First steps in pandemic preparedness research

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Preparing for the next pandemic

• Likely to be caused by a virus, zoonotic origin

• Respiratory, enteric, vector-borne transmission (this sequence of priorities)

• Clear scientific evidence for respiratory pandemics in the past by viruses other than influenza
Disease ecology perspective: two stages of viral emergence

Human adaptation

Sporadic acquisition
Epidemology perspective: chain of emergence

- Animal reservoir
- Human case
- Limited outbreak
- Pandemic
Chain of emergence

Preparedness (research)
- Animal reservoir
- Human case
- Limited outbreak
- Pandemic

Response
How basic research disciplines spell „preparedness“

Virology
• Viral diversity in reservoirs: genetic, functional

Ecology
• Intermediate hosts
  Frequency of spillover
  Conditions favoring spillover

Evolutionary biology
• Virus changes in early transmission chains
  E.g., adaptive vs neutral evolution
How outbreaks are detected

• Symptoms: case definition
• Number and distribution of cases
• Growth rate of case detection
• Transmission pattern
  • Human-to-human transmission chains
  • Not human-to-human (another source)

There is a disconnect between basic preparedness research and outbreak detection. Improving the latter is mainly a datascience challenge.
Most urgent gaps of knowledge when an epidemic/pandemic disease seems to emerge

• Acquisition: route, infectious dose
• Shedding: peak infectivity vs symptoms, end of infectivity
• Immunity: duration and correlates of disease protection, duration and correlates of transmission shielding

All of these questions of natural history, in addition to simple case detection, hinge on the availability of laboratory tests.
Testing: R+D timeline

Immediate
• RT-PCR, viral load

Early
• Antibody tests – neutralization tests – neutralization test surrogates

Late
• Antigen tests (lab-based and point of care / lat. flow devices)
• Cellular immunity surrogates
Fortunately, the lab test for which there is most urgent need has the shortest R+D turnaround time and takes the most benefit from basic research:

PCR detection
Biodiversity research: studies on coronaviruses in bats

Drexler et al., AVR, 2013
Biodiversity research enables virus recognition

Before SARS

10 years after SARS

Drexler et al., AVR 2014
Biodiversity research enables virus recognition

Before SARS

10 years after SARS

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Biodiversity research enables virus recognition

Before SARS

Gammapicornavirus

HCoV-OC43
BCoV
MHV

IBV

Cavally virus

FIPV
TGEV
PEDV

HCoV-229E

1
1
0.1

10 years after SARS

Gammacoronavirus

Deltacoronavirus

SARS

Cavally virus

Drexler et al., AVR 2014
Biodiversity research enables virus recognition

Before SARS

10 years after SARS

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Biodiversity research enables virus recognition

Before SARS

10 years after SARS

Drexler et al., AVR 2014
From supplements to Corman et al, Eurosurv 2020
Wuhan pneumonia cluster, 2019-20
A timeline, dates based on local reports

31 Dec
- Wuhan Municipal Health Commission (WMHC)
  - Medical experts arrived to examine "SARS" outbreak
  - 27 viral pneumonia cases isolated, 7 critically ill
  - No human-to-human (h2h) transmission
  - All believed to have visited Huanan Seafood Wholesale Market
  - Market also sells non-aquatic animals including birds, snakes, frogs, rabbits

03 Jan
- HK Govt to provide daily updates
- WMHC update
  - 44 cases, 11 critical
  - No h2h

1st protocol version
@WHO

08-9 Jan
- A novel coronavirus detected 07 Jan
  - 1 genome
  - 15 cases
  - Xu Jiajing via CCTV

05 Jan
- WMHC update
  - 59 cases, 7 critical, 163 close contacts
  - No h2h
  - Dec 12-29 onset
  - MERS-CoV, SARS-CoV, flu, ADV excluded

10 Jan
- 1st genome released from Prof Y-Z Zhang-led consortium Fudan University via virological.org

16 Jan
- Japan Ministry of Health confirms 1st case
  - 30s, male, Japan resident, pneumonia
  - Onset 03JAN
  - No markets but close contact of case in Wuhan

2nd protocol version
@WHO

Full paper
@Eurosurveillance

11 Jan
- WMHC update
  - Cases adjusted from 59 to 41, 739 contacts
  - 7 severe, 2 discharged
  - 1 death; 61-yr male with comorbidities
  - 5 genomes released to GISAID

13 Jan
- Thai Ministry of Public Health (TMPH) confirms 1st case
  - 61-yr female, Chinese citizen, 08JAN, pneumonia
  - Didn't visit Huanan market, Chinese citizen

15 Jan
- WMHC confirms 2nd death
  - 69-yr male, Chinese citizen

16 Jan
- TMPH confirms 2nd distinct case
  - 30s, male, Japan resident, pneumonia
  - Onset 03JAN
  - No markets but close contact of case in Wuhan

17 Jan
- TMPH confirms 2nd distinct case
  - 74-yr female, Chinese citizen, pneumonia

20 Jan
- S. Korea CDC confirms 1st case
  - 35-yr female, Chinese citizen, pneumonia
  - Onset 07JAN
  - No markets but close contact of case in Wuhan
  - Beijing confirms first cases
  - Guangdong confirms 1st case
  - 14 nosocomial cases
  - Zhong Nanshan

21 Jan
- Taiwan confirms 1st case
- United States confirms 1st case

22 Jan
- Hong Kong confirms 1st cases
- Macau confirms 1st case

23 Jan
- Wuhan city quarantined
- Huanggang city quarantined
- Ezhou city quarantined

Figure: Ian Mackay

Prepared by Ian M. Mackay, PhD
virologydownunder.com
Dates and information based on WMHC and media reports; not always verified by official sources
Version 7
Last updated 23JAN2019 AEST
Provision of essential clinical validation data along with protocol

<table>
<thead>
<tr>
<th>Clinical samples with known viruses</th>
<th>Clinical samplesa</th>
<th>Virus isolatesb</th>
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<tbody>
<tr>
<td>HCoV-HKU1</td>
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<td>1c</td>
</tr>
<tr>
<td>HCoV-OC43</td>
<td>16</td>
<td>2d</td>
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<tr>
<td>HCoV-NL63</td>
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<td>HCoV-229E</td>
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<td>MERS-CoV</td>
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<td>1g</td>
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<td>Influenza A(H3N2)</td>
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<td>Influenza A (untyped)</td>
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<td>Influenza A(H5N1)</td>
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<td>Influenza A(H7N9)</td>
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<td>Influenza B (Victoria or Yamagata)</td>
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<td>Rhinovirus/enterovirus</td>
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<tr>
<td>Respiratory syncytial virus (A/B)</td>
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<td>Parainfluenza 1 virus</td>
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<td>Parainfluenza 2 virus</td>
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<td>Human metapneumovirus</td>
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<td>Adenovirus</td>
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<tr>
<td>Human bocavirus</td>
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<td><em>Legionella</em> spp.</td>
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<td><em>Mycoplasma</em> spp.</td>
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<tr>
<td><strong>Total clinical samples</strong></td>
<td><strong>297</strong></td>
<td><strong>NA</strong></td>
</tr>
</tbody>
</table>

Corman et al, Eurosurg 2020
First steps toward clinical virology response

- Know, use, and monitor viral diversity for assay design
- Be prepared for clinical evaluation of assay performance:
  - Biobanked samples, standardized assay design procedures, proficient team of medical virologists and molecular biologists
- Use industry distribution channels in addition to provision of unrestricted access to protocols through qualified resources
- Rapidly publish protocols with peer review qualification to which diagnostic laboratories can refer in QA procedures