COVID UPDATE

Edward Buchel
Protocols

Shared health site for PPE outside of the operating room

Operative PPE
  - Assistants
  - Room changes

Reusable masks
  - Existing Industrial masks
  - Newly produced masks

Slates
Protocols

- On shared health website
- Have eliminated 5 day waiting period
- We have special investigation code for expedited viral testing
- Shared health site for PPE outside of the operating room
  - Confusion about EDCP outside of operating room.
  - Follow your sites information and shared health in formation
  - Regional coordination regarding PPE.
  - Each site now reporting usage and stock of PPE twice daily.
Operative PPE

The goal is safety with efficient use of PPE

- Assistants
  - MUST REDUCE THE NUMBER
  - MUST USE THE MOST TRAINED

- Room changes
  - NURSING WORKING ON DECREASING TURNOVER IN ROOMS
  - LIMIT STAFF IN AND OUT OF ROOM
  - STAFF STILL REMAINING AT END OF CASE AND FOR TIME OUT
Reusable masks
  - Existing Industrial masks
    - Nearly 800 on site
    - Coordinated fit testing
    - Wider distribution coming
  - Newly produced masks
    - Approval to use locally
    - 1-2 weeks for approval to use nationally
- Slates
  - More then a 50% reduction
  - Weekly adjustments
  - Next week no regional changes at present
- More to come.
The COVID-19 pandemic

Can the biology of other RNA respiratory viruses make this pandemic less “unprecedented”?

Sylvain Lother MD FRCPC DTMH
April 8, 2020
Objectives

- Review basic virology of SARS-CoV2
- Review transmission characteristics
- Review essential protective strategies for HCW
- Update:
  - Local experience
  - Diagnosis
  - Treatment studies

For live questions: Dr. Faisal Siddiqui
- Text: 204-510-7220
- Email: fsiddiqui@hsc.mb.ca

Send me questions anytime:
- slother@manitoba-physicians.ca
Disclosures

None
SARS-CoV2

• Beta-coronavirus
• ss +RNA (29,903 bp)
  • Not segmented
  • High mutation rate
  • Largest RNA virus genome!
• Enveloped
• 50-200 nm virion
• No vector-borne transmission
SARS-CoV2 cell entry

- Spike protein binds to human ACE2 (in type II pneumocytes)
- Spike protein – higher binding affinity than SARS

Letko. Nature. 2020
Shang. Nature. 2020
Transmission

Why is this virus so effective at propagating?
Many viral weapons!
SARS-CoV2 Viral weapons

- Pre-symptomatic spread
- Long incubation period
- Initial mild symptoms (and non-specific)/Long duration of mild symptoms
- High rates of illness severity
- No host immunity
- Effective person to person transmission (via droplets, possibly fomites)
- ?capacity to spread via airborne transmission
- ?Environmental stability
Pre-symptomatic spread

Intensive public health follow up from 243 cases in Singapore

243 cases (157 acquired locally)

10 of the 157 (6.4%) occurred prior to onset of symptoms in index

Pre-symptomatic transmission occurred 1-3 days before symptoms
Incubation period

• Longer incubation periods lead to longer generation times (time elapsed between symptom onset in primary case to symptom onset in secondary case)
• Long generation times mean days to weeks before localized outbreaks are identified
  • Meanwhile, horse is out of the barn

Median = 5.2 days

Symptoms

• Initially mild
• Very non-specific, diverse initial manifestations
• Some have cough, some have sore throat, some are weak and chills
• Fever 30-50% (probably lower)
• Most don’t progress to serious symptoms (> 80%)
• Those who do progress – usually present with SOB by day 6-10
• High illness severity (~14% require hospitalization/care)
Interpreting epidemiologic data

Range 10 – 25+ days delay
No host immunity

- Basic reproductive number
  $R_0 = 2$ to $3.5$
- Each new case of COVID-19 will cause 2 to 3.5 secondary cases

Modern Epidemiology (3rd ed.), Lippincott Williams & Wilkins, 2013
Transmission

- Review of 75,000 cases (Wuhan)
- COVID-19 is transmitted via respiratory droplets and possibly fomites (hand-to-face contact with contaminated articles) during close and unprotected contact.
- >80% of transmissions were within close contact in intra-familial settings
- No convincing evidence of airborne transmission

World Health Organization (WHO) Joint Mission, led by Canadian Dr. Bruce Aylward
Viral weapons

- Pre-symptomatic spread
- Long incubation period
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• ?Capacity to spread via airborne transmission
• ?Environmental stability
Aerosol generation
Definitions

• AGMP = aerosol generating medical procedures
• Aerosols = small particles (< 5 μm)
• Airborne transmission = spread of infectious agent via aerosols suspended in air (ex: TB)
Are AGMPs the only thing that create aerosol?

- NO!
- Coughing and sneezing create lots of aerosols
- Participants with influenza:
  - Patients expelled 900 to 302,200 particles per cough
  - Used a laser aerosol particle spectrometer (detects 0.35 to 10 \( \mu m \))
  - 63% of the detectable particle volume was in the range of aerosols
- No data to support other respiratory viruses transmit by the aerosols generated from coughing/sneezing -> droplets more important
Opportunistic airborne transmission?

Under “perfect” circumstances, can respiratory viruses spread via airborne aerosols?
SARS and influenza (seasonal and pandemic)

- Case-control studies: many studies
  - Hand hygiene alone has dramatic reduction in transmission\textsuperscript{1}
  - Droplet and contact precautions highly effective in controlling transmission\textsuperscript{2}

- Modeling data:
  - If airborne transmission was possible, hand hygiene and droplet/contact measures alone would not be as effective as reported\textsuperscript{3}

- General consensus: SARS and influenza cannot be transmitted via aerosols

COVID-19 and the Risk to Health Care Workers: A Case Report

Kangqi Ng, MBBS; Beng Hoong Poon, MBBS, MPH, MMed (Family Med); Troy Hai Kiat Puar, MBBS; Jessica Li Shan Quah, MBBS; Wann Jia Loh, MBBS; Yu Jun Wong, MD; Thean Yen Tan, MBBCh; Jagadesan Raghuram, MB BCh BAO

Article, Author, and Disclosure Information

- First Singapore COVID-19 patient (unknown when presented)
- Viral illness, needed O2, 2 days later intubated, difficult airway, 2 attempts, bougie, on vent 3 days, extubated, BiPAP post extubation
- 41 HCW exposed to AGMP, > 10 mins, < 2m from patient
- Surveillance x 2 weeks -> none with COVID-19
Environmental stability

Van Doremalen. NEJM. Mar 17
Protecting yourself
Stick to the basics!
What is **enhanced** droplet/contact?

- Usual droplet and contact pre-cautions
  - Surgical mask
  - Eye protection
  - Gown & gloves
- Enhancement - Use of N95 respirators for AGMP
PPE

• Using N95 mask:
  https://www.youtube.com/watch?v=syh5UnC6G2k

• Putting on/taking off PPE:
  https://professionals.wrha.mb.ca/old/extranet/ipc/ppe-videos.php
Overview

- **Don**
  - Put on all PPE in a clean area (outside patient room, or in ante-room)

- **Doff**
  - Gloves and gown off in room, wash hands
  - Always remove goggles and facemask in a clean area (outside patient room, or in ante-room)**
  - Always wash your hands before coming close to your face
    - Putting on, taking off, adjusting any mask
  - Never touch front or inside of your mask, only manipulate the elastics
# Down falls of “excessive” PPE

<table>
<thead>
<tr>
<th>Resources</th>
<th>Labor</th>
<th>Time</th>
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</thead>
<tbody>
<tr>
<td>Burn through PPE</td>
<td>More steps to wear PPE</td>
<td>Pt status may deteriorate rapidly</td>
</tr>
<tr>
<td></td>
<td>More room for error (doffing)</td>
<td></td>
</tr>
<tr>
<td>Expensive</td>
<td>Moving patients to All rooms (increases exposure to other pts, HCW, environments)</td>
<td>More time in patient rooms (enhanced cleaning)</td>
</tr>
<tr>
<td>Training &amp; other resources</td>
<td>Training</td>
<td>Delay in essential care or procedures pts need (policies)</td>
</tr>
</tbody>
</table>

Consider the **risks** (some evidence based increased risks) **VS.** the **benefits** (almost all unproven potential benefit)
Conclusions

• SARS-CoV2 - many virologic characteristics that increases transmissibility
• Conclusive supportive evidence that COVID-19 is spread by droplets
• No convincing evidence of aerosol/airborne transmission
• Convincing evidence that standard PPE (to protect against droplet/contact) reduces transmission
• Enhanced droplet/contact is added layer of protection
• Supported by governing bodies
  • WHO, CDC, PHAC, local guidelines

No evidence of airborne spread of SARS-CoV2
Local Experience
Provincial Epi

- 217 cases
  - 21 recovered

- 12 hospitalized
  - 6 currently in ICU
  - 1 ICU discharge
  - 3 ICU deaths

- 1 ICU discharge
- 3 ICU deaths
Canadian COVID-19 cumulative cases

First case in Canada: Jan 15
First case in MB: Mar 12

Take off: April 22nd?

MB vs. rest of Canada
## Canadian experience

<table>
<thead>
<tr>
<th></th>
<th>Canada</th>
<th>Manitoba</th>
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<tbody>
<tr>
<td>Outpatients</td>
<td>84.4%</td>
<td>94%*</td>
</tr>
<tr>
<td>Hospitalized (non-ICU)</td>
<td>11.5%</td>
<td>1.9%*</td>
</tr>
<tr>
<td>ICU</td>
<td>4.1%</td>
<td>4.4%*</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.9%</td>
<td>1.5%*</td>
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</table>

*Numbers will go up as progression to serious disease lags diagnosis by ~ week*
<table>
<thead>
<tr>
<th>Pt</th>
<th>Age/Sex</th>
<th>PMH</th>
<th>ARDS/Prone</th>
<th>AKI/CRRT</th>
<th>Shock</th>
<th>Super infxn</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>60s F</td>
<td>Obesity, DM</td>
<td>Sev/Prone</td>
<td>Yes/No CRRT</td>
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<tr>
<td>2</td>
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<td>DM, HTN</td>
<td>Mod/Prone</td>
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<td>8</td>
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<tr>
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<td>Stable</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>10</td>
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<td>No</td>
<td>No</td>
<td>ICU d/c</td>
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</table>
Diagnosis

- Real-time RT-PCR
- Several platforms: test characteristics Sn > 99%; Sp > 99%
- Total test in MB: 14,880 (1.4% positive rate)
- Pooled NAAT – 4 tests at once, capacity > 1200 tests per day, no backlog
  - Priority to HCW and hospitalized inpatients
  - Turn around < 24h from receiving specimen
Screening

- Asymptomatic screening
- Not great!
- Low viral titers 24-48h before symptoms
- Compromises sensitivity of test (FNs)
- Consider not screening
- Use enhanced droplet precautions with no screening
Treatment

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Waleed Alhazzani¹,², Morten Hylander Møller¹,³, Yaseen M. Arabi⁴, Mark Loeb⁵, Michelle Ng Gong⁶, Eddy Fan⁷, Simon Oczkowski¹,², Mitchell M. Levy¹,⁸, Lennie Derde⁹,¹⁰, Amy Dzierba¹¹, Bin Du¹², Michael Aboodi¹³, Hannah Wunsch¹⁴,¹⁵, Maurizio Cecconi¹⁶,¹⁷, Younsuck Koh¹⁸, Daniel S. Chertow¹⁹, Kathryn Maitland²⁰, Fayez Alshamsi²¹, Emilie Belley-Cote²², Massimiliano Greco²³,²⁴, Matthew Laundy²⁵, Jill S. Morgan²⁶, Jozef Kesecioglu²⁷, Allison McGeer²⁸, Leonard Mermel²⁹, Manoj J. Mamman³⁰, Paul E. Alexander³¹,³², Amy Arrington³³, John E. Centofanti³⁴, Giuseppe Citerio³⁵,³⁶, Bandar Baw³⁷,³⁸, Ziad A. Memish³⁹, Naomi Hammond⁴⁰,⁴¹, Frederick G. Hayden⁴², Laura Evans⁴³, Andrew Rhodes⁴⁴

Clinical Management of Patients with Moderate to Severe COVID-19 - Interim Guidance
April 2, 2020

No proven antiviral!
Local COVID-19 research & trials

A suite of trials spanning from PrEP, PEP, mild to severe COVID disease
Epidemiologic, translational, diagnostic studies
Rapid molecular diagnostics

- Xpert Xpress SARS-CoV2 (GeneXpert Xpress System)
- Spartan Cube (portable)
- Validation study
- Patients screened in parallel with lab-based testing (PHAC JC Wilt Lab)

Benefits:
- Rapid results, de-centralization of testing (reduce backlog)
- Help patient flow, IPAC
- Enroll quickly into clinical trials
- Improved access (northern/remote communities)
PEP and PET RCT

- Multinational, double blind RCT
- Novel internet-based trial
- PI: Dr. Ryan Zarychanski
- Coordinator: Nicole Marten
- Collaborators in QC, AB, UMN
- HCQ vs. placebo
- PEP group
  - Household contact or HCW within 4 days of exposure
- PET group
  - Within 4 days of symptoms, with COVID+ test or compatible symptoms after exposure

www.covid-19research.ca
CATCO – Canadian Treatments for COVID-19

• PIs: Drs. Yoav Keynan and Lauren Kelly
• Coordinators: Gary Annable & Dolores Friesen
• For Hospitalized patients with COVID-19 at GGH, SBGH, HSC
• Adaptive, randomized, open label, platform trial
• Follows global WHO SOLIDARITY PROTOCOL
• Several arms
  • Remdesivir for 10 days
  • Lopinavir/ritonavir for 14 days
  • HCQ for 11 days
  • SOC alone for 14 days
• Primary outcome: in-hospital all cause mortality
REMAP-CAP

• Global adaptive platform trial for ICU patients with pneumonia
• PI: Dr. Ryan Zarychanski
• Coordinator: Nicole Marten
• For CAP in ICU patients (within 48 hours of hospitalization) and requiring cardiovascular or respiratory support
• Several arms:
  • Lopinavir/ritonavir vs. SOC
  • HCQ vs. SOC
  • Interferon beta 1a vs. SOC
  • Heparin vs. SOC (global domain, led by Dr. Zarychanski)
HALO-COVID

- PI: Dr. Ryan Zarychanski
- Coordinator: Nicole Marten
- Two platforms:
  - Expanding HALO trial to include COVID-19 patients
  - Addition of HALO to the global REMAP-CAP platform
    - Immense international interest: Multiple heparin trials are coming
    - High d-dimers and macro/microthrombosis in COVID-19
    - Heparin interferes with SARS-CoV2 spike protein that mediates endothelial adhesion
- Intubated patients – UFH
- Ward patients – Enoxaparin
- Both trials planned 2000-3000 patients
  - Bayesian responsive adaptive randomization
## N95 sterilization

- PI: Dr. Anand Kumar
- Collaborators: NML

<table>
<thead>
<tr>
<th>Mask</th>
<th>Positive Control</th>
<th>Autoclave</th>
<th>EtO</th>
<th>iHP</th>
<th>VHP</th>
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<td><strong>SARS-CoV-2</strong></td>
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<td>3M 1860</td>
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<td>6.3 ± 0.7</td>
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</tbody>
</table>

Mean virus recovery post-decontamination (LogTCID<sub>50</sub> ± SD) compared to drying controls.
MB COVID-19 Clinical Research Team

Primary Supervisors
Ryan Zarychanski
Yoav Keynan
Lauren Kelly
Anand Kumar
Lauren MacKenzie
Dylan Mackay

Research Coordinators
Nicole Marten
Gary Annable
Dolores Friesen
Dayna Solvasen
Maggie Wilson

Trainees
Sylvain Lother
Thomas Fear
Milena Semproni
Carmen Tse, Izabella Supel

Sub-investigators & collaborators
Ken Kasper, Terry Wuerz, Amila Heendeniya, Glen Drobot, Jonathan Laxton, Zina Zaslawski, Helen Ferens

So many others!
Questions?

Thank you, for all that you do!!

For live questions: Dr. Faisal Siddiqui
• Text: 204-510-7220
• Email: fsiddiqui@hsc.mb.ca

Send me questions anytime:
• slother@manitoba-physicians.ca

Thanks to the following for their contributions to this talk, leadership and guidance:
• Dr. Ryan Zarychanski
• Dr. Yoav Keynan
• Dr. Ken Kasper
• Dr. Jarred Bullard
• Dr. Philippe Lagacé-Wiens
• Dr. Duane Funk
• Dr. Faisal Siddiqui
• Dr. Evelyn Lo
• Dr. Lauren MacKenzie
• Dr. Lauren Kelly
• Nicole Marten
Figure 2 - Number of positive influenza tests and percentage of tests positive, by type, Canada, weeks 2019-35 to 2020-13

Number of Laboratories Reporting in Week 13: 33 out of 36

Figure 2 – Number of positive influenza tests and percentage of tests positive, by type, subtype and report week, Canada, weeks 2018-35 to 2019-13
Convalescent plasma

• Led by Ryan Zarychanski and others
• ~2000 to 3000 pt RCT of convalescent plasma vs. SOC

• Collaboration with CBS and Hema Quebec
• Will enroll non-intubated patients first
  • Plan to expand to ICU population as product availability increases
Hyperimmune globulin

• RCT Led by Anand Kumar and Ryan Zarychanski
• Collaboration with emergent biosolutions
• Target population is healthcare workers (as prophylaxis)
• Trial in development at the moment
PrEP study

• HCQ vs. placebo for PrEP in HCWs
• PI: Drs. Lauren MacKenzie and Dylan Mackay
• Coordinator: Dayna Solvason
• More details to come....
SPRINT-SARI

- International, prospective observational study
- Comprehensive clinical and laboratory collection of data for emerging severe acute respiratory infections (SARIs) in the ICU
- All COVID-19 positive ICU patients enrolled locally

- 2 translational biology observational studies will be embedded