



## Addressing therapeutic questions to help Canadian physicians optimize asthma management for their patients during the COVID-19 pandemic

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This position statement aims to provide rapid guidance for Canadian physicians treating patients with asthma during the COVID-19 pandemic. The recommendations are informed by a very limited body of direct published data, inference from the indirect data, and recommendations from the guidelines of other international bodies. As such, these recommendations are primarily based on expert opinion and we recommend that treatment decisions be individualized.

*Readers seeking a complete review of current data are directed to the special article entitled "COVID-19: Pandemic Contingency Planning for the Allergy and Immunology Clinic" prepared by specialists in the areas of allergy, asthma and clinical immunology from Canada and the United States. The article is referenced,<sup>1</sup> is available on the Canadian Society of Allergy and Clinical Immunology website and is currently "in press" with the *The Journal of Allergy and Clinical Immunology: In Practice*.*

### Asthma management: General statement

In the absence of direct or indirect data that SARS-CoV-2 impacts the safety and efficacy of current asthma therapies, ***we recommend that maintenance and exacerbation management for asthma be continued according to current national and international asthma treatment guidelines. Optimal asthma control is expected to be the best protection against a SARS-CoV-2 exacerbation.***<sup>2-5</sup> The primary goal of asthma management is to control the disease and, by doing so, prevent or minimize the risk of short- and long-term complications, morbidity and mortality.<sup>2-5</sup>

### Risk of acquiring SARS-CoV-2 infection (COVID 19) by patients with asthma

***There does not appear to be an increased risk for asthma patients to acquire SARS-CoV-2 infection (COVID-19) compared to the general population***

**Rationale:** Two studies from China and one from Korea did not find that hospitalized patients with asthma were over-represented in the COVID-19 populations studied.<sup>6-8</sup>

### Risk and severity of asthma exacerbation caused by SARS-CoV-2 (COVID 19)

***We suggest that patients with asthma be advised to restart or continue their prescribed inhaled corticosteroid or inhaled corticosteroid steroid plus long-acting beta<sub>2</sub>-agonist maintenance therapy to improve disease control and to reduce the severity of viral-induced exacerbations including exacerbations that may be caused by SARS-CoV-2***

**Rationale:** There are no direct data to evaluate the risk of having an exacerbation or the severity of exacerbation associated with SARS-CoV-2.

**Risk:** It is probable that SARS-CoV-2 can trigger asthma exacerbations. Viral respiratory tract infections are a common cause of asthma exacerbations.<sup>9</sup> Exacerbations requiring emergency department visits and hospitalizations increase annually at times when viral infections increase, typically week 38 on the calendar.<sup>10</sup> Non-pandemic coronaviruses have been associated with asthma exacerbations.<sup>11,12</sup>

Improving asthma disease control is expected to reduce the frequency and severity of exacerbations.

**Severity:** As mentioned in the previous section, two studies from China and one from Korea did not find that hospitalized patients with asthma were over-represented in the COVID-19 populations studied.<sup>4-6</sup> One report from Italy reporting 481 deaths and one from China reporting 54 deaths did not identify asthma as a co-morbid risk factor.<sup>13,14</sup>

### **Safety of using systemic corticosteroids (prednisone) to treat asthma exacerbations during the SARS-CoV-2 (COVID 19) pandemic**

***We suggest using prednisone to treat severe asthma exacerbations as recommended in current national and international asthma guidelines during the SARS-CoV-2 (COVID 19) pandemic, whether or not the exacerbation is triggered by SARS-CoV-2***

#### **Rationale:**

A) Use of prednisone to treat an asthma exacerbation “not suspected” to be caused by SARS-CoV-2. Prednisone is recommended for the treatment of severe asthma exacerbations in international asthma guidelines including with viral induced exacerbations.<sup>2-5,15,16</sup> Non-pandemic coronavirus infection contributes to these exacerbations.<sup>9,12</sup> If prednisone-requiring exacerbations are not treated, patients may require an avoidable emergency department visit or hospitalization (which could also expose them to SARS-CoV-2). There is no available evidence of harm caused by using prednisone to treat asthma exacerbations during the pandemic. The brief course of prednisone used to treat acute asthma exacerbation is not expected to compromise the immune system sufficiently to increase chances of acquiring SARS-CoV-2 and/or developing COVID-19.

B) Use of prednisone to treat an asthma exacerbation “suspected” to be caused by SARS-CoV-2. There is a concern that prednisone may prolong viral replication.<sup>17</sup> It remains unclear as to whether prednisone is helpful or harmful in the treatment of COVID-19. Russell and colleagues reviewed observational data and concluded there was no benefit to using prednisone to treat SARS-CoV-2 lung injury.<sup>18</sup> Front-line physicians from the Chinese Thoracic Society challenge this assertion and take the position that since the evidence is inconclusive and since SARS-CoV-2 lung injury is profoundly inflammatory that corticosteroids make play an important role. They recommend that physicians should follow basic principles when using corticosteroids: “(1) the benefits and harms should be carefully weighed before using corticosteroids; (2) corticosteroids should be used prudently in critically ill patients with SARS-CoV-2 pneumonia; (3) for patients with hypoxemia due to underlying diseases or who regularly use corticosteroids for chronic diseases, further use of corticosteroids should be cautious; and (4) the dosage should be low to-moderate ( $\leq 0.5-1$  mg/kg per day methylprednisolone or equivalent) and the duration should be short ( $\leq 7$  days).”<sup>19</sup> Arabi and colleagues found that after adjusting for confounders, there

was no mortality signal associated with prednisone use in the Middle East Respiratory Syndrome.<sup>20</sup>

In the absence of evidence of harm and an expectation of a low risk of harm, we prioritized the high value of current evidence-based care recommendations to treat asthma exacerbations with prednisone to reduce the need for urgent health service utilization.

### **Safety of using inhaled steroids**

***We suggest that patients with asthma restart or continue to use their inhaled asthma controller medications during the COVID-19 epidemic***

**Rationale:** There is no current evidence that inhaled corticosteroids increase the risk of acquiring SARS-CoV-2 infection (COVID-19) or that inhaled corticosteroids increase the severity of infection. To the contrary, it is likely that the SARS-CoV-2 could cause an asthma exacerbation, making it a high priority to achieve well controlled asthma as protection against a severe asthma exacerbation. In the absence of evidence of harm and an expectation of a very low risk of harm from inhaled corticosteroids, we prioritized the high value of asthma control to reduce the frequency and severity of exacerbations.

### **Use of biologics to manage severe asthma**

***We suggest that anti-IgE and anti-IL5 monoclonal antibodies (biologics) be continued during the COVID-19 pandemic. If biologic therapies are interrupted temporarily, we suggest stepping-up other controller therapies on an individualized basis which may include adding low dose prednisone, high or very high dose inhaled corticosteroid with long-acting beta2-agonist therapy, or long-acting anti-muscarinic therapy. Where available, providers may consider switching patients to self-administration of biologics at home***

**Rationale:** Anti-IgE and anti-IL5 monoclonal antibodies are currently approved for use in Canada to treat severe allergic and severe eosinophilic asthma.<sup>3</sup> A primary benefit of biologic agents is to reduce the frequency of severe asthma exacerbations. Discontinuing these medications during the COVID-19 pandemic would be expected to increase the frequency of severe exacerbations and increase the likelihood that patients would need to enter the health system through an urgent physician visit, emergency department visit, or hospitalization. Furthermore, the loss of asthma control associated with discontinuing medications may make the patient more vulnerable to a severe exacerbation associated with a viral infection. Mechanistically and based on the published literature on biologic agents, including long-term follow-up studies, we do not expect that the immune response to viral infection would be impaired by these agents. Notably, Esquivel and colleagues identify that Omalizumab may protect against viral induced exacerbations.<sup>21</sup> In the absence of evidence of harm and an expectation of a low risk of harm, in high risk severe asthma patients, we

prioritized the high value of biologic agents to treat severe asthma to improve control and to reduce exacerbations including the need for urgent health service utilization.

### Safety of nebulizer use in asthma

**We suggest that nebulizers be replaced by metered dose inhalers with spacing devices or dry powder inhalers to administer inhaled-corticosteroids and short-acting bronchodilators inside healthcare facilities including nursing homes to reduce the risk of aerosol spread of virus particles. Patients who are already using nebulizers to administer therapy at home should continue until such time as their provider can discuss switching to metered dose inhalers with a spacing device or dry powder inhalers**

**Rationale:** Metered dose inhalers with spacing devices are more effective than nebulization and the preferred method of delivery even for acute exacerbations in the emergency department and hospital, and even under non-pandemic circumstances. Dry powder inhalers are another alternate. A recent nebulization experiment elevates concern that clinical nebulization devices pose a risk of aerosolization of SARS-CoV-2, placing healthcare workers and caregivers at risk for infection.<sup>22</sup> The recommendation to avoid nebulization applies to all patients, not only to patients that have confirmed or suspected COVID-19. We placed a high value on selecting the most effective method of delivery while reducing any potential risk of disease transmission.

### Physical distancing for asthma patients

**We suggest that all patients with asthma follow current local, national public and global health advisories with respect to the indications for physical distancing and isolation. Patients with mild-moderate asthma should work from home if feasible. Patients with severe asthma should also work from home if feasible and, if not feasible, should remain off work for medical reasons until such time as the WHO or local public health authorities declare that physical distancing is no longer necessary**

**Rationale:** Longitudinal experience with seasonal influenza has been extended to infer that patients with chronic lung disease are at risk for severe complications of SARS-CoV-2 infection (COVID-19). Physical distancing is an important public health measure to “flatten the curve” of community spread of the virus. The workplace is a social environment that may expose patients to others in their community, particularly if physical distancing in the workplace setting is difficult to implement. Until we fully understand the risks associated with SARS-CoV-2 infection in patients with chronic lung disease, we have placed a high value on limiting exposure based on prior experience with influenza.

### We will review our recommendations at least every two weeks and as more information becomes available

The pandemic is a rapidly evolving situation. Clinicians are advised to look to the Canadian Thoracic Society website for resources and links to asthma action plans and tutorial videos for children and adults for the proper use of inhalers and puffers as well as further updates on COVID-19 and lung diseases.

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