April 10, 2020
4th Edition

COVID-19 Report

Finding the evidence for you

A weekly report to answer clinically relevant questions by summarizing the most recent evidence.

This information is intended for health care professionals.

Clinical Description & Epidemiology

What is the clinical presentation and outcome of SARS-CoV-2 infection in pregnant women?

- Studies are limited, but current data suggests that pregnant women are not at greater risk of developing severe COVID-19 than the general population. Clinical characteristics are similar to non-pregnant adults with most having mild to moderate symptoms.[1] Some were asymptomatic until they developed postpartum fever and/or mild respiratory symptoms.[2] Two cases from Iran reported maternal death after delivery due to acute respiratory distress syndrome (ARDS).[3]
- A systematic review identified 32 pregnant women of which 15 (47%) had preterm delivery.[4] As well, only 23 of the 32 women had reported maternal outcome, of which two required ICU admission.
- No cases of severe disease or fatal outcome was reported in nine generally healthy Chinese women infected with SARS-CoV-2 during late third trimester.[5] Of note, six were given an antiviral and all of the women were provided with oxygen support and empiric antibiotics. Post infection onset, two women experienced premature rupture of membrane and fetal distress was noted in two other women. Four of the women had preterm labour, although all were past 36 gestational weeks and the etiology was felt to be unrelated to COVID-19.
- Although there is limited data, and most are from women infected in their third trimester, the outcomes of COVID-19 in pregnancy appear less severe compared to

SARS and MERS.[6]

Are there different clinical presentations and outcomes in COVID-19 patients with malignancy or transplant?

- Malignancy: In a Chinese prospective cohort study of 1,590 symptomatic COVID-19 patients, 1% (18 patients) had malignancy, most commonly lung cancer. There was an increased risk of severe disease and mortality in those with a history of cancer. Active disease, chemotherapy or surgery within a month of infection increased likelihood of poor outcomes.[1] A preprint retrospective cohort study of 28 COVID-19 patients with cancer from Wuhan had similar findings.[2]
- Organ recipients: Nine COVID-19 case studies following a total of 17 organ transplant recipients: two cardiac,[3] four hepatic,[4,5] ten renal,[6,7,8,9,10,11] and an allogeneic bone marrow transplant[11] were reviewed. In general, presentations and timeline were similar to immunocompetent populations. Two died, three were intubated, and most required adjustment of immunosuppressive regimen. Currently, there is little data to support increased or decreased risk of severe disease or mortality for COVID-19 patients on immunosuppressive therapy for organ transplantation. Opinions are divided as to whether immuno-suppressive therapy may be somewhat protective from severe disease and adverse outcomes, while recommendations to minimize exposure to COVID-19 for immunosuppressed patients are consistent.

What is the incidence of laboratory-acquired infection of COVID-19?

- As of April 8, 2020, there have been no reported cases of laboratory-acquired infection (LAI) with SARS-CoV-2 in Canada with the completion of approximately 360,000 tests.
- There have been four cases of laboratory-acquired SARS-CoV infection since 2003.[1] All of these were attributed to a lack of understanding or adherence to safety procedures and involved laboratories where virus was being grown in cell culture. No LAI has been reported for MERS-CoV.[2]
- The WHO has provided interim guidance on laboratory safety related to COVID-19.[3] Public health labs across Canada are processing SARS-CoV-2 specimens for molecular detection in containment level 2 labs with use of appropriate PPE and biosafety cabinets.

What is the psychiatric impact of pandemic or mass casualties on healthcare practitioners? What are some strategies to mitigate the impact?

- 1,257 healthcare workers in China surveyed during the COVID-19 outbreak reported symptoms of depression (50.4%), anxiety (44.6%), insomnia (34.0%), and distress (71.5%).[1]
- During the SARS outbreak in 2003, health care workers in Toronto reported feelings of anxiety, anger, frustration, as well as fear of contagion and infection of loved ones.[2] Mental distress was exacerbated by uncertainty, changes in isolation procedures, and colleagues entering quarantine or treatment. Approximately 10% of hospital employees, at an affected Beijing hospital, reported post-traumatic stress symptoms at some point during the 3 year period post SARS outbreak.[3]
- For protection of mental well-being during the COVID-19 pandemic, staff should be provided with realistic, timely situational updates to allow for psychological preparedness. Health care workers should seek early interventions from informal support networks (such as peer supports or colleagues) with swift escalation to professional support as needed, and self-care should be practiced.[4,5]

Diagnostics & Surveillance

Does viral load correlate with symptoms or infectivity?

- Initial studies suggest that severe cases of COVID-19 are associated with higher viral loads[1] and longer lasting viral detection as compared to mild cases. 90% of mild cases are PCR-negative at 10 days post symptom onset.[2]
- Contrary to this, recent work has suggested that in mild cases of COVID-19, viral RNA detection may peak 3-8 days post symptom onset.[3] As well, sputum samples remained positive longer than upper respiratory specimens.
- Viral load detection in asymptomatic patients has not been thoroughly studied. Carriage and transmission of SARS-COV-2 have been described previously, but their contribution to population prevalence of SARS-CoV-2 is not clear.[4,5,6]

Why are we not screening asymptomatic people? Can healthcare workers (HCW) become infected from asymptomatic patients?

- Resource shortages have led to most countries restricting their testing. For Manitoba, see Shared Health's April 9, 2020 update, but for the most updated information check Info for Staff.
- Truly asymptomatic patients (never develop symptoms) may be a cause of potential super-spreading since presymptomatic patients are likely to self-isolate once symptoms develop.[1,2,3]

- Although less comparable to urban settings, mathematical modelling studies from the infamous Diamond Princess cruise-ship (Feb 2020) demonstrated that 51.7% of all cases were presymptomatic, and only 17.9% never developed symptoms.[4]
- Currently, there have been no documented cases of transmission to a HCW from a truly asymptomatic COVID-19 patient. Still, literature suggests that transmission can and does occur from both asymptomatic and presymptomatic patients, although this is likely the minority of cases.[5,6]

Therapeutics

What clinical trials for treatment of COVID-19 are currently ongoing in Canada?

- The Solidarity trial is a global initiative led by the World Health Organization to investigate four treatment options (remdesivir, lopinavir/ritonavir +/- interferon beta-1, and chloroquine or hydroxychloroquine) against standard of care to assess their effectiveness against COVID-19.[1] CATCO, the Canadian arm, will soon be recruiting hospitalized patients to evaluate lopinavir/ritonavir.
- Two other independent Canadian trials are actively recruiting to investigate hydroxychloroquine both as treatment and prophylaxis in COVID-19.[2]
- The REMAP-CAP trial is an international adaptive trial that evaluates numerous therapies (including steroids, monoclonal antibodies, antibiotics and antivirals) for the management of severe community-acquired pneumonia and was recently extended to include therapies for COVID-19.[3]
- Canadian Blood Services announced earlier this April they will be launching a trial to study the use of convalescent plasma for the treatment of COVID-19, and are in the process of securing Health Canada approval.[4]
- To stay updated, there is a geographically-organized registry of the COVID-19 trials underway throughout Canada as well as a table of all the Health Canada authorized clinical trials.

Is there any evidence for Zinc in the treatment of COVID-19?

- *In vitro*, zinc inhibited SARS-CoV-1 RNA polymerase activity and viral replication.[1] The applicability of this study is limited by its use of likely supraphysiologic zinc concentrations and an ionophore to increase cellular zinc levels. It is not known if similar effects would be seen for SARS-CoV-2.
- Zinc deficiency impairs immune response.[2] Low serum zinc correlated with all-cause mortality in an observational study of elderly patients living in a personal care home.[3] In areas of the developing world where zinc deficiency is endemic,

supplementation has shown benefit in some situations such as decreasing childhood pneumonia incidence.[4,5]

- In the setting of critical illness, low serum zinc is frequently demonstrated without correlation to clinical outcome.[6,7] It is not known whether supplementation would confer benefit in cases of severe COVID-19.

- Frequent zinc lozenges have been shown to reduce the duration of common cold symptoms in adults.[8,9] However, as coronavirus is only responsible for a minority of colds, the majority being due to rhinovirus, the efficacy of zinc supplementation in mild COVID-19 is unclear.

What are the best management strategies for patients already on inhaled steroids or who need to start a short course of oral steroids for another indication (eg: asthma or COPD), in the setting of possible exposure to SARS-CoV-2 or confirmed COVID-19 infection?

- There is presently no published evidence for the effects of inhaled or low dose oral steroids in patients with asthma or COPD in the presence of COVID-19.
- Literature from SARS-COV1 and MERS, extrapolated to SARS-COV2, indicates that intravenous steroids may cause harm.[1] Of note, doses used to treat severe COVID-19 are much higher than what is typically used to treat asthma or COPD exacerbations.
- Current guidelines by the Global Initiative for Asthma 2019 and the American Academy of Allergy, Asthma & Immunology suggest continuing inhaled corticosteroids and oral corticosteroids as indicated to treat asthma and asthma exacerbations.[2,3]
- Reducing or stopping chronic inhaled corticosteroids increases the risk of an asthma exacerbation and severe infection (RR 2.35).[4]
- In the setting of suspected or confirmed COVID-19, it is recommended to avoid nebulized medications as there is the potential for increased transmission. Inhaled medications should preferentially be delivered via metered-dose inhaler with a spacer or a valved holding chamber.[5]

Infection Prevention & Control

What have we learned from the COVID-19 outbreak in King County, Washington? Why are long term care facilities prone to COVID-19 outbreaks?

- As discussed earlier (March 27th edition) long-term care facilities (LTCFs) are particularly at risk for COVID-19 outbreaks.[1,2]

- During a COVID-19 outbreak in King County, Washington, USA, the index patient resided in a LTCF. 16 days after their diagnosis, 30% of residents in that facility tested positive for SARS-CoV-2, ~50% of whom were asymptomatic at time of testing.[3] The virus then spread to other facilities, resulting in a total of 167 positive cases.[4] LTCF residents with confirmed COVID-19 had a hospitalization rate of 54.5% and fatality of 33.7%. In comparison, fatality rates were 6.2% among visitors, and 0% among health care workers.[4]
- Some patients in this outbreak presented with few or atypical symptoms (e.g. malaise and nausea).[3] Physicians must have a high index of suspicion in this population, and consider LTCF residence as a potential exposure. Rapid case identification can prompt infection control measures that limit further spread.

- An epidemiological investigation[4] identified factors that likely contributed to this outbreak:
    - Delayed recognition because COVID-19 was not suspected, was difficult to identify based on clinical features, and limited availability of testing.
    - Transfers of patients between facilities and staff working in multiple facilities.
    - Challenges to implementing infection control practices: inadequate supplies of PPE, poor familiarity with PPE, and poor adherence to PPE recommendations.
    - Some staff worked while symptomatic

- The World Health Organization (WHO) and Shared Health Manitoba have created IP&C guidelines for LTCFs in the context of COVID-19.

Are surgical procedures in asymptomatic patients a risk for transmission of COVID-19? Can infection control measures limit this? How useful is screening or other measures to reduce transmission of COVID-19 in this setting?

- Periprocedural transmission of SARS-CoV-2 to healthcare workers has likely occurred following C-section or lower-limb surgeries performed on COVID-19 positive patients from Wuhan, China who underwent spinal anaesthesia.[1] Further, it is known that patients without symptoms contribute to viral spread and can have viral loads similar to those with symptoms.[2]
- Stringent and multi-faceted infection prevention and control measures can prevent perioperative viral transmission, even during high-risk procedures. Institutions that were able to protect all of their OR staff from contracting infections from infected surgical patients during the SARS epidemic attributed their success to: 1) enhanced personal protection (e.g. positive air-powered respirator for high-risk procedure or patient), 2) OR/ICU reorganization (e.g. geographic segregation, negative-pressure rooms, and minimizing staff involved), 3) minimizing intraoperative exposure to

aerosolized secretions (e.g. surgical technique, reduced suction use), and 4) safe equipment disposal/decontamination.[3]

- The choice of institutional strategies must take into account the local disease prevalence, testing capacity, and institutional capacity to implement preventative measures perioperatively:
    - Screening asymptomatic patients: CT scans and PCR tests will identify some patients without symptoms. However, currently no evidence confirms either their reliability in the setting of high disease prevalence, or their efficiency in the setting of low prevalence, when used for this purpose.
    - Universal use of enhanced infection and control measures: Routine implementation of comprehensive measures is resource-intensive and not feasible in all institutions.
    - Deferral of non-emergent surgery: Evidence from modeling studies suggests this may be effective. Additionally, observational data has raised the concern that asymptomatic SARS-CoV-2 positive patients who undergo surgery may develop worse COVID-19 related outcomes.[4,5]
- Current guidelines for COVID-19 screening prior to essential surgeries in Manitoba can be found on the Shared Health website at under Resources for Specialty Areas – Surgery/Procedures. If possible, patients requiring non-emergent surgery should first undergo 14 days of self-isolation. If surgical patients are symptomatic, they are screened for COVID-19 using RT-PCR.

Public Health Interventions

How effective is the use of temperature monitoring to screen for COVID-19 amongst healthcare workers or the general public? What method of temperature measurement is most effective – contact thermometry vs infrared?

- Contact thermometry methods include rectal, oral, tympanic, and axillary – in decreasing order of accuracy.[1] Oral measurement is more accurate than infrared thermometry, but is more time consuming, has increased risk of contact with bodily fluids, and is more invasive.[2] Infrared thermometry accuracy is affected by many variables including individual factors (age, sex, facial hair, and cosmetic use) and external factors (model of device used and environmental settings).[1]
- Thermal screening for healthcare workers has been described, but there is no data on its effectiveness for detecting COVID-19.
- For screening the general population, most studies have focused on the airport setting. All studies on this topic found that temperature monitoring, in isolation, is an

inadequate screening tool. One study estimated that as many as 46% of SARS-CoV-2 positive patients may be missed by this method.[3]

- The challenges of relying on temperature screening alone for COVID-19 are multifactorial and include (i) asymptomatic or presymptomatic infection,[4] (ii) fever is not present in all symptomatic cases as discussed in our March 21st edition, (iii) purposeful deception by people taking antipyretics and thus masking their fever,[5] and (iv) thermometry equipment factors.
- If employed, thermal monitoring should be used in conjunction with other screening methods for the detection of COVID-19.

Pediatric Corner

Which laboratory findings are associated with COVID-19 in pediatric patients? Do they differ from adult findings?

- In the current literature, laboratory abnormalities including lymphopenia are less common in children compared to adults.[1] In a systematic review of 66 children[2] and another study of 171 children[4], leukocyte counts were within normal range in 69.6%-73.7% of cases, with lymphopenia found in only 3.0-3.5%. The latter study also reported elevated procalcitonin in 64% of cases, but similar to adult patients, it is felt that this is most likely indicative of bacterial co-infection.
- A small study of 36 children reported that lymphopenia, elevated procalcitonin, elevated D-dimer, and elevated CKMB had statistically significant association with moderate disease compared to asymptomatic or mild cases.[3] Leukocyte count, CRP, CK, and liver enzymes were abnormal in a minority of cases with no statistically significant relationship to illness severity.

What are the critical care guidelines for pediatric patients with COVID-19?

- Most cases of COVID-19 in children are mild, with only 0.6% of cases requiring admission to intensive care in a large Chinese case series.[1] Pediatric deaths are rare.[1,2]
- To date, there is no literature specifically documenting the ICU management of pediatric patients with COVID-19. An expert consensus statement from China recommends early invasive mechanical ventilation with low tidal volumes to decrease ventilator-related lung injury.[3] They describe a two hours trial of non-

invasive ventilation as acceptable, but providers should be cognizant that CPAP and BiPAP are aerosol-generating modalities and appropriate personal protective equipment is required.

- In the absence of COVID-19-specific literature for severely ill children, consider the pediatric acute respiratory distress syndrome (ARDS) guidelines.
- At this time, there have been no recommendations for specific vasoactive medications or fluid consideration.
- National and local pediatric ICU guidelines for COVID-19 are currently being discussed.

What is the psychological impact of a pandemic or mass casualties on children?

- Disasters, including pandemics, can detrimentally impact the psychological well-being of children.[1,2] Clinicians should discuss this potential with pediatric patients and their families. Pandemics raise unique challenges due to physical distancing measures.
- Previous research has shown that following a disaster, many children experience adjustment reactions, which include sleep and eating problems, depression, anxiety, concentration difficulties, substance abuse, and developmental or social regression. These symptoms may be more likely with separation from important caregivers and disruption in daily routines.[1]
- A study of pandemic disasters that interviewed 398 parents found that of those who were quarantined or isolated, 33.4% reported that their children began using mental health services related to their experience. Common diagnoses were acute stress disorder, adjustment disorder, and grief. Children who experienced isolation or quarantine were more likely to meet criteria for PTSD based on parental report than those who did not (30% vs. 1.1%).[3]
- In a small study, children 6 to 18 years old with probable or suspected SARS in 2003, reported feelings of sadness attributed to being alone, worrying about family members, and feelings of being punished while hospitalized and isolated from their caregivers.[4] Similarly, 21 children aged 5 to 19 years who were hospitalized during the period of strict infection control practices reported feeling isolated.[5] They also described feelings of anxiety, fear, and confusion related to a lack of information and conflicting messages about SARS.

The information presented reflects the data that is currently available to us. In the context of a pandemic where rapid dissemination of information is essential, we have included information from evolving medical literature which may be awaiting peer-review.

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