SARS “eradication”

Leo Poon
Overview:

• History
• How did we contain SARS
• Look forward
SARS: the first pandemic of the 21st century

http://www.nature.com/nature/focus/sars/map.html

5 July
– SARS was contained worldwide
Economic Impact of selected infectious disease outbreaks

Figures are estimates and are presented as relative size. Based upon bio-era, World Bank, and UNDP data. Chart updated by EcoHealth Alliance.
SARS outbreak - emerged from southern China
Official index case: Nov 2002

6 Feb 2003: 218 cases in this province
Rumours of SARS in early 2003

Fear factor!

Fujian province in February 11, 2003

Sale price of a bottle of vinegar:
10 yuan to 1000 yuan

H5N1 pandemic scare:
2 imported H5N1 cases in Hong Kong
The Hong Kong outbreak

21 Feb 2003  AA: Index case
Guangzhou

AA (index case)
SARS

- 11th March 03:
  - 20 HCW in Hanoi
  - 23 HCW in PWH, Hong Kong
- 12th March 03: WHO Global alert
- 14th March 03: Canada
- 15th March 03: Singapore, Germany
- 15th March 03: WHO Travel advisory
- 17th March 03: WHO Network of SARS Labs
A Novel coronavirus is associated with SARS

Coronavirus as a possible cause of severe acute respiratory syndrome

J S M Peiris, S T Lai, L L M Poon, Y Guan, L Y C Yam, W Lim, J Nicholls, W K S Yee, W W Yan, M T Cheung, V C C Cheng, K H Chan, D N C Tsang, R W H Yung, T K Ng, K Y Yuen, and members of the SARS study group*

Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome

Christian Drosten, M.D., Stephan Günther, M.D., Wolfgang Preiser, M.D., Sylvie van der Werf, Ph.D., Hans-Reinhard Brodt, M.D., Stephan Becker, Ph.D., Holger Rabenau, Ph.D., Marcus Panning, M.D., Larissa Kolesnikova, Ph.D., Ron A.M. Fouchier, Ph.D., Annemarie Berger, Ph.D., Ana-Maria Burguière, Ph.D., Jindrich Cinatl, Ph.D., Markus Eickmann, Ph.D., Nicolas Escrivou, Ph.D., Klaus Grywna, M.Sc., Stefanie Kramme, M.D., Jean-Claude Manuguerra, Ph.D., Stefanie Müller, M.Sc., Volker Rickerts, M.D., Martin Stürmer, Ph.D., Simon Vieth, Hans-Dieter Klenk, M.D., Albert D.M.E. Osterhaus, Ph.D., Herbert Schmitz, M.D., and Hans Wilhelm Doerr, M.D.

A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome

Thomas G. Ksiazek, D.V.M., Ph.D., Dean Erdman, Dr. P.H., Cynthia Goldsmith, M.S., Sherif R. Zaki, M.D., Ph.D., Teresa Peret, Ph.D., Shannon Emery, Suxiang Tong, Ph.D., Carlo Urbani, M.D.,* James A. Comer, Ph.D., M.P.H., Wilina Lim, Pierre E. Rollin, M.D., Scott Dowell, M.D., M.P.H., Ai-Ee Ling, M.D., Charles Humphrey, Ph.D., Wun-Ju Shieh, M.D., Jeannette Guarnier, M.D., Christopher D. Paddock, M.D., Paul Rota, Ph.D., Barry Fields, Ph.D., Joseph DeRisi, Ph.D., Jyh-Yuan Yang, Ph.D., Nancy Cox, Ph.D., James Hughes, M.D., James W. LeDuc, Ph.D., William Bellini, Ph.D., Larry J. Anderson, M.D., and the SARS Working Group†
Koch's postulates fulfilled for SARS coronavirus

- The microbe must be present in every case of the disease
- The microbe must be isolated from the diseased host and grown in pure culture
- The disease must be reproduced when the microbe is introduced into a non-disease susceptible host (animal)
- The microbe must be recovered from an experimentally-infected host

Newly discovered coronavirus as the primary cause of SARS!

How did we stop the SARS epidemic?

a) Use of highly non-specific case definitions

As more information has become available, WHO-recommended SARS case definitions have been revised as follows:

**Suspect Case**

A person presenting after 1 February 2003 with history of:

- high fever (>38°C)

AND

- one or more respiratory symptoms including cough, shortness of breath, difficulty breathing
- close contact* with a person who has been diagnosed with SARS
- recent history of travel to areas reporting cases of SARS

**Probable Case**

A suspect case with chest x-ray findings of pneumonia or Respiratory Distress Syndrome

OR

A person with an unexplained respiratory illness resulting in death, with an autopsy examination demonstrating the pathology of Respiratory Distress Syndrome without an identifiable cause.

Schrag et al., EID 2004
B) Strict Infectious disease control

SARS outbreak in hospital settings

Hong Kong


- Prompt guideline on management of severe acute respiratory syndrome (SARS)
  - PPE
  - Patient management
  - etc

Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS)

W H Seto, D Tsang, R W H Yung, T Y Ching, T K Ng, M Ho, L M Ho, J S M Peiris, and Advisors of Expert SARS group of Hospital Authority*

*Members listed at end of report

Goh et al., Ann Acad Med Singapore 2006

Lancet 2003
C) Aggressive contact tracing and quarantine policy

Isolation

School closure

Cumulative numbers of persons under quarantine during the SARS outbreak, Taiwan, 2003, and the quarantined SARS patients classified by their status*

<table>
<thead>
<tr>
<th>Level and reason for quarantine</th>
<th>No. quarantined persons</th>
<th>No. quarantined officially confirmed SARS-CoV case-patients</th>
<th>No. quarantined laboratory-confirmed, antibody-positive SARS case-patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level A</td>
<td>7,921</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Family members</td>
<td>7,921</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Classmates and teachers</td>
<td>16,564</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Healthcare workers</td>
<td>2,409</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Others†</td>
<td>19,224</td>
<td>6‡</td>
<td>1</td>
</tr>
<tr>
<td>All others§</td>
<td>9,514</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>55,632</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Level B</td>
<td>95,828</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>151,460</td>
<td>17</td>
<td>7</td>
</tr>
</tbody>
</table>

50% drop in population contact rates
50% reduction in hospital transmission
70% reduction in total transmission

D) Early travel advisory and intensive updates from WHO

Emergencies preparedness, response

World Health Organization issues emergency travel advisory
15 March 2003

Figure 3. Number of arriving and departing air passengers in Hong Kong (1 March 2003 to 31 August 2003)

23 May:
HK was removed from the list

Situation Updates - SARS

96 updates within 4 months

Numerous press conferences for general public and teleconferences for expert group meetings

Transparency and accountability!
E) We were lucky in some sense.....

i) SARS patients were not highly infectious in the first week of disease onset.

ii) SARS-CoV is not highly transmissible

https://www.quora.com/What-is-the-most-contagious-disease-on-Earth
F) Managed to find the animal source and prompt control measures

SARS is emerged from animals

May 2003: Banning of selling masked palm civets in China
Aug 2003: The ban was relaxed
Jan 2004: New human cases, leading to a complete ban of selling masked palm civets
4 laboratory infections in 2003-2004, one led to a human-to-human transmission.
Will SARS come back?

Chinese Horseshoe bats as the nature reservoir of SARS-like coronaviruses

All precursor viruses for SARS-CoV can be found in the same cave at Yunnan (Hu et al., PLoS Path 2017)

SARS-CoV might be generated by recombination events:

SARS-CoV in civet

Genome nucleotide position

Evolution
Explosion on coronaviruses of bat origins since 2003

2003
- Murine hepatitis virus strain NL63
- Murine hepatitis virus
- Murine hepatitis virus strain 2
- Murine hepatitis virus strain (H51)
- Bovine coronavirus
- Bovine coronavirus
- SARS virus, Hong Kong isolate
- Near related 4634 strain
- Near related 4634 strain (Beaudette C67)
- Transmissible gastroenteritis virus
- Human coronavirus 229E
- Porcine epidemic diarrhea virus

2005
- Accession number
- Group
- HCoV-229E
- HCoV-NL63
- Bat-CoV
- PEDV
- Canine CoV
- FIPV
- TGEV
- IBV
- SARS-CoV
- HCoV-OC43
- MHV

2010
- Alphacoronaviruses
- Betacoronaviruses
- BCoV (Bovine)
- DC42 (Human)
- MHV (Mousae)
- HKU1 (Human)
- SARS-CoV (Human)


Studies from other groups at different geographical regions

Lancet 2003
Science 2003
J Virol 2005
J Virol 2006
J Gen Virol 2006
J Gen Virol 2008
Emergence of MERS-CoV

MERS-CoV

Unknown bat host

Another intermediate host?

• ~2200 confirmed cases;
• ~800 deaths;
• Several hospital outbreaks: 1 single introduction

181 confirmed cases

Camel is an important reservoir for MERS-CoV
Chan and Poon mBio, 2013

Chu et al., EID 2014
Hemida et al., EID 2014
Chu et al., Eurosurveillance 2015
Chu et al., PNAS 2018
Fatal swine acute diarrhoea syndrome caused by an HKU2–related coronavirus of bat origin

Peng Zhou1,12, Hang Fan2,12, Tian Lan3,4,12, Xing–Lou Yang1, Wei–Feng Shi5, Wei Zhang1, Yan Zhu1, Ya–Wei Zhang2, Qing–Mei Xie3,4, Shailendra Mani6, Xiao–Shuang Zheng1, Bei Li1, Jin–Man Li2, Hua Guo1, Guang–Qian Pei2, Xiao–Ping An2, Jun–Wei Chen3,4, Ling Zhou3,4, Kai–Jie Mai3,4, Zi–Xian Wu3,4, Di Li3,4, Danielle E. Anderson6, Li–Biao Zhang7, Shi–Yue Li8, Zhi–Qiang Mi2, Tong–Tong He2, Peng Cong9, Peng–Ju Guo9, Ren Huang9, Yun Luo1, Xiang–Ling Liu1, Jing Chen1, Yong Huang2, Qiang Sun7, Xiang–Li–Lan Zhang2, Yuan–Yuan Wang2, Shao–Zhen Xing2, Yan–Shan Chen3,4, Yuan Sun3,4, Juan Li3, Peter Daszak10*, Lin–Fa Wang6*, Zheng–Li Shi1*, Yi–Gang Tong7,11*, & Jing–Yun Ma3,4*

Nature 2018

- An outbreak killed 24,693 piglets in four farms at Guangdong
- The virus is genetically similar to HKU2–like bat coronaviruses
- A highly similar virus can also be detected in bats in Guangdong Province

Implications:
- Food security?
- Trading?
- Facility host switching?
WHO R&D Blueprint

List of Blueprint priority diseases

- Crimean-Congo haemorrhagic fever (CCHF)
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipavirus diseases
- Rift Valley fever (RVF)
- Zika
- Disease X
Lesson learned by Hong Kong

- Preparedness Plan
- Early Case Detection, Surveillance, and Notification
- Infection Control Preparedness
- Laboratory Preparedness
- Clinical Management Preparedness
- Development of Surge Capacity
- Effective Communication Preparedness Plans
- Interdisciplinary/Multidisciplinary Approach

H5N1, 2009 H1N1 pandemic and H7N9
Conclusion

• SARS in 2003 was caused by a zoonotic virus;
• Aggressive measures were used to contain SARS;
• There was a huge investment in pandemic preparedness in the SARS aftermath;
• The precursor viruses of SARS-CoV still circulate in bats;
• CoVs in bats and other animals continuous pose threats to human (health and food security);
• The current MERS outbreak highlights the strengths and weaknesses of preparedness plan.
WHO Network of Laboratories

SARS

- Federal Laboratories for Health Canada, Winnipeg, Canada
- Health Canada, Ottawa, Canada
- Public Health Laboratory Centre, Hongkong SAR China
- Prince of Wales Hospital, Hongkong SAR China
- The University of Hongkong, Hong Kong SAR, China
- Institut Pasteur, Paris, France
- Bernhard-Nocht Institute, Hamburg and Johann Wolfgang Goethe Universitat, Frankfurt, Germany
- National Institute of Infectious Disease, Tokyo, Japan
- Erasmus MC, Rotterdam, The Netherlands
- Singapore General Hospital, Singapore
- Central Public Health Laboratory, London, UK
- Centers for Disease Control & Prevention, Atlanta, USA

AFDC, Hong Kong
The University of Hong Kong: School of Public Health: Malik Peiris, Daniel Chu, Mahen Perera, M Chan, Chris Mok, Renee Chan, Eric Lau, Y Guan, John Nicholls, P Wang
National Research Centre, Giza, Egypt: G Kayali, MA Ali
King Faisal University, KSA: MG Hemida, A Al Naeem
King Fahad Medical City, KSA: S Fagbo, A Hakawi
Seoul National University College of Medicine, Myoung-don Oh, SW Park, WB Park, PG Choe, SJ Choi, JY Chun, HS Oh, KH Song et al
Guangzhou Medical University, 1st Affiliated Hospital: NS Zhong, Ling Chen et al.
CIRAD: Eve Miguel, V Chevalier, F Roger
Institut Pasteur: Maria van Kerkhove
Abu Dhabi Food Control Authority: Z Al Hammadi, YM Yassir, SS Al Muhairi
University of Iowa: S Perlman, J Zhao
Transboundary State Central Veterinary Laboratory, Mongolia: B Damdinjav, B Khisgee
University of Queensland: Rafat Al Jassim

R Fouchier, B Haagmans, M Koopmans (Erasmus MC), C Drosten, M Muller (U Bonn), Aron Hall (US CDC); Bernard Faye