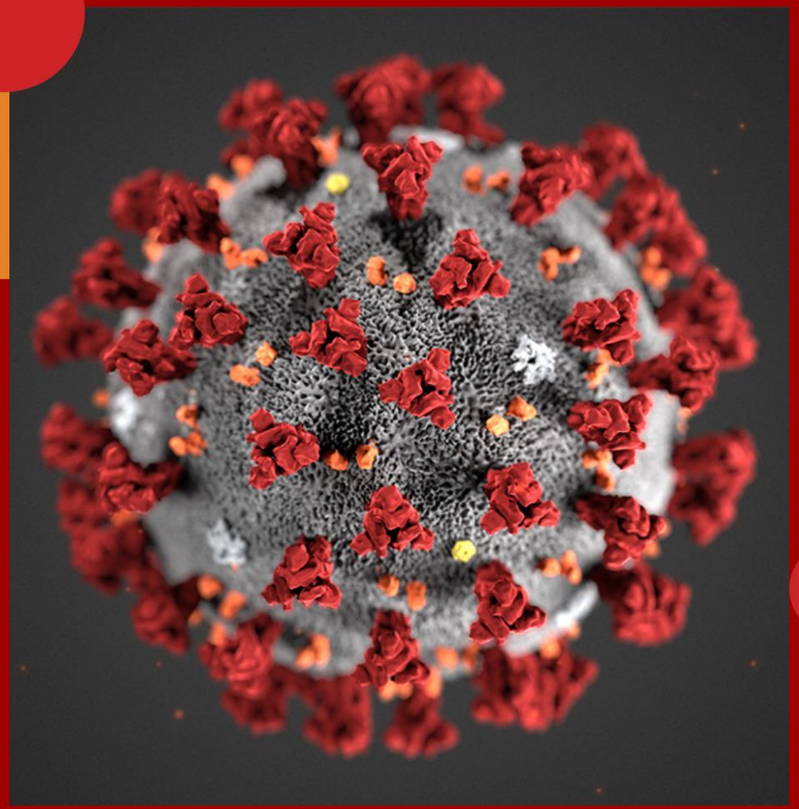
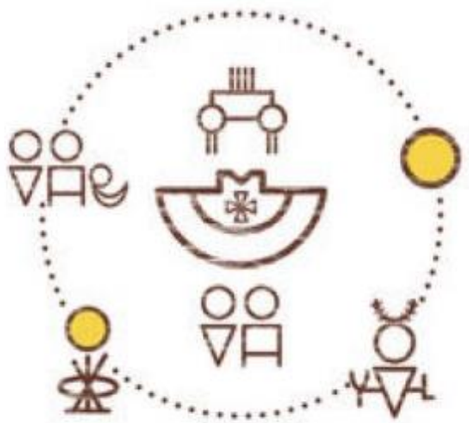
SARS-CoV-2 Modes of Transmission and Related IPC Measures



Tuesday, April 28, 2020|

John Conly, University of Calgary and Alberta Health Services, Calgary, Canada

Territorial Acknowledgement



ii' taa'poh'to'p

Source: https://www.ucalgary.ca/indigenous

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- Appointed as a member of the Order of Canada in 2018 for pioneering contributions in IPC, antimicrobial resistance and healthcare innovations.

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Sorting the Message

- Mainstream media and social media in **total overdrive**
- First major pandemic in the "modern age" of **instant social messaging**
- Lots of "papers" now published online before even reviewed
- "Science" may be correct but may jump to premature or incorrect conclusions or be incomprehensible; some will never be published
- Even in top quality peer-viewed journals the articles may be premature / over interpreted / incomplete and without necessary limitations
- Many letters and short reports
- Authors, reviewers and journals are under immense pressure to be fast and first in publishing
- **Be careful and use your critical appraisal skills and common sense**

Basic Viral Facts

- The SARS-CoV-2 causes COVID-19 infection.
- Single strand RNA virus in coronavirus family named from morphology
- It is a respiratory virus (contact droplet **not** airborne tran**smission**)
- Only a few coronaviruses cause human illness (mostly **respiratory** such as colds but also serious respiratory infections SARS and MERS)
- Uses human ACE 2 receptor(Angiotensin converting enzyme 2)
- **VERY high affinity** for receptor vs. SARS (i.e. readily latches onto respiratory cells ? few viruses needed for infection)

SARS -CoV-2

- SARS-CoV-2 likely originated from Asian bats into intermediary animal host (the pangolin) and then to humans
- Virus not mutating significantly. So vaccine more possible but virus less likely to “flame out” or become less pathogenic
- Variation is, however, enough for phylogenetic studies https://nextstrain.org/narratives/ncov/sit-rep/2020-03-27
- IgG and IgM Antibody tests are close: Will be very useful for determining natural history and possible health care staffing
- No one is immune

Natural History in Humans

- Proportion of asymptomatic infections unknown and critical for understanding possible transmission and HCW immunity.
- Estimates range 0-6% but models higher
- Incubation period after exposure likely 2-14 days (median ~5 days)
- 97.5% develop symptoms within 11 days
- Of those diagnosed
  - 80% have self-limited mainly respiratory illness probably of ~ 14 days duration
  - 15% have more severe illness requiring medical care +/- hospitalization
  - 5% go to intensive care +/- ventilation
- Risk in hospitalized is mainly respiratory then multi organ failure requiring ventilation and high risk of death ~ 70% ventilated patients
- Progression risk and rate down pathway below is unclear

Diagnostic Clinical Challenges

Influenza-like-illness (ILI)

- **New or changed cough**

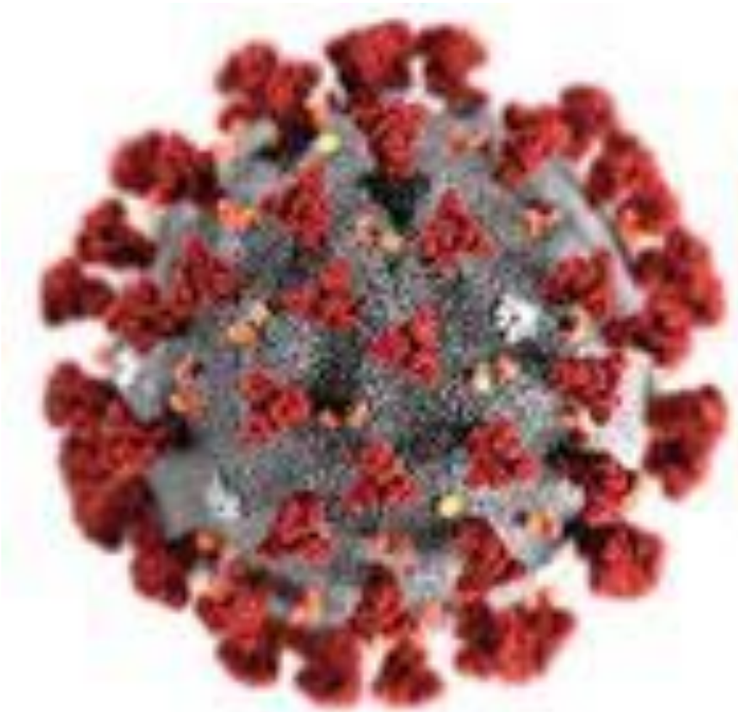
AND one or more of the following:

- **Fever** (or history of fever in the last 24 hours)
- **Muscle aches**
- **Severe exhaustion/weakness**
- Sore throat
- Joint pain

COVID-19

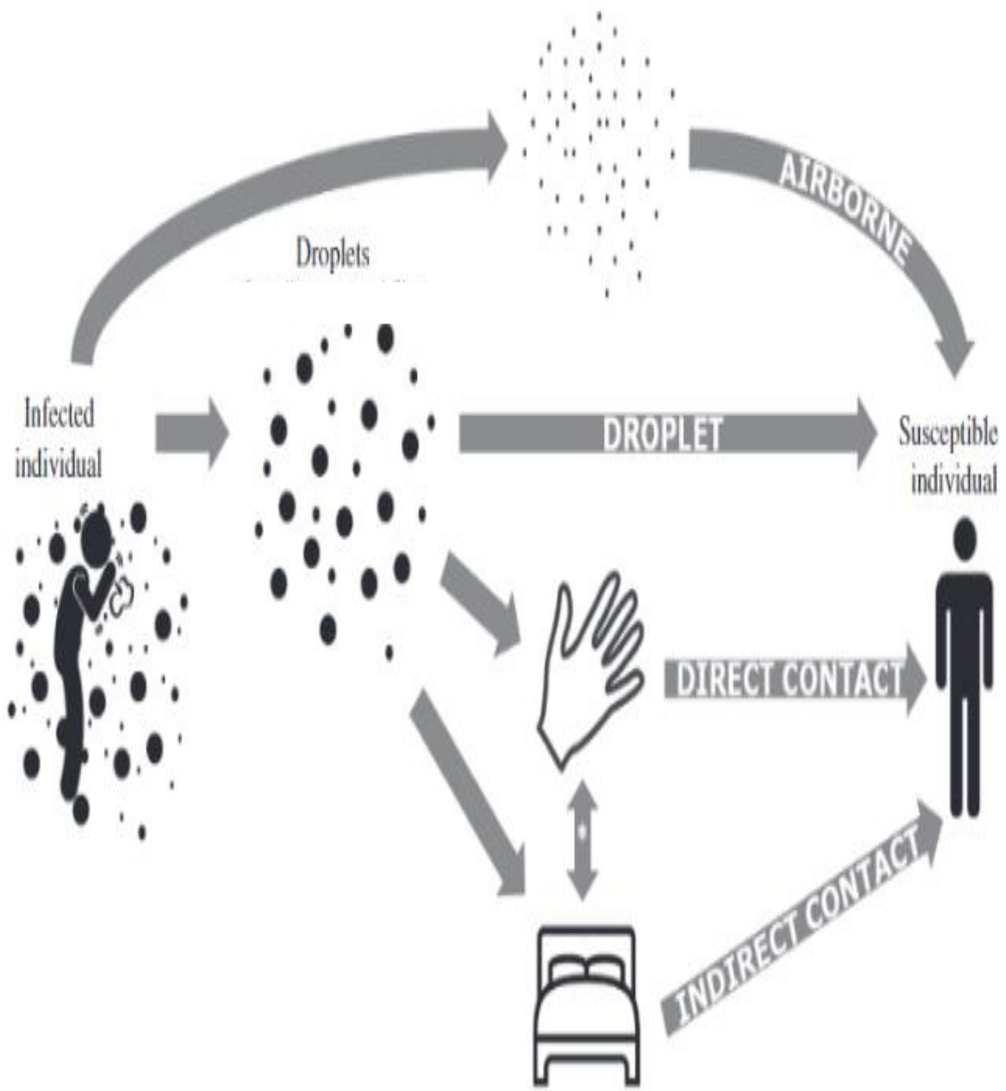
- **Fever** (98%)
- **Cough** (76%)
- **Myalgia or fatigue** (44%)
- Sore throat
- Sputum production (28%)
- Headache (8%)
- Mild Diarrhea (? 3%)
- Hemoptysis (5%)
- Additional symptoms – skin lesions, strokes

COVID-19 and SARS-CoV-2
Infection Prevention and Control



SARS-CoV-2

Transmission Routes



Source: J.A. Otter et al. / Journal of Hospital Infection 92 (2016) 235e250

Transmission Routes

- Droplet and airborne routes create most debate
- Continuum of droplet and airborne routes an important concept
- Particles of a variety of sizes are expelled from the human airway during coughing, sneezing, talking and medical procedures
- Size of these particles and the distance propelled is complex
  - particle sizes variable
  - distance they will be propelled is dependent on the force generated by the individual or the procedure
  - particles may or may not contain the infectious agent
  - infectious agent may or may not be viable
  - concentration of particles affected by many factors: the relative humidity, evaporation level, ,settling velocity, direction of air flow, the number of air changes per hour, temperature, crowding and other environmental factors
- Airborne may be obligate or preferential or opportunistic and refers to particles that stay aloft for minutes or hours (less than 5-10 µm in diameter) and can be carried by air currents over a measurable distance
- Droplet spread refers to large droplets (>5-10um) that fall within 1 metre

Exposure, Transmission and Invasive Infection

- Exposure to microorganisms
- Not all exposures lead to transmission and invasive infection.
- Exposure occurs when a host comes into contact with an infected source or contaminated environment (e.g., inanimate/animate object or particles in the air)
- Probability of transmission followed by invasive infection →many factors
  - host susceptibility
  - presence of host receptors
  - receptivity of host receptors
  - inoculum
  - viability
  - virulence
  - effectiveness of the hierarchy of controls

SARS-CoV-1/ MERS-CoV Findings Relevant to IPC

- **Droplet and contact** – multiple studies demonstrated **compliance with gloves, gowns and medical masks or N95s** were adequate to prevent transmission for SARS

- **Major risks** exposure of eye and mucous membranes to **respiratory secretions and AGMPs**, ie intubation (**opportunistic airborne);** no association with contact with urine/stool

- **HCW spread -** associated with **inconsistent or improper PPE use** for SARS/MERS-CoV outbreaks; **Infections in HCWs: 22% and 25%** for SARS and MERS, respectively

- **Risk factors for nosocomial spread** of MERS-CoV in two large outbreaks in Saudi Arabia and South Korea found ER/Ward **overcrowding and sub-optimal control of visitors** were major factors

- **Transmission** of MERS-CoV **was not documented** in one investigation of mostly **asymptomatic** and **pauci-symptomatic** cases and their household contacts

- **Asymptomatic cases reported but uncommon** – one study of MERS cases found 80% of "asymptomatic" persons actually had symptoms on close questioning

Seto WH et al Lancet 2003;Raboud J et al Plos One 2010; Jefferson et al Cochrane Rev 2011; Oboho IK et a NEJM 2015;Kim SW CID 2017; Cheng VC et al Antiviral Res 2013; Van Kerkhove MD et al Sci Rep. 2019.

SARS-CoV-2 Detection

Patient specimens

- **BAL** samples (Zhu NEJM) + viral isolation
- **Nasopharyngeal/oropharyngeal** (NP/OP) swabs
  - multiple reports of detection of 2019-nCoV RNA in NP/OP swabs; sensitivity varies 71-100% and depends on operator, timing and site of specimen; specificity near 100%
  - shedding over time varies but recent studies elucidating
  - viable virus does not correlate well with RT-PCR depending on time
- **Serum**
  - Chan (Lancet 2020) also showed + RT-PCR of serum in one patient
- **Stool**
  - Investigators in Shenzhen and Washington State have detected 2019-nCoV RNA in the stool of infected patients (Holshue NEJM 2020)

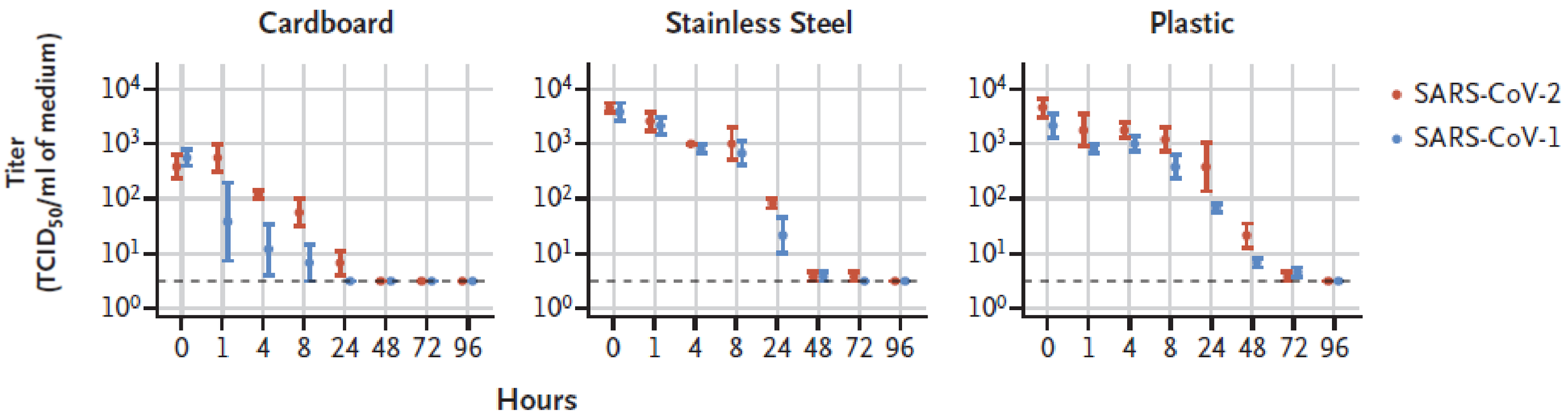
Table I
Persistence of coronaviruses on different types of inanimate surfaces

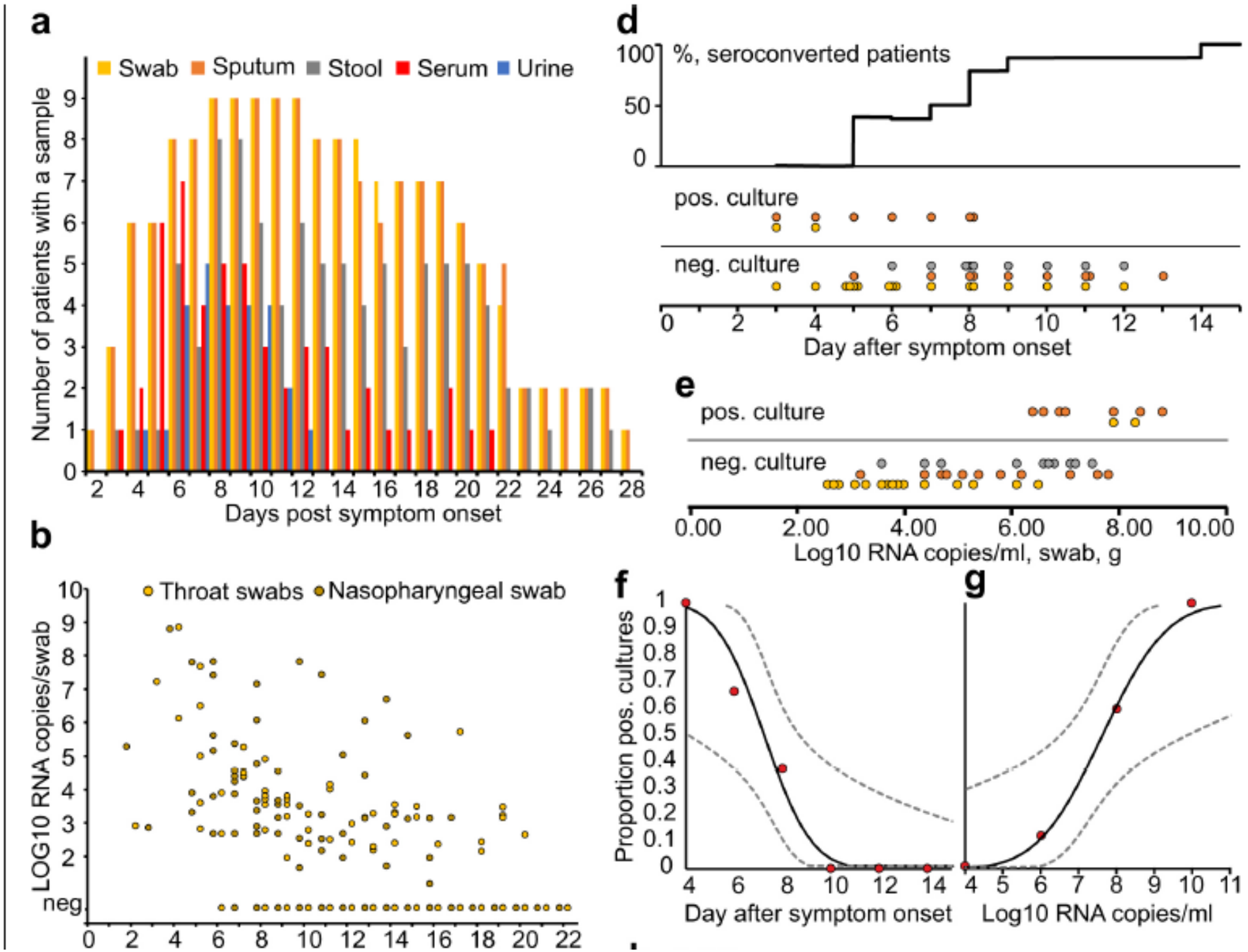
Type of surface	Virus	Strain / isolate	Inoculum (viral titer)	Temperature	Persistence	Reference
Steel	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C	48 h	[21]
				30°C	8–24 h	
	TGEV	Unknown	10^6	4°C	≥ 28 d	[22]
				20°C	3–28 d	
				40°C	4–96 h	
	MHV	Unknown	10^6	4°C	≥ 28 d	[22]
				20°C	4–28 d	
				40°C	4–96 h	
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Aluminium	HCoV	Strains 229E and OC43	5×10^3	21°C	2–8 h	[24]
Metal	SARS-CoV	Strain P9	10^5	RT	5 d	[25]
Wood	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
Paper	SARS-CoV	Strain P9	10^5	RT	4–5 d	[25]
	SARS-CoV	Strain GVU6109	10^6	RT	24 h	[26]
			10^5		3 h	
			10^4		< 5 min	
Glass	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Plastic	SARS-CoV	Strain HKU39849	10^5	22°-25°C	≤ 5 d	[27]
	MERS-CoV	Isolate HCoV-EMC/2012	10^5	20°C	48 h	[21]
				30°C	8–24 h	
	SARS-CoV	Strain P9	10^5	RT	4 d	[25]
	SARS-CoV	Strain FFM1	10^7	RT	6–9 d	[28]
	HCoV	Strain 229E	10^7	RT	2–6 d	[28]
PVC	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Silicon rubber	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Surgical glove (latex)	HCoV	Strains 229E and OC43	5×10^3	21°C	≤ 8 h	[24]
Disposable gown	SARS-CoV	Strain GVU6109	10^6	RT	2 d	[26]
			10^5		24 h	
			10^4		1 h	
Ceramic	HCoV	Strain 229E	10^3	21°C	5 d	[23]
Teflon	HCoV	Strain 229E	10^3	21°C	5 d	[23]

MERS = Middle East Respiratory Syndrome; HCoV = human coronavirus; TGEV = transmissible gastroenteritis virus; MHV = mouse hepatitis virus; SARS = Severe Acute Respiratory Syndrome; RT = room temperature.

Kampf G et al J Hosp Inf 2020

Survival SARS-CoV-2

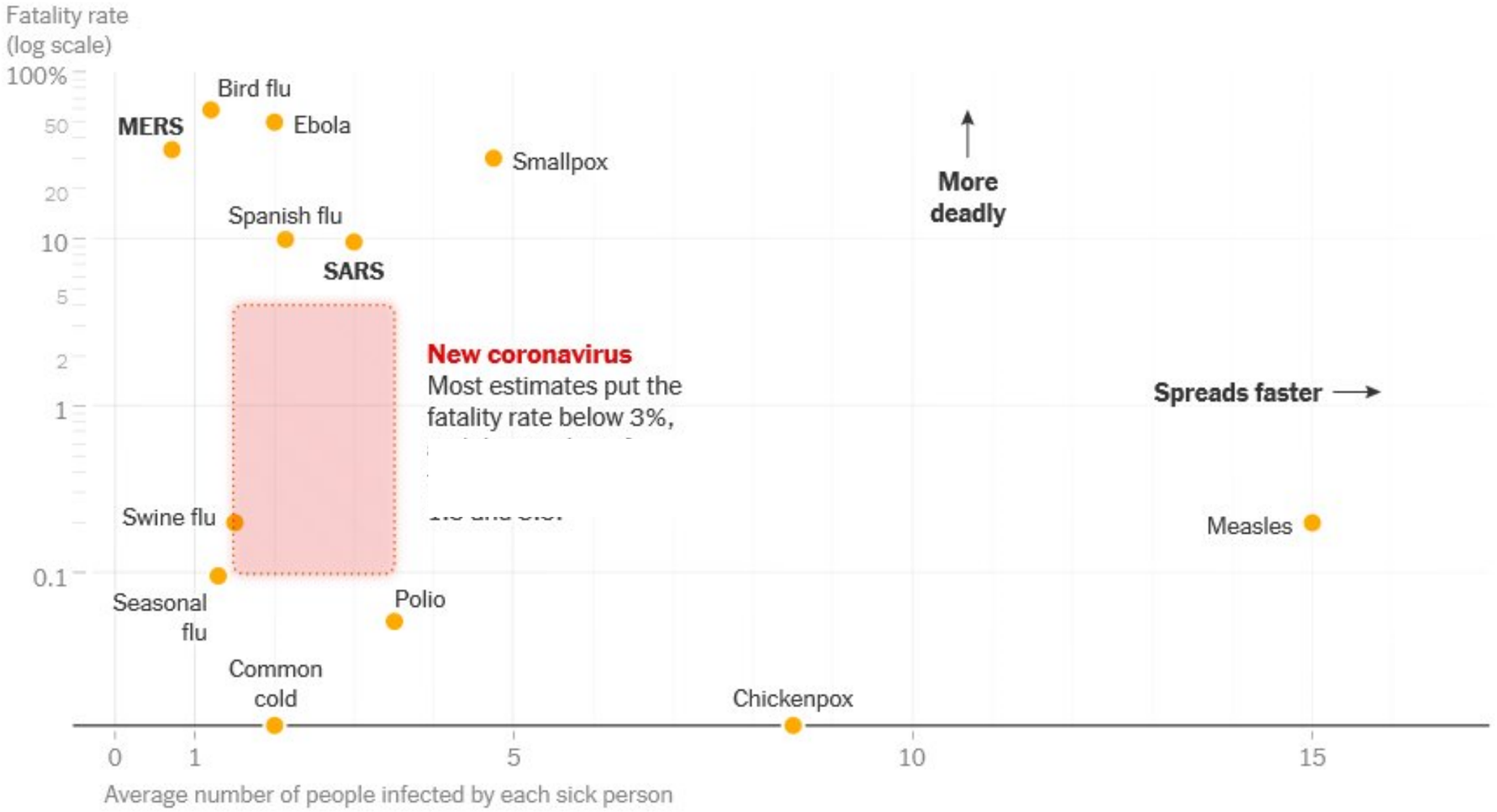




- Virus was readily isolated during the first week of symptoms from a considerable fraction of samples (16.66% in swabs, 83.33% in sputum samples)
- No isolates of virus obtained from samples taken after day 8 in spite of ongoing high viral loads by RT-PCR

Wolfel et al Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x. [Epub ahead of print]

How SARS-CoV-2 spread compares to other viruses



Basic reproductive number (R_0)
the average number of individuals infected by a case over the infectious period, in a fully susceptible population.
Most major studies suggest it is falling into range of
2.20 -2.68
Korea and Italy of 2.60
(based on initial case growth)

Li Q et al N Engl J Med. 2020 Mar 26;382(13):1199-1207; Wu JT Lancet. 2020 Feb 29;395(10225):689-697
Zhynag Z et al. Int J Infect Dis. 2020 Apr 22. pii: S1201-9712(20)30259-9.

Mode Transmission SARS-CoV-2

- Droplet - contact considered predominant route
  - Consistent with SARS-CoV-1, MERS-CoV
  - Consistent with R_0 of other droplet-contact respiratory viruses
  - WHO-China Joint Mission on COVID-19 in China with 75,465 cases supported person-to-person droplet and fomite transmission
    - 78-85% of the investigated infection clusters occurred within families, with an intra-household 2^0 attack rate of 3-10%, not consistent with airborne transmission

`

References: WHO- China Joint Mission Report 2020

Reports against/for Airborne Transmission for CoVs

- 41 HCW exposure over 10 minutes within 2 meters to a COVID-19 patient during multiple AGMPs, 85% surgical masks and no transmission events
- COVID-19 + who was nursed in an open cubicle of a general ward before the diagnosis was made and 76 tests 52 contacts, some without PPE and no transmissions
- No evidence of COVID-19 transmission to passengers seated around a COVID+ passenger long flight
- No transmission events in 5544 continuous person hours HCW exposure to 132 inpatient COVID+ pts using medical masks as part of PPE routine care

References:; Ng K et al Ann Int Med.16 Mar 2020; Wong SC-Y. J Hosp Inf 2020; :Schwartz K et al. CMAJ 24 March 2020; Conly J Unpublished

- Amoy Garden outbreak Sars-CoV-1 > 300 residents possible aerosol event vs rats
- Report of a bus transmission 4.5 meters distance in Chinese report (translated)
- Outbreak in air-conditioned (AC) restaurant China with 10 persons with 1 meter distance between tables along flow of air from the AC
- Experimental study with 3-jet Collison nebulizer creating aerosol of viable SARS-CoV-2
- Systematic review of droplet dispersion but mainly modelling studies; no clinical settings or epidemiologic data

References: Yu IT et al N Engl J Med. 2004 Apr 22;350(17):1731-9; Luo Y et al. Pract Prev Med. 2020-03-05. Lu J et al. MMWR 26:7 July 2020; Van Doremalen N et al. N Engl J Med.2020 Apr 16;382(16):1564-1567; Bahl P et al. JID 2020;XX:1–8

Reports against/for Airborne Transmission for CoVs

- SARS-CoV-2 (RT-PCR) in 1/13 (7.7%) environmental samples but 0/8 air samples collected 10 cm from the patient's chin in Hong Kong
- SARS-CoV-2 (RT-PCR) in 17/22 (77%) environmental samples but 0/5 air sample sites including beside the patient collected in Singapore
- None/10 air samples for SARS-CoV-2 (RT-PCR) with samplers with fresh DMEM 2 to 5 m away from the patient (severely ill)

Cheng V, et al. ICHE 2020; Ong SW, et al. JAMA 2020; Faridi S et al. Science of The Total Environment 2020

- SARS-CoV-2 (RT-PCR) in 20/37 air samples at 1-113 copies/m^3 highest ICU – multiple areas hospital
- SARS-CoV-2 (RT-PCR) in 126/163 samples (77.3%) collected in this study, 0 to 1.75 copies/µL and air samples 2.86 copies/L including outside pt rooms; no viable virus cultivated in any of the 163 samples
- SARS-CoV-2 (RT-PCR) high touch surface contamination was shown in 10/15 (66.7%) rooms 1840 to 3380 RNA copies per m^3 ; viabilty not done

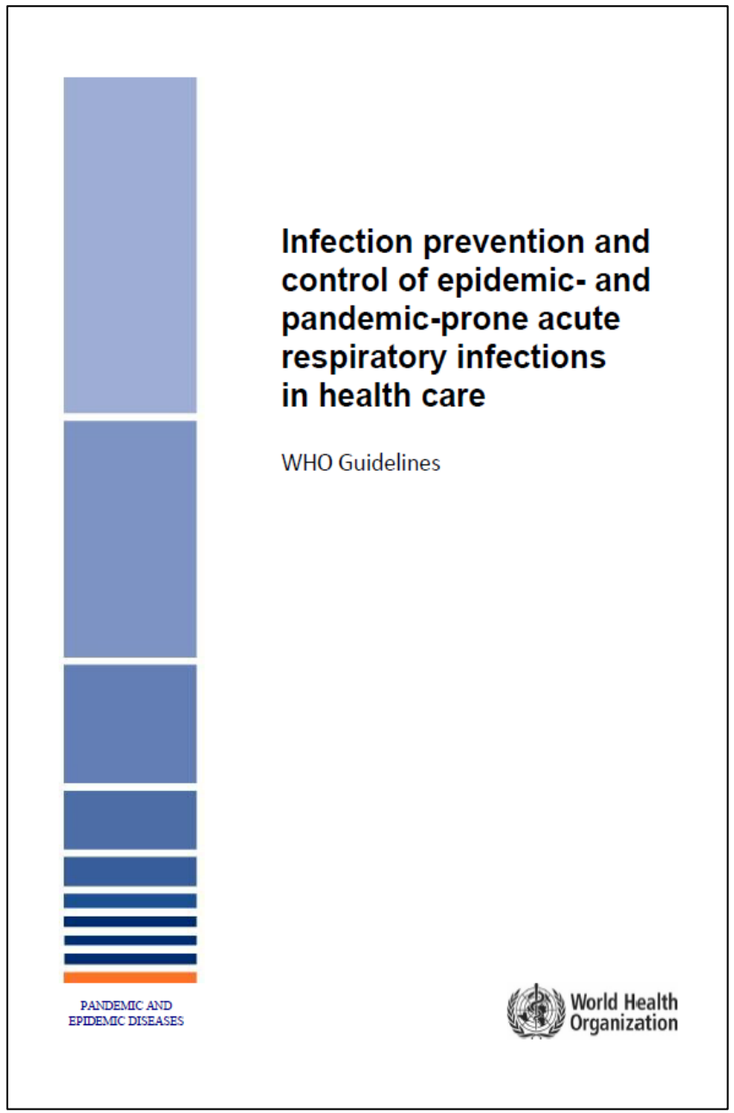
References: Liu Y et al Nature Med. 2004 Apr 27; Santarpia JL et al 2020 medRxiv preprint; Chia PY, 2020, medRxiv preprint

Transmission Risks of SARS-CoV-2

- Prospective cohort study of 4,950 persons who had a close contact with confirmed COVID-2019 patients (n=129;2.6% [6.2% asymptomatic/38% mild/51.9% moderate/3.9% severe])
- RT- PCR q2 days; daily temp and symptom check
- Uni- and multivariable regression analysis (SAS) were performed for risk factors for developing COVID-19
- Age (1.8-4.2% 0-17 to > 60 yrs); household and multiplicity of contacts (10.2-13%) highest risk whereas public transport and HCW lowest (1.0 and 0.1%) and severity were (0.33 % asymptomatic/3.3% mild/5.6% moderate/6.2% severe]) and sputum production and fever all significant risk factors in MV analysis
- RT-PCR sensitivity **71.9%;** 93.2%; 96.9% **100%** at **1**,2 ,3 and **6 tests**

Luo L et al. Modes of contact and risk of transmission in COVID-19 among close contacts; medRxiv preprint doi: https://doi.org/10.1101/2020.03.24.20042606. Guangzhou Center for Disease Control and Prevention

Building upon key existing WHO guidance



https://www.who.int/csr/bioriskreduction/infection_control/publication/en/

Seto WH. Conly JM, Pessoa -Silva et al EMHJ 2013

Infection prevention and control during health care for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection

Interim guidance

Updated October 2019

WHO/MERS/IPC/15.1 Rev 1

World Health Organization

https://apps.who.int/iris/bitstream/handle/10665/174652/WHO_MERS_IPC_15.1_eng.pdf;jsessionid=718B13F93CBB3B2DD7CCAA2623321BDF?sequence=1

2019 n-CoV: WHO guidance

Home care for patients with suspected novel coronavirus (nCoV) infection presenting with mild symptoms and management of contacts

Interim guidance
20 January 2020

World Health Organization

https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts

https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125

Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected

Interim guidance

25 January 2020

World Health Organization

Infection prevention and control during health care when COVID-19 is suspected

Interim guidance
19 March 2020

World Health Organization

https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125

Principles of IPC Strategies associated with Health Care for Suspected COVID-19

1. Ensuring triage, early recognition, and source control (isolating patients with suspected COVID-19)
2. Applying standard precautions for all patients
3. Implementing empiric additional precautions (droplet and contact and, whenever applicable, airborne precautions) for suspected cases of COVID-19
4. Implementing administrative controls
5. Using environmental and engineering controls

Ensuring triage, Early Recognition, and Source Control

- Encourage HCWs to have a high level of clinical suspicion
- Establish a well-equipped triage station at the entrance to the facility, supported by trained staff
- Institute the use of screening questionnaires according to the updated case definition; refer to the Global Surveillance for human infection with coronavirus disease (COVID-19) for case definitions
- Post signs in public areas reminding symptomatic patients to alert HCWs

Applying Standard Precautions for all Patients

- Ensure that all patients cover their nose and mouth with a tissue or elbow when coughing or sneezing
- Offer a medical mask to patients with suspected COVID-19 while they are in waiting/public areas or in cohorting rooms
- Perform hand hygiene after contact with respiratory secretions
- Hand hygiene includes either cleansing hands with an alcohol-based hand rub or with soap and water
- Alcohol-based hand rubs are preferred if hands are not visibly soiled
- Wash hands with soap and water when they are visibly soiled

Implementing Empiric Additional Precautions

- Contact and droplet precautions
  - Gloves, gowns, medical masks, eye protection
  - Donning and doffing appropriately
  - Requires education for HCW populations
  - Single use or dedicated equipment
  - Limit visitors
  - Refrain touching face/mask/eyes
  - Disinfect high touch surfaces
- Airborne precautions for aerosol-generating procedures
  - Well ventilated room
  - Use a particulate respirator at level of a NIOSH-certified N95 or (EU) standard FFP2, or equivalent

Alberta Health Services

Infection Prevention and Control

Putting on (Donning) Personal Protective Equipment (PPE)

1 HAND HYGIENE

A Using an alcohol-based hand rub is the preferred way to clean your hands.

B If your hands look or feel dirty, soap and water must be used to wash your hands.

2 Gown

A Make sure the gown covers from neck to knees to wrist.

B Tie at the back of neck and waist.

3a Procedure/Surgical mask

- Secure the ties or elastic around your head so the mask stays in place.
- Fit the moldable band to the nose bridge. Fit snugly to your face and below chin.

3b N95 respirator

There are different styles of N95 respirators (pictured below). They include: a) molded cup, b) duckbill, c) flat-fold and d) v-fold

All styles have the same basic steps for donning; molded cup and duckbill are pictured below. Refer to the manufacturer for specific donning instructions.

A Pre-stretch both top and bottom straps before placing the respirator on your face.

B Cup the N95 respirator in your hand.

C Position the N95 respirator under your chin with the nose piece up. Secure the elastic band around your head so the N95 respirator stays in place.

D Use both hands to mold the metal band of the N95 respirator around the bridge of your nose.

E Fit check the N95 respirator.

4 Eye protection or face shields

- Place over the eyes (or face).
- Adjust to fit.

5 Gloves

- Pull the cuffs of the gloves over the cuffs of the gown.

May 2014

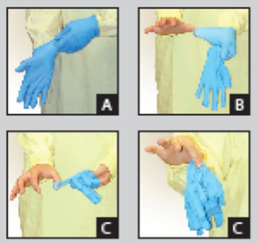
www.albertahealthservices.ca

Alberta Health Services

Infection Prevention and Control

Taking off (Doffing) Personal Protective Equipment (PPE)

1 Gloves



A Grasp the outside edge of the glove near the wrist and peel away from the hand, turning the glove inside-out.

- Hold the glove in the opposite gloved hand.

B Slide an ungloved finger or thumb under the wrist of the remaining glove.

C Peel the glove off and over the first glove, making a bag for both gloves.

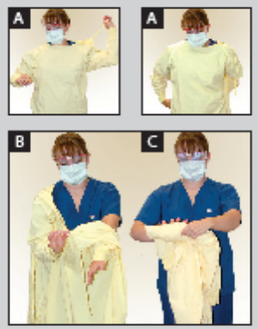
- Put the gloves in the garbage.

2 HAND HYGIENE

A Using an alcohol-based hand rub is the preferred way to clean your hands.

B If your hands look or feel dirty, soap and water must be used to wash your hands.

3 Gown



A Carefully unfasten ties.

B Grasp the outside of the gown at the back of the shoulders and pull the gown down over the arms.

C Turn the gown inside out during removal.

- Put in hamper or, if disposable, put in garbage.

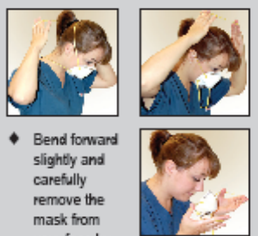
4 HAND HYGIENE

- Clean your hands. (See No. 2)
- Exit the patient room, close the door and clean your hands again.

5 Eye protection or face shield

- Handle only by headband or ear pieces.
- Carefully pull away from face.
- Put reusable items in appropriate area for cleaning.
- Put disposable items into garbage.

6 Mask or N95 respirator



- Bend forward slightly and carefully remove the mask from your face by touching only the ties or elastic bands.
- Start with the bottom tie, then remove the top tie.
- Throw the mask in the garbage.

There are different styles of N95 respirators but all styles have the same basic steps for doffing.

7 HAND HYGIENE

- Clean your hands. (See No. 2)

May 2014

www.albertahealthservices.ca

Images; AHS Donning and Doffing

Administrative Measures related to Health Care Workers

- Provision of adequate training for HCWs
- Ensuring an adequate patient-to-staff ratio
- Establishing a surveillance process for acute respiratory infections potentially caused by COVID-19 virus among HCWs
- Ensuring that HCWs and the public understand the
- Importance of promptly seeking medical care
- Monitoring HCW compliance with standard precautions and providing mechanisms for improvement

Using Environmental and Engineering Controls

- Address basic infrastructure of the health care facility[14] and aim to ensure adequate ventilation
- Maintain adequate environmental cleaning
- Separation of at least 1 metre between all patients
- Ensure that cleaning and disinfection procedures are followed consistently and correctly
- Manage laundry, food service utensils and medical waste in accordance with safe routine procedures

References

- World Health Organization
  - http://covid19.who.int

- Questions ?