2012/13 Novel Coronavirus Case Study

Ontario’s Approach to Preparation, Management and Response

February 19th, 2013
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Shelly Bolotin MSc PhD MScPH
Outline of Presentation

• Intro to coronaviruses
• Initial epidemiology of novel Coronavirus (nCoV)
• Ontario response/Important Health Notices (IHN)
• Public Health Ontario Labs response
• Final observations
Coronavirus Virology

Large, enveloped, positive strand, RNA viruses
Pleomorphic, roughly spherical, 80 to 160 nm in size

Spike glycoprotein (S)
Envelope small membrane protein (E)
Membrane protein (M)
Hemagglutinin-esterase (HE)
Nucleoprotein (N)
Genomic RNA
Overview of coronaviruses

- 4 genetic groups
  - alpha: Human CoVs 229E and NL63 and animal CoVs.
  - beta: Human CoV OC43, HKU1, SARS
  - gamma: avian CoVs, Baluga whale CoV.
  - delta: animal coronaviruses.

SARS virions in tissue culture
Human coronaviruses: 229E, NL63, OC43, HKU1

- Frequent cause of “common cold” and also associated with LRTIs.
- Mostly transmitted by respiratory tract secretions.
- Incubation period 2-5 days.
- Mostly infectious in early days of illness.
Human Coronaviruses: 229E, NL63, OC43, HKU1

• Distributed worldwide.

• Outbreaks in winter in temperate climates.

• Laboratory detection:
  • Molecular assays (clinical)
  • Grown in specialized cell lines, serology (research)

• Treatment – no proven antiviral therapy.
Commercial molecular detection kits

• Luminex RVP - Detects 20 different respiratory targets

• Seeplex® RV15 ACE
  • Influenza A/B virus, RSV A, RSVB, parainfluenza virus 1-4, adenovirus
  • Coronavirus 229E/NL63, OC43, rhinovirus, enterovirus, metapneumovirus
  • Bocavirus
Discovery of the novel coronavirus

- Jedda, Saudi Arabia, June 2012: microbiologist (Dr Zaki) isolated and cultured a virus from a man who had died of severe pneumonia and acute renal failure.
- Zaki contacted Ron Fouchier, Erasmus Medical Center (EMC) in Rotterdam, the Netherlands.
  - Advised he test for a coronavirus, which came up positive.
- Zaki mailed a sample of the virus to Fouchier
  - Fouchier sequenced it and found that it was a previously unknown human coronavirus, closely related to one from bats.
- On 20 September, 2012: Zaki announced the discovery on ProMED-mail.
- The virus has since been provisionally named human betacoronavirus 2c EMC (hCoV-EMC), after the Rotterdam centre.
- Researchers wishing to acquire samples of its virus are now required to first sign an EMC material-transfer agreement (MTA).
HCoV-EMC is in lineage C of beta coronavirus, similar to bat coronaviruses.
Genomic Characterization of a Newly Discovered Coronavirus Associated with Acute Respiratory Distress Syndrome in Humans

Sander van Boheemen,a Miranda de Graaf,a Chris Lauber,b Theo M. Bestebroer,a V. Stalin Raj,a Ali Moh Zaki,c Albert D. M. E. Osterhaus,a Bart L. Haagmans,a Alexander E. Gorbalenya,d,e Eric J. Snijder,b and Ron A. M. Fouchiera

Viroscience Lab, Erasmus MC, Rotterdam, The Netherlands; Molecular Virology Laboratory, Department of Medical Microbiology, Center of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands; Dr. Soltman Fakeeh Hospital, Jeddah, Saudi Arabia; and Faculty of Bioengineering and Bioinformatics, Lomonosov Moscow State University, Moscow, Russia2

Whole genome sequence published November 20, 2012

• Observed some differences to the coronavirus that cause the 2002/2003 SARS outbreak.

• Blocking the SARS coronavirus receptor, ACE2, inhibits growth of SARS virus, but not novel coronavirus.
  • This suggests it uses another, as yet unidentified, receptor.

• Observed that virus can grow well in several different animal cell types including bat, swine, and human cells.
  • This feature may allow it to spread across different animal hosts.
Human Betacoronavirus 2c EMC/2012–related Viruses in Bats, Ghana and Europe.

• Screened fecal specimens of 4,758 bats from Ghana and 272 bats from 4 European countries (Netherlands, Germany, Ukraine, Romania) for betacoronaviruses.

• Viruses related to the novel human betacoronavirus EMC/2012 detected in 46 (24.9%) of 185 *Nycteris* bats and 40 (14.7%) of 272 *Pipistrellus* bats.

• **Genetic relatedness indicated EMC/2012 originated from bats.**
24 April 2012: Amman, Jordan

- Cluster of 11 respiratory cases at a hospital, including eight health-care workers.
- Two of the cases died
- Laboratory tests were negative for coronavirus and several other respiratory viruses.

## Case Count

<table>
<thead>
<tr>
<th></th>
<th>Active/Recovered</th>
<th>Fatal</th>
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<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>-</td>
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</table>

13 June 2012: Jeddah, Saudi Arabia

- 60 YO male admitted to hospital with pneumonia + acute renal failure.
- Laboratory tests negative for several respiratory viruses.
- **24 June, 2012:** Patient dies.
- Post-mortem pan-coronavirus RT-PCR was positive.
- **15 September, 2012:** Saudi doctor announces isolation of new coronavirus (nCoV) on ProMED. Fouchier lab (Netherlands) follows with GenBank sequence.
- No evidence of transmission to HCW or other contacts.

### Case Count

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<tr>
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<th>Fatal</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
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</table>
23 September 2012: Doha, Qatar and London, UK

- UK Health Protection Agency confirms new case of nCoV.
- 49 YO male from Qatar, fell ill with pneumonia + renal failure on 3 September and transferred to London hospital for ECMO treatment.
- Travelled to Saudi Arabia >10 days prior to symptom onset, where he experienced mild respiratory illness that resolved.
- When back in Qatar, he spent time on a farm.
- No epidemiological link with first case. Possibly zoonotic?
- No evidence of transmission to HCW or other contacts.
- First WHO Global Alert and Response (GAR) issued.

Case Count

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

TOTAL 2
25 September, 2012: WHO interim case definition

Clinical criteria:
- A person with acute respiratory syndrome which may include fever and cough requiring hospitalization.
  AND
- With suspicion of lower airway involvement not explained by any other infection or any other aetiology.

Epidemiological criteria:
- Close contact within the last 10 days before onset of illness with a probable or confirmed case of novel coronavirus infection while the case-contact was ill.
  OR
- Travel to or residence in an area where infection with novel coronavirus has recently been reported or where transmission could have occurred (Qatar, Saudi Arabia).

Probable novel coronavirus case
- A person fitting the clinical definition AND epidemiological criteria above but no laboratory confirmation.

Confirmed novel coronavirus case
- A person with laboratory confirmation of infection with the novel coronavirus.

WHO releases case finding and management scheme on 29 September, 2012. No screening recommendations or travel advisories are released.

Important Health Notice
Information for Health Workers and Health Sector Employers
Novel Coronavirus
September 27, 2012 – Page 1 of 4

This information requires knowledgeable interpretation and is intended primarily for use by health workers and health sector employers in all settings.

Highlights
- Two confirmed cases of a novel coronavirus have occurred globally since June 2012: one has died and the other remains in severe condition.
- The cases are a resident of Saudi Arabia and a resident of Qatar who travelled to Saudi Arabia.
- As this virus has only been recently identified, there is limited information on clinical features, transmission and severity at this stage; it is not yet clear if the severe respiratory illness in the two cases is typical of this virus.
IHNs- What are they?

- Issued by MOHLTC in response to abnormal events needing rapid communication of Ministry direction/instruction
- Require “knowledgeable interpretation”
- Primarily for HCWs and their facilities/organizations:
  - Hospitals
  - LTCFs
  - Community-based health services
  - Public Health
  - Emergency services
  - Pharmacies
## IHNs - Frequency

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of IHNs</th>
<th>Topics</th>
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</thead>
<tbody>
<tr>
<td>2004</td>
<td>11</td>
<td>SARS updates, avian influenza (H7, H5N1)</td>
</tr>
<tr>
<td>2005</td>
<td>11</td>
<td>H5N1 update, rubella, LTCF FRI outbreak</td>
</tr>
<tr>
<td>2006</td>
<td>3</td>
<td>Botulism, enterics</td>
</tr>
<tr>
<td>2007</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>35</td>
<td>pH1N1, listeriosis, medical isotopes</td>
</tr>
<tr>
<td>2010</td>
<td>2</td>
<td>pH1N1 update, listeriosis</td>
</tr>
<tr>
<td>2011</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>3</td>
<td>nCoV, botulism</td>
</tr>
</tbody>
</table>
IHN Processes

• Science input → EMB review → CMOH approval → CIB approval/translation
• Almost 45,000 recipients, fax for 49% (74% for physicians)
• Length of IHN determines speed of transmission
• No formal evaluation of impact
• Can be cumbersome if science/response evolves rapidly
27 September, 2012: Initial nCoV IHN

- Addressed background, case definition, IP&C precautions, lab issues.
- Early in evolution of understanding of epi/clinical/lab/PH aspects
- Required travel to/residence in areas where cases detected
- Raised issue of end-October international travel to Hajj
- Recommended contact/droplet/airborne precautions (legacy of SARS), but missed emphasizing eye protection.
- Uncertainty re. person-person transmission, especially HCWs
- Timeliness concerns re. other provinces, especially BC
- Length of IHN and time needed to electronically distribute (% faxes)
Interim issues following IHN

• To correct or not? is it good enough?
• Expectations of all signatory countries to the International Health Regulations
• Planning for the Hajj, 3,500 Ontarians* estimated to attend Oct. 24-27, 2012
  • No PHAC/WHO travel restrictions
  • Importance of influenza vaccination
  • Concerns re. post-Hajj surveillance/case detection
• Initial conclusions re. no evidence of person-person transmission
• No change to Ontario IP&C recommendations (MOL)
• No post-Hajj cases even with heightened international vigilance

*Kamran Khan, Bio.Diaspora project- personal communication
4 October, 2012: Eurosurveillance publications

Rapid Communications

The United Kingdom public health response to an imported laboratory confirmed case of a novel coronavirus in September 2012

Rapid Communications

Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012
4 Nov 2012: Riyadh, Saudi Arabia

- No epidemiological links to other cases.
- No travel history, but patient visited a farm one week before symptom onset.
- Preliminary investigations of contacts revealed no secondary cases.
- Patient recovered.
Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia

23 Nov 2012: Riyadh, Saudi Arabia

- A new cluster of four cases of respiratory disease is identified as part of enhanced nCoV surveillance.
- Cases are epidemiologically linked (same family).
- Three of the cases in the cluster were laboratory confirmed. Of these, two died and one recovered.
- Fourth case in cluster recovered but laboratory tests (PCR) were negative.
23 Nov 2012: Doha, Qatar and Germany

- A second Qatari case is announced by Germany’s Robert Koch Institute (RKI).
- Case developed symptoms in October, and was transferred to Germany.
- nCoV detected in samples by both the HPA and RKI.
- Case recovered.

<table>
<thead>
<tr>
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<th></th>
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</thead>
<tbody>
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<tr>
<td>Fatal</td>
<td>3</td>
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<tr>
<td>TOTAL</td>
<td>7</td>
</tr>
</tbody>
</table>
30 November 2012: Amman, Jordan

- Samples from two fatal cases from April 2012 respiratory cluster in Jordan were retested for nCoV. Both samples were positive.
- WHO team sent to Jordan in November could not determine index case of cluster.
- WHO team noted that some cases in the cluster were mild. No cases in this cluster had renal failure.
- There was no history of travel or contact with animals among confirmed or probable cases.

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<td>Fatal</td>
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<td>TOTAL</td>
</tr>
</tbody>
</table>
28 November/3 December 2012: WHO Guidance

• Wider geographic area, persisted for at least 5 months
• These factors + uncertainties re. person-person transmission
• Test for nCoV (concurrent with other respiratory pathogen testing)
  • Clusters of SARI (especially requiring ICU care)
  • HCW with pneumonia caring for SARI of ?etiology
  • Removed travel to/residence in affected areas
  • Consider testing patients with unusual/severe course of disease
Issues with WHO guidance

• Not justified by the epidemiology → no cases in 2+ months with international surveillance

• PCR test characteristics with human specimens
  • Extremely low PPV even with excellent sensitivity/specificity
  • Based on expected range of prevalence of nCoV as cause of SARI

• Likely impacts of concurrent testing for nCoV + other etiologies
  • “Precautionary” implementation of full airborne precautions
  • ? Wise use of isolation and other IP&C resources

• Likely impacts of false positive results given likely PPV of nCoV testing
  • Implementation of full airborne precautions
  • Re-invoking of SARS post-traumatic stress disorder reactions
  • Media/political attention
  • Costs of clarifying true vs. false-positive results
17 December 2012: Second IHN

- IHN directed to web-based clinical guidance document
- Briefer document → shorter dissemination (3 hours)
- Ease of editing/updating guidance document
- Reinforced broader nCoV testing as per WHO recommendations
- Clarified IP&C measures
11 February, 2013: Manchester, UK
• A 60 YO male UK resident is diagnosed with a nCoV and A(H1N1)pdm09 co-infection.
• In the 10 days prior to symptom onset, the patient travelled to Saudi Arabia and Pakistan (developed symptoms while in Saudi Arabia).
• The patient is currently undergoing ECMO in ICU.
• 13 February, 2013: A family member of the Manchester case is hospitalized with nCoV. This case has no travel history outside the UK, suggesting human-to-human transmission. Patient died.
• 15 February, 2013: A third case of nCoV in this cluster is announced. The patient is a family member of the other two cases, has no travel history outside the UK and experienced mild illness. The case is quarantined at home.
• WHO risk assessment or advice with regards to screening, travel or trade remains unchanged.

Case Count
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<tr>
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<tbody>
<tr>
<td>Active/Recovered</td>
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<tr>
<td>Fatal</td>
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<tr>
<td>TOTAL</td>
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</table>
## Case counts to date

<table>
<thead>
<tr>
<th>Country</th>
<th>Active/Recovered</th>
<th>Died</th>
<th>Jordan</th>
<th>UK</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saudi Arabia</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Qatar</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Jordan</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6</strong></td>
<td><strong>6</strong></td>
<td><strong>6</strong></td>
<td><strong>6</strong></td>
<td><strong>6</strong></td>
</tr>
</tbody>
</table>
DETECTION OF A NOVEL HUMAN CORONAVIRUS BY REAL-TIME REVERSE-TRANSCRIPTION POLYMERASE CHAIN REACTION

V M Corman¹, I Eckerle¹, T Bleicker¹, A Zaki², O Landt³, M Eschbach-Bludau¹, S van Boheemen⁴, R Gopal⁵, M Ballhause³, T M Bestebroer⁴, D Muth¹, M A Müller¹, J F Drexler¹, M Zambon⁵, A D Osterhaus⁴, R M Fouchier⁴, C Drosten (drosten@virology-bonn.de)¹

1. Institute of Virology, University of Bonn Medical Centre, Bonn, Germany
2. Virology Laboratory, Dr Soliman Fakeeh Hospital, Jeddah
3. TibMolbiol, Berlin, Germany
4. Department of Virology and Virosciences, Erasmus Medical Centre, Rotterdam, The Netherlands
5. Health Protection Agency (HPA), London, United Kingdom

• Provisional genome sequence and isolate of hCoV-EMC were obtained from RM Fouchier on 24 September, after notification of second case (admitted in UK).

• Sequence used for assay design; virus was used for initial validation.
DETECTION OF A NOVEL HUMAN CORONAVIRUS BY REAL-TIME REVERSE-TRANSCRIPTION POLYMERASE CHAIN REACTION

- PCR contained 2 targets
  - Screen: A region upstream of envelope gene (UpE)
  - Confirmation: Open reading frame 1b (ORF 1b).

### Table 1
Results of sensitivity and specificity tests for hCoV-EMC assays, 2012*

<table>
<thead>
<tr>
<th>Experiment</th>
<th>upE assay</th>
<th>ORF1b assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection end point for cell culture-derived virus</td>
<td>0.01 TCID50/reaction</td>
<td>0.1 TCID50/reaction</td>
</tr>
<tr>
<td>Technical LOD</td>
<td>3.4 RNA copies/reaction</td>
<td>64 RNA copies/reaction</td>
</tr>
<tr>
<td></td>
<td>(95% CI: 2.5–6.9 copies/reaction)</td>
<td>(95% CI: 47–126 copies/reaction)</td>
</tr>
<tr>
<td>Cross-reactivity with hCoV-229E</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
</tr>
<tr>
<td></td>
<td>(3 x $10^6$ RNA copies/mL)</td>
<td>(4 x $10^6$ copies/mL)</td>
</tr>
<tr>
<td>Cross-reactivity with hCoV-NL63</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
</tr>
<tr>
<td></td>
<td>(4 x $10^6$ copies/mL)</td>
<td>(3 x $10^6$ copies/mL)</td>
</tr>
<tr>
<td>Cross-reactivity with hCoV-OC43</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
<td>No reactivity with virus containing $10^5$ PFU/mL</td>
</tr>
<tr>
<td></td>
<td>(3 x $10^6$ copies/mL)</td>
<td>(3 x $10^6$ copies/mL)</td>
</tr>
<tr>
<td>Cross-reactivity with SARS-CoV</td>
<td>No reactivity with virus containing $3 x 10^6$ PFU/mL</td>
<td>No reactivity with virus containing $3 x 10^6$ PFU/mL</td>
</tr>
<tr>
<td></td>
<td>(5 x $10^6$ copies/mL)</td>
<td>(5 x $10^6$ copies/mL)</td>
</tr>
</tbody>
</table>

CI: confidence interval; CoV: coronavirus; LOD: limit of detection; ORF: open reading frame; PFU: plaque forming units; TCID50: median tissue culture infective dose; upE: upstream of the E gene.
How could we validate the test in Ontario?

• Challenge – no actual virus to test against.

• Solution – use synthetic nucleic acid control material
  • Purchased control genetic material from Germany and validated in parallel with NML.
UpE Realtime PCR (10-fold serial dilutions)

LOD calculated base on original concentration of plasmid and number of bps of target

<table>
<thead>
<tr>
<th>ssRN A</th>
<th>UpE (copy/ul)</th>
<th>ORF1b (copy/ul)</th>
<th>NSP12 (copy/ul)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ssRN A</td>
<td>7.88</td>
<td>7.94</td>
<td>8.38</td>
</tr>
<tr>
<td>dsRN A</td>
<td>2.93</td>
<td>2.99</td>
<td>3.17</td>
</tr>
</tbody>
</table>

No cross reactivity with other human coronaviruses
ASSAYS FOR LABORATORY CONFIRMATION OF NOVEL HUMAN CORONAVIRUS (HCoV-EMC) INFECTIONS

V M Corman¹,2, M A Müller¹,2, U Costabel³, J Timm⁴, T Binger¹, B Meyer¹, P Kreher⁵, E Lattwein⁶, M Eschbach-Bludau¹, A Nitsche⁵, T Bleicker¹, O Landt⁵, B Schweiger³, J F Drexler¹, A D Osterhaus⁸, B L Haagmans⁸, U Dittmer⁴, F Bonin³, T Wolff⁵, C Drosten (drosten@virology-bonn.de)¹

Additional realtime-PCR targeting Orf1a target
Sequencing targets (RdRp, N)
Recommendations from WHO expert consultation on laboratory testing (28 November 2012)

- Use the \textit{upE} assay for first-line screening.
- Confirmatory testing with any validated RT-PCR assay for alternative targets: orf1a or orf1b)
- If real-time PCR positive, follow by sequencing of at least a portion of one viral gene and compare to Genbank sequences.
Who should be tested......

- 1. Patients under investigation

- A person with an acute respiratory infection, which may include history of fever or measured fever ($\geq 38^\circ C, 100.4^\circ F$) and cough

- AND

- Suspicion of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome (ARDS)), based on clinical or radiological evidence of consolidation.

- AND

- Residence in or history of travel to the Arabian Peninsula* or neighbouring countries within 10 days before onset of illness.

- AND

- Not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines. It is not necessary to wait for all test results for other pathogens before testing for novel coronavirus.
Who should be tested......

• 2. Ill contacts

Individuals with acute respiratory illness of any degree of severity who, within 10 days before onset of illness, were in close physical contact with a confirmed or probable case of novel coronavirus infection, while the case was ill.

• 3. Clusters

Any cluster of severe acute respiratory infection (SARI), particularly clusters of patients requiring intensive care, without regard to place of residence or a history of travel

• AND

• Not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.
Who should be tested......

- 4. Health care workers:
  - WHO advises that Health care workers who care for patients with severe acute respiratory infections, particularly patients requiring intensive care, who develop unexplained pneumonia without regard to place or residence or history of travel should be tested.
  - AND
  - Not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.
  - PHO does not think it is absolutely necessary to test ill health care workers if there is no relevant travel history, but will consider testing on request.
Specimens for novel coronavirus testing

- Respiratory tract samples (e.g. NPS, BAL)
- Urine
- EDTA (purple top) blood
- Stool (dry sterile container)

- Serology not currently requested by NML
  - Likely to change once serology test widely available

- Contact PHOL customer service for microbiologist approval prior to submission.
PHOL Testing Algorithm:

• NP/BAL: Influenza A/B PCR, respiratory viral multiplex PCR, *Mycoplasma/Chlamydophila pneumoniae* PCR, novel CoV PCR.

• BAL (or sputum): Legionella PCR

• Urine: *Legionella* urinary antigen, novel CoV PCR

• Stool (if diarrhea): novel CoV PCR

• EDTA blood: novel CoV PCR

• Test broadly, continue to test for novel coronavirus even if a pathogen found
**Assessment for Testing**

- acute respiratory infection, which may include fever (≥ 38°C, 100.4°F) and cough; **AND**
- suspicion of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome (ARDS)) based on clinical or radiological evidence of consolidation; **AND**
- hospitalized or in Emergency planning to admit **AND**
- travel to or residence in an area where infection with novel coronavirus has recently been reported or where transmission could have occurred in 10 days before illness onset **OR**
- contact with a confirmed case
- inform client to also contact their local Health Unit about the suspect case

**Sample Collection**

- NP Swab (NP&BAL if intubated)
- EDTA Blood
- Urine
- Stool in Dry Sterile Container (if gastrointestinal symptoms)

**Test Ordering**

Record the travel history, onset date, and clinical symptoms:

- One PHL General Test Requisition per sample:
- Test Ordered - "Novel Coronavirus"
- Travel History (Country of travel) ______
- Date of Return
- Date of Onset ______
- Signs & Symptoms ______

**FOR CSC:**

- Date: ______
- Time of Call: ______

**Patient Identifier:**

- Name: ______
- Health Card: ______
- Date of Birth: (yyyy/mm/dd) ______
- Collection Date: (yyyy/mm/dd) ______

**Doctor/Hospital/Laboratory/Submitter:**

- ______

**PLEASE PHONE RESULT TO:**

- ______

**Phone number (MUST BE DIRECT LINE OR CELL PHONE OF ORDERING CLINICIAN):**

- ______

**Other tests requested ______**

- inform client these may be tested after the coronavirus test

**APPROVED BY (MM/CM) ______**

---

**CS:** fax to DASH, DE, MOL DIAG, DNA CORE, VIRUS DETECTION, MM/CM Suite (include others if other tests requested)
PHAC Biosafety Advisory: Human Coronavirus Erasmus Medical Centre (HCoV-EMC/2012), Jan 23, 2013

- HCoV-EMC/2012 classified as Risk Group 3 human pathogen
- Containment Level 3 for all proliferative *in vitro* or *in vivo* activities

<table>
<thead>
<tr>
<th>Sample Type and Activity</th>
<th>Minimum Containment Level Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Proliferative Clinical/Diagnostic Activities (processing specimens for packaging and distribution to laboratories, diagnostic testing activities (excluding culture), molecular testing using non-infectious material, etc.)</td>
<td>CL2 †</td>
</tr>
<tr>
<td>Work Involving Positive Cultures (culturing of specimen, processing positive cultures for packaging and distribution to laboratories, etc.)</td>
<td>CL4 †</td>
</tr>
<tr>
<td><em>In Vivo Work</em></td>
<td>CL3 †</td>
</tr>
<tr>
<td>† Additional Operational and Physical Requirements</td>
<td></td>
</tr>
</tbody>
</table>

**Transportation** For air shipments:
- cultures (i.e. propagated virus) should be shipped as Category A, UN2814.
- patient/primary sample specimens should be shipped as Category B, UN3373.
Lessons to date - nCoV

- Morbidity/mortality associated with nCoV
- ? Limited person-person transmission vs. common exposure for clusters
- Expect more emerging ID signals needing coordinated international response
- IHR requirements regarding public health emergencies of international concern
Lessons to date - IHNs

• Alternatives to IHNs, especially when broad alerts necessary
  • Limitations of existing PH Alerts/CNPHI postings
• Alternative purposes/structure of IHN
  • Direct to web-based guidelines/resources
  • High-level summaries
  • ? Subsequent IHNs if significant changes to guidelines
• Expedited review/approvals of IHNs
• Evaluation of uptake/impact
Not all coronas have global success!

Thanks To....

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- Tom Appleyard