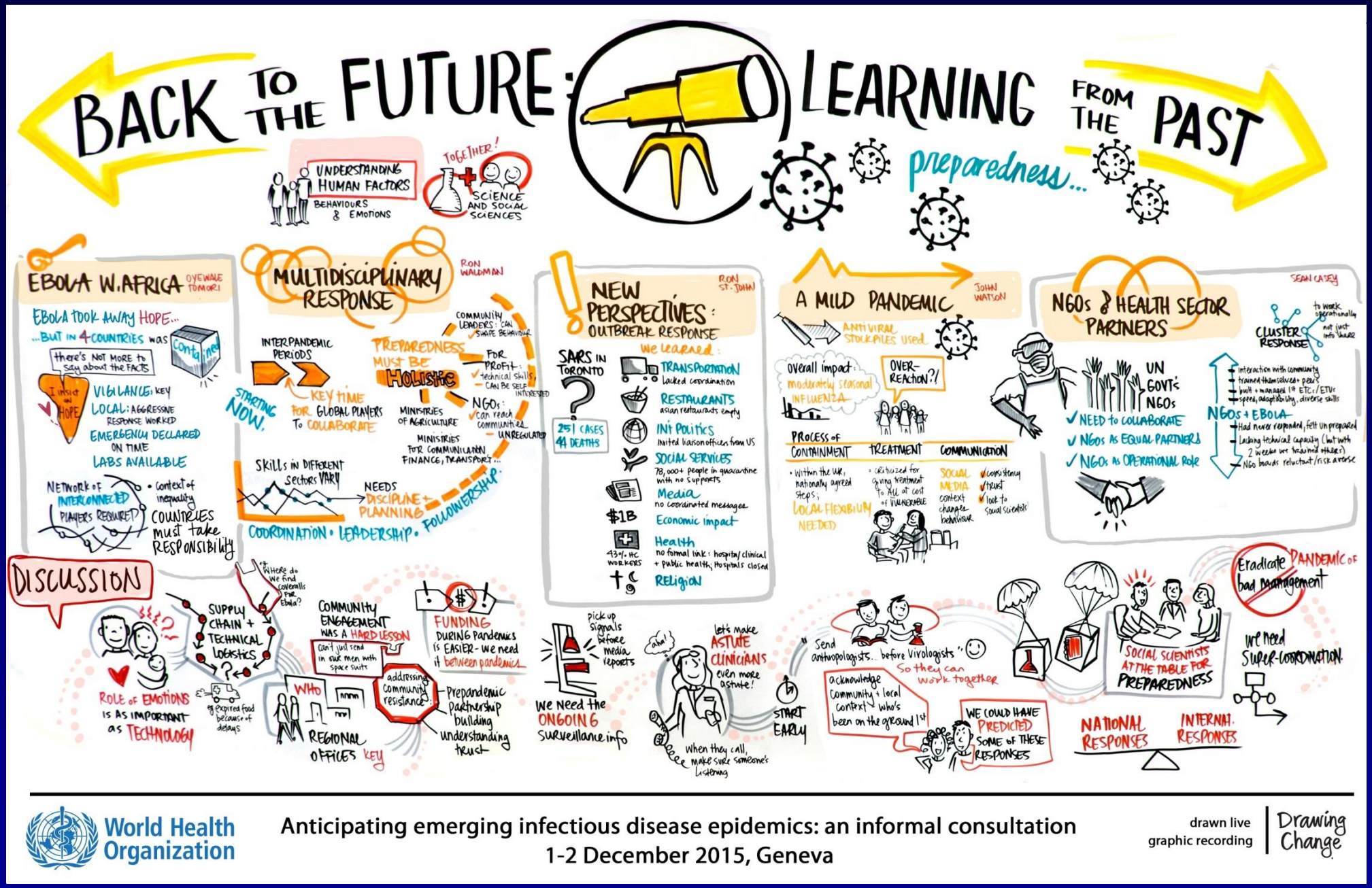
Footnote:

*Subjects may have already been given empiric antibiotics prior to urine samples being sent to laboratory for microbiological analysis. Therefore, total duration of antibiotic therapy could range from 3-5 days for subjects in the 'short course' therapy arm. Upon reporting of results from microbiology laboratory, typically 24-48 hours after sample is sent for analysis, subjects with:

1. Negative urine cultures OR
2. Resistant urine cultures but clinically stable OR
3. Resistant urine culture with persistent fever,

Thanks to collaborators/contributors (and NMRC!)

- SAF/DSO
  - Vernon Lee, Tan Boon Huan
- NUHS
  - K Jeyaseelan , Neoh KG, Prof Evelyn Koay, Dr Julian Tang, Hsu Li Yang, KO Lee, Raymond Lin
  - Ramandeep K Virk , Anupama Vasudevan, Vithia Gunalan + Sebastian Maurer-Stroh
  - Jaminah b Mohd Ali, Sarah Sidek, Isaac Low
- IIDE/TTSH: Leo YS, David Lye, Shawn Vasoo and many more



World Health Organization

Anticipating emerging infectious disease epidemics: an informal consultation
1-2 December 2015, Geneva

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http://www.who.int/csr/disease/anticipating_epidemics/ae-meeting-audiovisual/en/

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SYMPOSIUM SESSIONS		
1. Dengue: Insights from bed to bench 2. Tuberculosis: Drug resistance and new therapeutics 3. Antimicrobial Resistance: A One-Health approach 4. Malaria: Drug resistance and new insights 5. Outbreak diagnostics: Detecting the new and unknown 6. Outbreak control: Learning from the past to prepare for the future	1. Zika: Experience from around the world 2. Mycology: Insights from bed to bench 3. Antimicrobial Resistance: Approach to treating the untreatable 4. SARS, MERS and pneumonia 5. Outbreak clinical trials: Can it be done? 6. Outbreak host response	1. Chikungunya and Zika: The threat of arboviruses 2. HIV: Is an end to the pandemic possible? 3. Influenza: Insights from genomics to modelling 4. Dengue: Debate on Wolbachia and dengue vaccines 5. Microbiome and infectious diseases 6. Outbreak predicting the next big one

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Physicians/Scientists	$700	$850	$1000
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