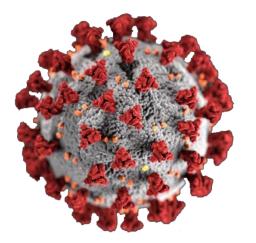


Singapore from the Frontlines





Matthias Maiwald

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Singapore was hit quite badly by the 2003 SARS outbreak

Probable cases of SARS by country and territory, 1 November 2002 - 31 July 2003^[5] Fatality Country or region Cases + Deaths + ŧ (%) Mainland China^[a] 5,327 349 6.6 Hong Kong 1,755 299 17.0 Taiwan^{[b][6][7]} 346 73 21.1 Canada 251 44 17.5 Singapore 238 33 13.9 5 7.9 \star Vietnam 63 Total excluding Mainland China 2,769 454 16.4 Total (29 territories) 8,096 811 9.6

A map of the infected countries of the epidemic of SARS between 1 November 2002 and 7 August 2003 Countries with confirmed deaths Countries with confirmed infections Countries with confirmed cases

b. ^ After 11 July 2003, 325 Taiwanese cases were 'discarded'. Laboratory information was insufficient or incomplete for 135 of the discarded cases; 101 of these patients died.

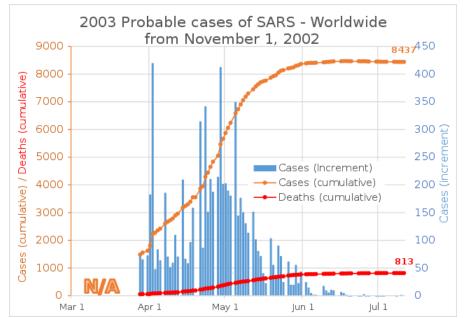
a. A Figures for China exclude Hong Kong, Macau and Taiwan, which are reported

Singapore also had 5 deaths among healthcare workers

separately by the WHO

Painful Lesson:

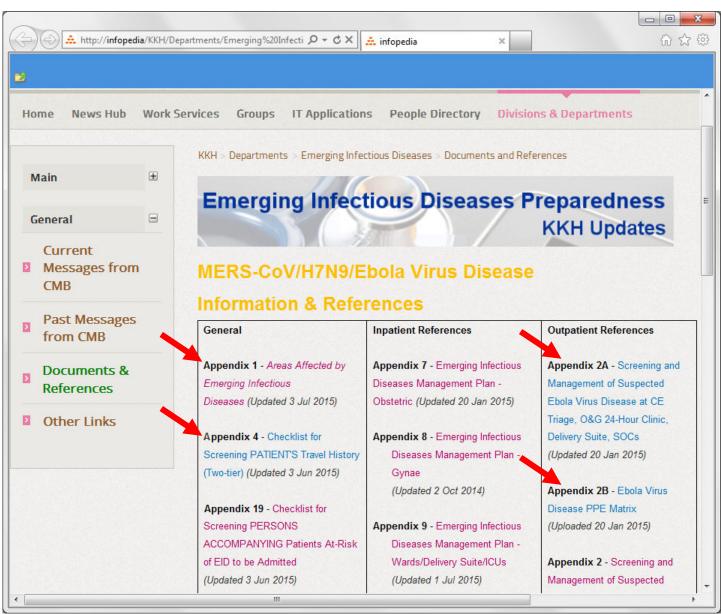
 Due to its exposed location as trade and travel hub, SG is extremely vulnerable to imported infections!



Since 2003, Singapore kept doing pandemic planning: Our hospital's Emerging Infectious Diseases Pages

Page from **2015**

(when MERS, Ebola and Flu A H7N9 were around)



Screening **Procedures** from 2015

Novel Coronavirus (MERS)

SOUTH KOREA

MIDDLE EAST

Middle Fast includes:-

The Arabian Peninsula &

neighbouring countries in the

- United Arab Emirates (UAE)

The affected areas in Africa

Ebola Virus Disease

٠

- Jordan

- Kuwait

- Oman

- Qatar

- Yemen

includes:-Guinea

Liberia

Sierra Leone

-

-

-

- Lebanon

- Saudi Arabia

		1st screen Screening staff	2nd Screen Ward staff					
	1) Travel history or resident of country	Yes No	Yes No	MERS-CoV	H7N9 China (last 10 days)	Ebola Africa (last 21 days)		
S	(refer Appendix 1)			(last 14 days)	(last to days)			
	2) Close contact with confirmed or suspect ca	ase		Last 14 days	Last 10 days	Last 21 days		
	3) Symptoms			Fever or cough o	or SOB	Fever		
	Tick if any of					Vomiting,		
	symptoms present					Diarrhoea,		
		_				Headache,		
<u>Influenz</u>	<u>a A (H7N9)</u>					Abdominal pain,		
CHIN	IA					Sore throat,		
	ed municipalities /					Rash,		
provinces - Anhui	in China includes:- 安徽					Red eyes,		
- Beijing	女 徽 北京					Bleeding, (mucous membranes/		
- Fujian 福建						venipuncture sites)		
- Guangdo	-					/		
- Guizhou 贵州			MERS-CoV & H7N9					
- Guangxi 广西 - Hebei 河北								
- Henan	河南		If patient has (1 or 2) +3					
- Hunan 湖南 - Staff must don <u>Full PPE</u> . Patient to v						•		
- Jiangxi	江西	- Adm	mit patient to the ward with negative pressure room.					
- Jiangsu - Jilin	Jiangsu 江苏 Ebola							
- Shandor								
- Shangha								
- Xinjiang	injiang 新疆 Send to TTSH							
- Zhejiang	, 浙江		* If patient is an 'At-Risk (Low Risk/ High Risk) ' case - Admit to Ward 46 (negative pressure with isolation room), or					
		· · ·						
- Delivery Suite Room 1-4 (when in labour).						,		
			For all other scenarios, discuss with ID physician					

2nd Screen

1st screen

Exercise "Sparrowhawk" (I and II)

- Mock patient with serious infection arrives at the hospital
- Role-play
- Conducted for Ebola 2015 – Enhanced PPE with respirators
- For "Respiratory X" disease – Full PPE with N95 mask, eye protection, gowns, gloves



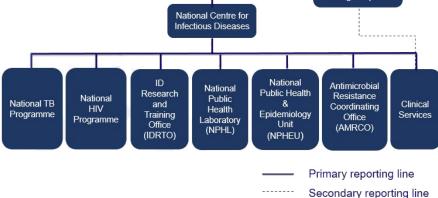


Images: KKH Infection Control Unit

Singapore National Centre for Infectious Diseases (NCID)

- Purpose-built medical facility within the public healthcare system
- 17 wards, 330 beds, 2 ICUs
- High-level isolation ward capable of handling Ebola, Marburg, anthrax
- Research and diagnostic facilities
- National Public Health Laboratory (NPHL)
- Formally opened on 7 Sept. 2019 (just in time)





Images: Wikipedia (top), NCID (bottom)

KK Women's and Children's Hospital SingHealth

KK Women's and Children's Hospital (KKH)

- 830-bed pediatric & OB/Gyn hospital
- Tertiary-level academic teaching hospital for National University of Singapore (NUS) and Duke-NUS
- My workplace -- I am a clinical microbiologist at the hospital's Department of Pathology & Laboratory Medicine
- Relatively small microbiology section



Images: Unabiz (top), Google Maps, User KSY (bottom)

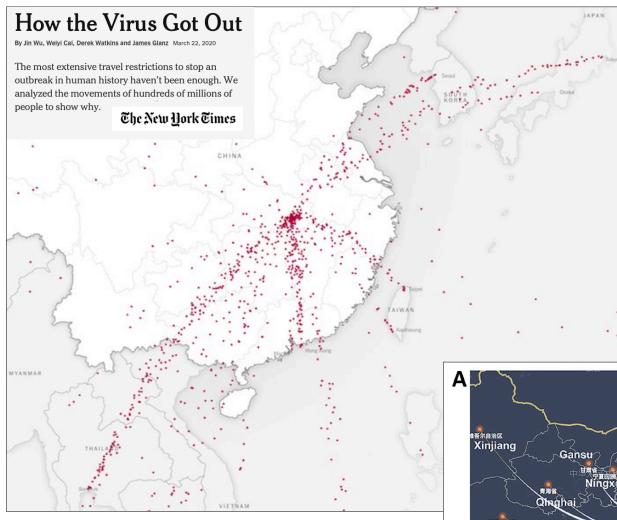
4 Jan 2020 – The Straits Times

A8 | TOPOF THE NEWS

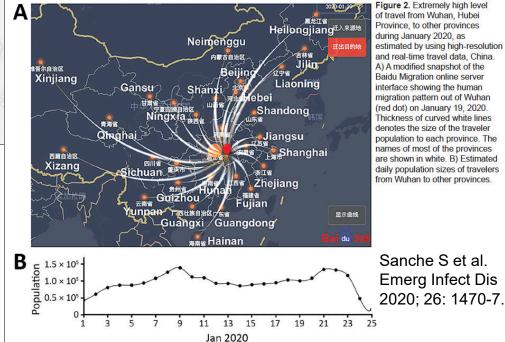
| THE STRAITS TIMES | SATURDAY, JANUARY 4, 2020 |







- Wuhan "Exodus"
- Wuhan Lockdown
 23 Jan 2020
- About 5 million people left Wuhan
- Chinese New Year 25-26 Jan 2020
- Biggest yearly travel period



• Travel inside China

 Travel to Thailand, Singapore, Bali, Hong Kong, Taiwan, Japan, S. Korea (--> "First Wave")

Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases Interim guidance 17 January 2020

WHO/2019-nCoV/laboratory/2020.3

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance

Early PCR Assays (Jan 2020) 2020)

- Drosten Group, Charité, Berlin Germany
- School of Public Health, University of Hong Kong, Hong (Leo Poon, Daniel Chu and Malik Peiris)
- China CDC (National Institute for Viral Disease Control and Prevention)
- Department of Medical Sciences, Ministry of Public Health, Thailand
- National Institute of Infectious Diseases, Tokyo, Japan

PCR protocol available 13 Jan 2020

Berlin, 13.01.2020



Diagnostic detection of Wuhan coronavirus 2019 by real-time RT-PCR

-Protocol and preliminary evaluation as of Jan 13, 2020-

Victor Corman, Tobias Bleicker, Sebastian Brünink, Christian Drosten Charité Virology, Berlin, Germany

Olfert Landt, Tib-Molbiol, Berlin, Germany

Marion Koopmans Erasmus MC, Rotterdam, The Netherlands

Maria Zambon Public Health England, London

Additional advice by Malik Peiris, University of Hong Kong

RESEARCH

Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR

Victor M Corman¹, Olfert Landt², Marco Kaiser², Richard Molenkamp³, Adam Meijer⁴, Daniel KW Chu⁵, Tobias Bleicker¹, Sebastian Brünlnk¹, Julia Schneider¹, Marie Luisa Schmidt¹, Daphne GJC Mulders³, Bart L Haagmans³, Bas van der Veer⁴, Sharon van den Brink⁴, Lisa Wijsman⁴, Gabriel Goderski⁴, Jean-Louis Romette⁶, Joanna Ellis⁷, Maria Zambon⁷, Malik Peiris⁵, Herman Goossens⁸, Chantal Reusken⁴, Marion PG Koopmans³, Christian Drosten¹

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- 4. National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
- 5. University of Hong Kong, Hong Kong, China
- 6. Université d Aix-Marseille, Marseille, France
- 7. Public Health England, London, United Kingdom 8. Department of Medical Microbiology, Vaccine and Infectious Diseases Institute, University of Antwerp, Antwerp, Belgium

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Citation style for this article

Corman Victor M, Landt Olfert, Kalser Marco, Molenkamp Richard, Meljer Adam, Chu Daniel KW, Bleicker Toblas, Brünink Sebastian, Schneider Julia, Schmidt Marle Luisa, Mulders Daphne GjC, Haagmans Bart L, van der Veer Bas, van den Brink Sharon, Wijsman Lisa, Goderski Gabriel, Romette Jean-Louis, Ellis Joanna, Zambon Maria, Peiris Malik, Goossens Herman, Reusken Chantal, Koopmans Marion PG, Drosten Christian. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):pli=2000045. https://doi.org/10.2807/1560-7947.ES.2020.25.3.2000045

7 Feb. 2020

Health Organization has d

31,207

MAINLAND CHIN

WUHAN VIRUS OUTBREAK: IN NUMBERS train of coronavirus that originated in the Chinese city of Wuhan lass r

27 territories beyond mainland China

CONFIRMED

85 33 25

25 24

16

15 15

13

12 12

10

1

31,532

0

.0 0

638

DEATH

COUNTRY/TERRITORY

TOTAL CINCL. MAINLAND CHINA)

VISIT YAHOO.COM FOR THE LATEST NEWS COVERAGE

- is mutating. The Wo

ie (SARS), which killed ne

23 Jan. 2020

Singapore

Singapore confirms first case of Wuhan virus



Employees at Singapore's National Centre for Infectious Diseases putting on protective gear before carrying out testing for the novel coronavirus.

SINGAPORE: Singapore on Thursday (Jan 23) announced a confirmed case of the Wuhan virus, a new coronavirus that has sickened hundreds of people and killed at least 17.

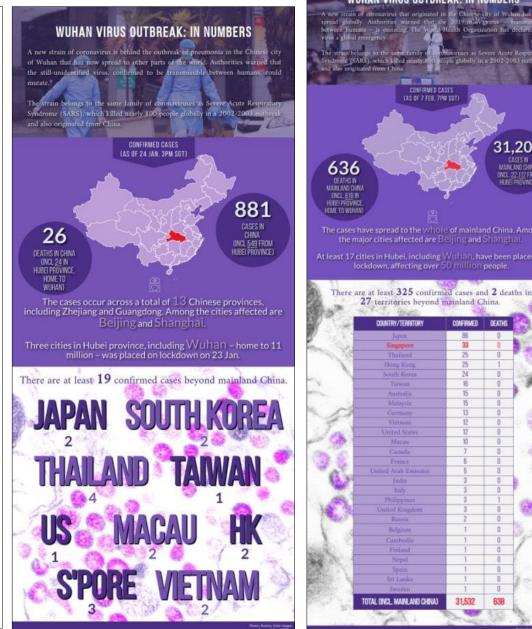
In a media briefing on Thursday evening, the Ministry of Health said the patient is a 66-year-old Chinese man. The Wuhan resident, who arrived in Singapore with his family on Jan 20, flew from Guangzhou via China Southern flight CZ351.

He is currently in isolation at the Singapore General Hospital and is in stable condition.

- READ: Wuhan virus Number of confirmed cases in China exceeds 570
- ▶ READ: Wuhan virus What we know about the fatalities

▶ READ: "Verge of tears" - Residents of virus-hit Wuhan call for support amid food shortage worries

25 Jan. 2020



Adoption of Testing in Singapore

National Public Health Laboratory (NPHL)

 Designed own PCR (N gene, ORF1ab gene); JAMA 2020

JAMA | Original Investigation

Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore

Barnaby Edward Young, MB, BChir; Sean Wei Xiang Ong, MBBS; Shirin Kalimuddin, MPH; Jenny G. Low, MPH; Seow Yen Tan, MBBS; Jiashen Loh, MBBS; Oon-Tek Ng, MPH; Kalisvar Marimuthu, MBBS; Li Wei Ang, Msc; Tze Minn Mak, PhD; Sok Kiang Lau, PhD; Danielle E. Anderson, PhD; Kian Sing Chan, MBBS; Thean Yen Tan, MBBCh; Tong Yong Ng, MBBS; Lin Cui, PhD; Zubaidah Sald, MSc; Lalitba Kurupatham, MPH; Mark I-Cheng Chen, PhD; Monica Chan, BMBS; Shawn Vasoo, MBBS; Lin-Fa Wang, PhD; Boon Huan Tan, PhD; Raymond Tzer Pin Lin, MBBS; Vermon Jian Ming Lee, PhD; Yee-Sin Leo, MPH; David Chien Lye, MBBS; for the Singapore 2019 Novel Coronavirus Outbreak Research Team

JAMA. 2020;323(15):1488-1494. doi:10.1001/jama.2020.3204 Published online March 3, 2020. Corrected on March 20, 2020.

Singapore General Hospital (SGH) Dept. Molecular Pathology

• Adopted German assay late Jan.

Other Hospital Labs (public & private)

 Received panels of coded samples from NPHL; when all correct, approval for testing by Ministry of Health (MOH)

We at KKH

• PCR testing approved 11 Feb.

Subsequently

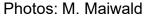
- Commercial PCR kits became available
 - TIB Molbiol Berlin, Germany
 - Fortitude Kit, A*Star Singapore
 - Roche cobas 6800 or 8800
- Ramping up test capacity (~500/day in our small lab)
- Some bigger labs 1500-2000 per day
- Serology (Abbott IgG) started at KKH 22 May
- Singapore (pop. 6.6 m) aims at test capacity 40,000 PCRs per day

Biosafety of Testing

- Needed to design lab protocols
- (1) Microbiology & Mol. Micro. Lab
- (2) Other Clinical Laboratories
- (a) "Respiratory type" specimens (higher risk)
- (b) "Non-respiratory" specimens (lower risk)
- COVID suspect specimens double-bagged and labeled

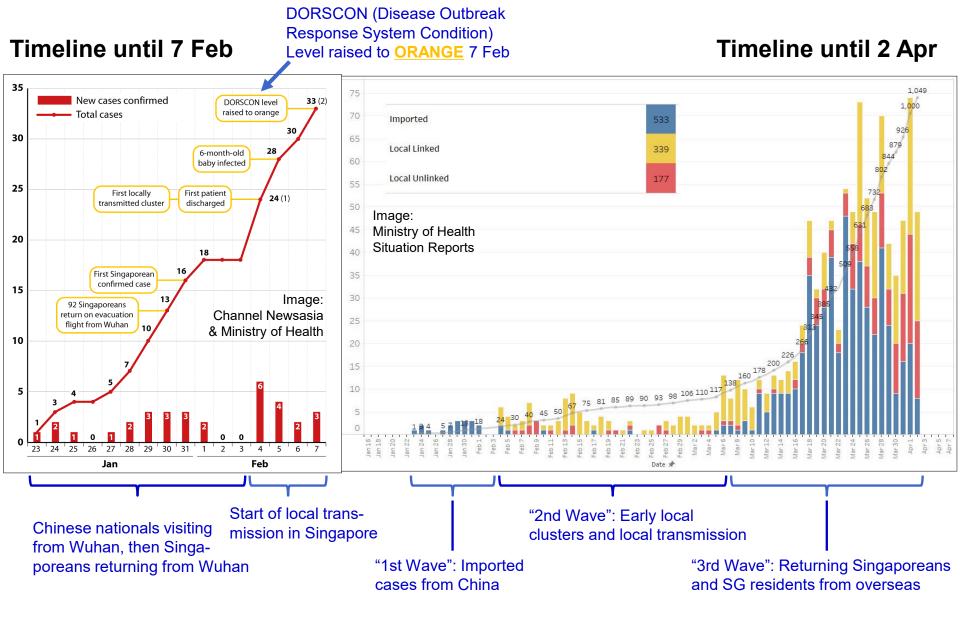


- For (a): Biosafety cabinets (BSCs), goggles, N95 masks, gowns, gloves for specimen processing
- Pregnant women & staff on immunosuppressant medication exempted



Our "Hunting Trophy Wall"

Early COVID-19 Timeline in SG



PPE Measures at the Hospital

Triage

• Counter Staff: surg. mask (ext. use); Clin. Staff: N95 mask (ext.)

Patient Care

- Suspected/confirmed pats.: N95 mask + goggles (ext. use) + gown + gloves (single use)
- Non-suspect patients: surg. mask (ext. use)

Aerosol-generating Procedures

- **<u>Suspected/confirmed pats.</u>**: N95 + goggles (or PAPR) + gown + gloves (all single use)
- Other pats.: N95 mask + goggles (ext. use) + gown + gloves (single use)

Environmental Cleaning

• N95 mask + goggles (ext. use) + gown + gloves (single use)

Admin. Staff, Patients, Visitors

• Surgical mask (ext. use); or cloth mask

Notes

 Ext. use = extended use for one shift (N95 mask in new zip-lock bag or plastic lunch box when temporarily removed)

Other Measures during DORSCON Orange

Hospital Staff

- All staff to take temperature 2 x daily and record on staff intranet
- Anyone with fever, flu-like sympt., sore throat, runny nose MUST report to staff clinic, get COVID-19 tested and placed on 5 d mandatory home quarantine (10 k fines for breach)

Leave

- All leave outside SG is disallowed, including conferences
- Staff arriving from other countries must serve 14 d Stay-Home Notice (SHN)

Meetings, Education, Research

- Inter-hospital movement of HCWs restricted, incl. resident rostering
- Meetings & education via teleconferencing (Zoom, WebEx)
- Research is restricted; guidelines issued

Patients, **Visitors**

- Visitor access registration & control; only 1 visitor per patient
- Elective procedures & clinic visits restricted
- Isolation wards for suspect/confirmed pats.; discharge when PCR neg. on 2 consec. days

Patient Categories & Indications for Testing

	Before 26 March	From 26 March	From 8 May
1.	Suspect/Confirmed Case fulfilling MOH criteria	Meet MOH's suspect case definition	Meet MOH's suspect case definition
2.	Enhanced Surveillance for Community-Acq. Pneumonia (inpat. & outpatient)	Pneumonia surveillance (inpatient or outpatient)	Other clinical, e.g. fever, ARI, atypical symptoms
3.	ARI/ Other Conditions fulfilling KKH At-risk criteria (includes travel history/ pre-surgery/ etc)	Other clinical conditions, e.g. fever, ARI, atypical symptoms	Surveillance of confirmed case
4.	N/A	Surveillance of confirmed case	Other reasons not clinically indicated, e.g. patient's request (chargeable)
5.	Pats. not fulfilling MOH criteria or KKH at-risk criteria (chargeable)	Other reasons not clinically indicated (chargeable)	N/A

- Patient Categories evolved during the pandemic
- MOH = Ministry of Health; ARI = Acute Respiratory Infection; KKH = KK Women's and Children's Hospital

Case of Paucisymptomatic Child

- 6 mo/old infant admitted for testing & isolation b/c mother was infected
- Asymptomatic except mild fever 38.5°C
- Low Ct value 13.7
 ≈ 6 billion virus copies per NP swab
- NP samples pos. up to day 16
- Child likely highly infectious

A Well Infant With Coronavirus Disease 2019 With High Viral Load

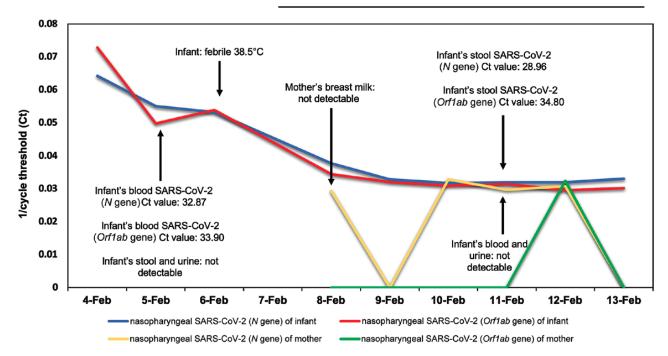
Kai-qian Kam,^{1,©} Chee Fu Yung,¹ Lin Cui,² Raymond Tzer Pin Lin,² Tze Minn Mak,² Matthias Maiwald,³ Jiahui Li,¹ Chia Yin Chong,¹ Karen Nadua,¹ Natalie Woon Hui Tan,¹ and Koh Cheng Thoon¹

¹Infectious Disease Service, Department of Pediatrics, KK Women's and Children's Hospital, Singapore, Singapore, ²National Public Health Laboratory, National Centre for Infectious Diseases, Singapore, Singapore, and ³Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital, Singapore, Singapore

A well 6-month-old infant with coronavirus disease 2019 (COVID-19) had persistently positive nasopharyngeal swabs up to day 16 of admission. This case highlights the difficulties in establishing the true incidence of COVID-19, as asymptomatic individuals can excrete the virus. These patients may play important roles in human-to-human transmission in the community.

Keywords. COVID-19; SARS-CoV-2; infant; 2019 novel Clin. Infect. Dis. Online Ahead of Print.

 Our lab's lowest recorded Ct value:
 9.7 (in an adult)
 ≈ 100 billion virus copies per NP swab



Environment of Infected Child

- 6 mo/old infant with high viral load
- Paucisymptomatic
- In isolation room
- Sampled & tested: Bed, Cot Rail, Table (+) HCW's face shield, N95 mask, gown (-)
- Infected but well infants with no resp. symptoms can easily contaminate environment
- Child likely highly infectious

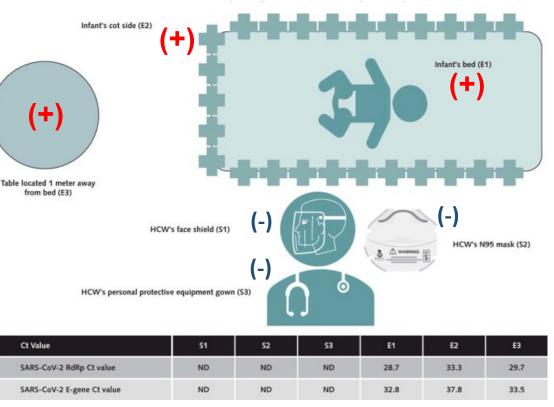
Yung CF, Kam KQ, Wong MSY, Maiwald M, Tan YK, Tan BH, Thoon KC. Ann Intern Med. 2020 Apr 1; M20-0942. Online ahead of print.

Annals of Internal Medicine

OBSERVATION: BRIEF RESEARCH REPORT

Environment and Personal Protective Equipment Tests for SARS-CoV-2 in the Isolation Room of an Infant With Infection

Background: Severe acute respiratory syndromecoronavirus 2 (SARS-CoV-2) is suspected to be spread from an infected person to a susceptible host primarily via droplet and possibly direct contact (1). The roles of transmission by indirect contact (fomites) or by long-range airborne route are uncertain. Currently, there are no data on the risk for transmission from infants or young children with coronavirus disease 2019 (COVID-19) who may be asymptomatic or pauci-symptomatic.



Clinical Utility of Buccal Swabs for Severe Acute Respiratory Syndrome Coronavirus 2 Detection in Coronavirus Disease 2019–Infected Children

Kai-qian Kam,^{13,5,0} Chee Fu Yung,^{13,4} Matthias Maiwald,^{23,6} Chia Yin Chong,^{13,4,5} Han Yang Soong,² Liat Hui Loo,² Natalie Woon Hui Tan,^{13,4,5} Jiahui Li,^{13,5} Karen Donceras Nadua,^{13,5} and Koh Cheng Thoon^{13,4,5}

¹Infectious Disease Service, Department of Pediatrics, KK Women's and Children's Hospital, Singapore; ²Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital, Singapore; ²Duke-NUS Medical School, Singapore; ⁴Lee Kong Chian School of Medicine, Imperial College London, Nanyang Technological University, Singapore; ⁵Yong Loo Lin School of Medicine, National University of Singapore, Singapore; and ⁶Department of Microbiology and Immunology, National University of Singapore, Singapore

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detected from at least 1 buccal specimen in 9 of 11 coronavirus disease 2019 (COVID-19)–infected children (81.8%). Viral loads in buccal specimens were substantially lower than those in nasopharyngeal specimens. Buccal swabs are not good as COVID-19 screening specimens in children.

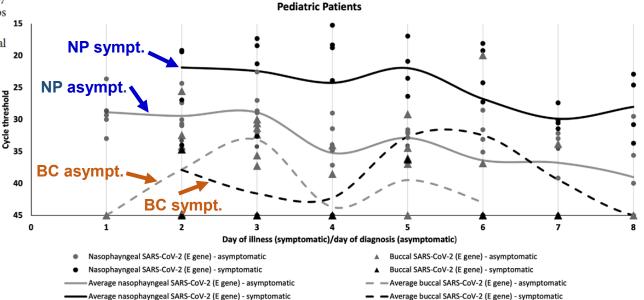
Keywords. COVID-19; buccal; saliva; SARS-CoV-2; viral load.

J Pediatric Infect Dis Soc. 2020 May 28; piaa068. Online ahead of print.

Buccal swabs vs. NP swabs

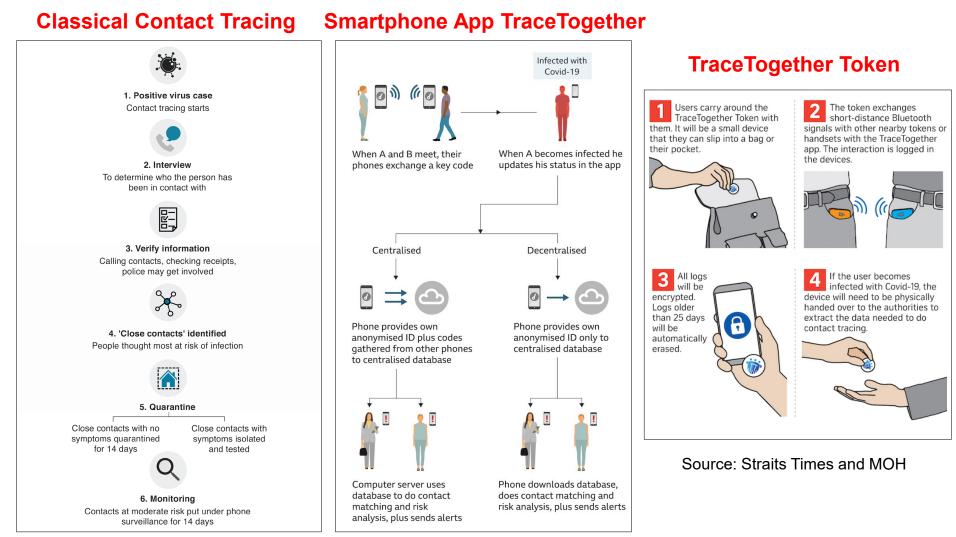
- 11 infected children; 6 asympt., 5 symptomatic
- Symptomatic all had mild illness
- Buccal swabs are less invasive, easier
- Buccal & NP collected same day, same session
- 2/11 children had neg. buccal swabs (82% sens.)
- Buccal swab Ct values avg. 10.7 higher than NP (P<0.001; factor 1000) --> not a good specimen

Nasopharyngeal and Buccal SARS-CoV-2 Cycle Threshold Trend for Asymptomatic and Symptomatic



Public Health Measures

Singapore has been exemplary in contact tracing, isolating and identifying clusters



Source: BBC News

Source: BBC and MOH

Coronavirus Jokes

Um nicht mit Coronavirus in Verbindung gebracht zu werden: Mexikanische Biermarke in "Ebola" umbenannt VON DER POSTILLON

In order not to be associated with Coronavirus, Mexican beer brand renamed in "Ebola"

22. JANUAR 2020





Source: Tagesschau.de









A Turn of Events

- Until late March, SG did extremely well
- Cases were under control with aggressive isolation and contact tracing efforts
- Shops, schools were open, public life unaffected

Then, cases emerged at Foreign-Worker Dormitories (from 30 March)

- SG has ~300,000 low-income foreign workers, mostly in construction (e.g. India, Bangladesh, Myanmar)
- Housed in crammed conditions, e.g. 15-20 people in one bedroom
- Virus got foothold, spread like 'wildfire'
- All dormitories quarantined (Armed Forces involved)
- Comprehensive testing and relocation strategy to Government Quarantine Facilities (GQFs)

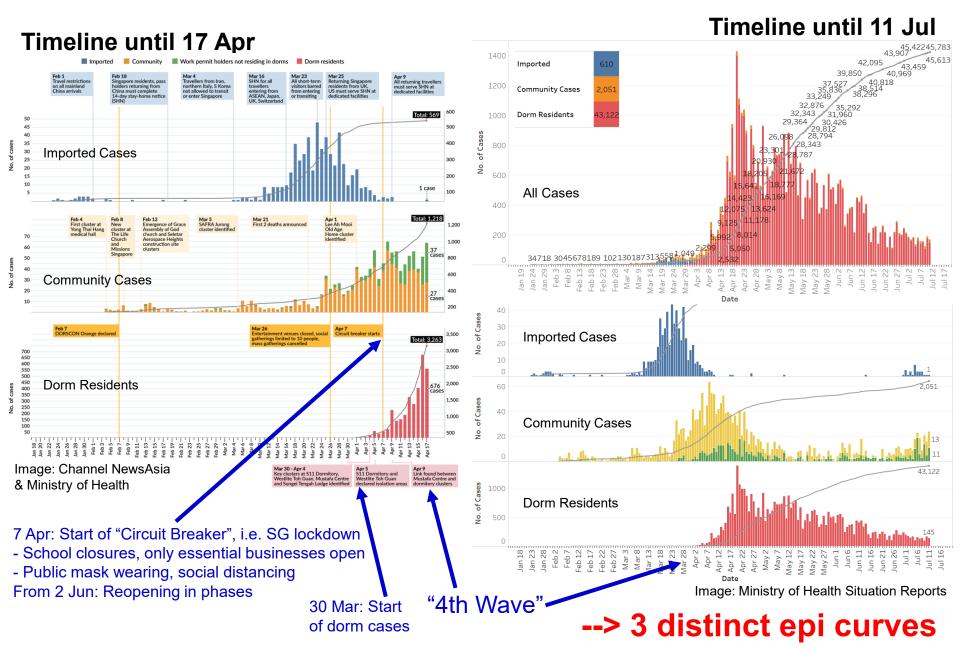






Photos: Channel NewsAsia from AFP, Reuters, MINDEF

Subsequent Timeline in SG

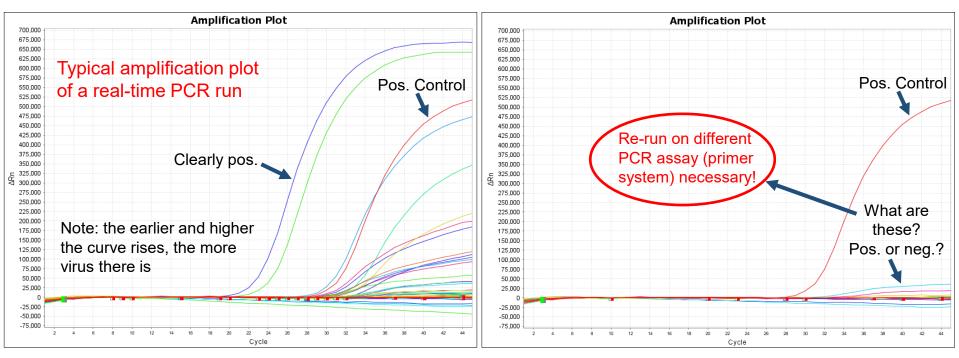


Coping with Increased Testing

- To cope with increasing test demand, MOH set up Testing Operations Centre (TOC)
- TOC would allocate cases from dorms and Government Quarantine Facilities (GQFs) across all public and private labs

Testing in high-prevalence settings is difficult!

- Many samples with low-level or borderline amplification curves (stages of infection)
- Extensive re-testing with confirmatory assays is necessary!



Photos: M. Maiwald

Measures for the General Public

Before April 2020

- Relatively normal situation; public life not much affected
- Some panic-buying after DORSCON Orange 7 Feb; quickly subsided

From 7 Apr: "Circuit Breaker"

- School closures, only essential businesses open, public mask wearing (cloth or surg.)
- Only takeout at restaurants, gatherings restricted (only families), no gyms
- No religious gatherings, travel restrictions, working from home
- Public accepted these measures well, but economic conseq. & hardship
- Access control/recording in public places & shopping centers

Reopening in Phases from 2 June

• "Safe Reopening" (phase 1), "Safe Transition" (phase 2) and "Safe Nation" (phase 3)



Conclusions and Outlook

- Singapore generally managed the crisis very well benefitted from preparedness
- As of 2 July, 44,000 cases, 26 deaths remarkably low death rate
- Outbreak in the foreign workers' dormitories constituted a lapse of attention to this vulnerable part of the population resulted in rapid spread; majority of SG's cases

On the Ground

- Work on the ground was challenging
- So far no major PPE shortages stockpiled before the pandemic
- Temporary lab reagent shortages overcome with centralized procurement & alternatives

Capacity Building & Maintaining

- Completion of NCID (long planned) in 2019 was fortuitous
- Our lab was underresourced & understaffed improved & rec'd help from hospital leaders
- Capability of Lab-Developed Tests (LDTs) "saved" us in the lab
- Maintaining clinical & lab capacity, staffing & skill sets essential for outbreak response

Future

• Unclear how pandemic will progress – unlikely relief before vaccine (2021?) availability