



# npcurrent

Canadian Journal for Nurse Practitioners

2021  
ISSUE 7

## **Acute Migraine Treatment**

A new combination therapy

## **Asthma Management**

An update

## **Multiple Sclerosis**

The role of the nurse practitioner

## **SARS-CoV-2 in Children**

Most predictive symptoms  
of a positive test

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retinitis pigmentosa



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parathyroid failure



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atypical cerebral palsy, learning  
disabilities



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5420 Highway 6 North, Suite 434  
Guelph ON N1H 6J2  
[www.npcurrent.ca](http://www.npcurrent.ca)

ISSN 2561-8059

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## Information for Authors

### Types of Contributions

We welcome all contributions that are of potential interest to nurse practitioners, including but not limited to the following categories:

**Original Research** – Please follow the standard format of scientific manuscripts with the inclusion of an abstract, introduction, methods, results, discussion and conclusion. Tables and figures must be submitted in an editable word file.

**Key Concepts** – Brief contributions on topics of interest to nurse practitioners, such as new therapeutic approaches or frequently encountered clinical conditions.

**Practice Perspectives** – An article that illustrates diagnosis, treatment or management concepts, including innovative NP-led initiatives.

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Submitted articles must not have been previously published (abstracts and theses excluded) or under consideration for publication in the same format elsewhere.

### Authorship

All authors must have made substantial contributions to the development of the article.



# Acute Migraine Treatment: Recent Advance in Combination Therapy

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## Migraine: A common problem

Nurse practitioners (NP) working with clients in primary or emergency care are likely to encounter migraines as a frequent illness that must be treated; it is estimated that 2.7 million Canadians suffer from migraines.<sup>1</sup> Migraines have significant impact on day-to-day functioning, with those suffering migraines reporting missing work, school and social events (Table 1).<sup>2</sup> Worldwide, migraine is the 6<sup>th</sup> highest cause of years lost to disability.<sup>3</sup> Not only are there concerns for the impact on overall quality of life for migraineurs, but there is an associated cost to this disabling condition. CIHI data has found that the direct and indirect costs of headaches on the health system are on par with those associated with other neurologic conditions such as epilepsy and multiple sclerosis.<sup>4</sup>



Unfortunately, the most recent Health Canada survey on the topic, found that the average time to diagnosis from onset of symptoms was 3.6 years and only 42% of migraineurs had ever tried a prescription medication.<sup>1</sup> That migraines are often under-recognized and under-treated is a concern given the significant impact they have on both patients, often in their most productive years of life, and the health care system.

## Migraines: How to recognize them

The Lipton 3 item ID migraine screener is a tool NPs can use to help them diagnose migraines.

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**Table 1.** How does migraine impact patients and families?

School, Work, and Social Impact in Previous 3 Months	
Missed $\geq 1$ day of work/school	25%
Work/school productivity reduced by $\geq 50\%$	28%
Did no household work	48%
Household productivity reduced by $\geq 50\%$	34%
Missed family or social activity	29%

Lipton RB et al., Neurology. 2007;68:343-349

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# Acute Migraine Treatment: Recent Advance in Combination Therapy

Continued from page 3

With a positive response to 2 of the 3 items there is a 93% predictive value, making it a quick, simple and effective tool (Table 2).<sup>5</sup> Although effective, it is critical to always keep in mind during clinical assessments for headache, the SNOOP4 red flags (Table 3).<sup>6</sup> Migraine headache is frequently misdiagnosed as sinus headache. In a study of patients who had a history of HCP- or self-diagnosed sinus headache, 80% of patients met the International Headache Society criteria for migraine.<sup>7</sup> Migraine symptoms that closely resemble sinus headache symptoms include facial pain and pressure over frontal sinuses and nasal congestion.<sup>8</sup>

## Migraines: How and when to treat

It is important that clinicians understand not only how a migraine presents but also how and when to treat to most effectively manage the migraine. To do so, a review of the physiologic changes that occur with migraine and the associated symptoms is useful.

Migraines are a complex neurologic condition involving the trigeminal vascular system, neurogenic inflammation, and CNS hyperexcitability. They occur in 4 phases: prodrome, aura, headache, and postdrome.

**Table 2.** 3-Item ID migraine screener

During the last three months, did you have any of the following with your headaches?	Yes / No	
You felt <u>nauseated or sick</u> to your stomach when you had a headache?	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<u>Light bothered you</u> (a lot more than when you don't have headaches?)	Yes <input type="checkbox"/>	No <input type="checkbox"/>
Your headaches <u>limited your ability</u> to work, study or do what you need to do for at least one day?	Yes <input type="checkbox"/>	No <input type="checkbox"/>

**Table 3.** Red flags in headache: SNOOP4

<b>S</b>	<b>S</b> ystemic signs or symptoms	Fever, myalgias, weight loss, malignancy, HIV
<b>N</b>	<b>N</b> eurologic signs or symptoms	Hemiparesis, hemi-sensory loss, diplopia, dysarthria
<b>O</b>	<b>O</b> nset sudden	Thunderclap – Sudden onset is split-second & out of the blue
<b>O</b>	<b>O</b> lder	Onset after age 50
<b>P</b>	<b>P</b> attern change	<b>P</b> rogressive headache – loss of headache-free periods <b>P</b> recipitated by Valsalva maneuver <b>P</b> ostural aggravation – worse standing or lying <b>P</b> apilledema

Dodick D. Pearls: Headache. Semin Neurol. 2010;30:74-81.

Continued on page 6

# Acute Migraine Treatment: Recent Advance in Combination Therapy

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## Patient Assessment Questions to Guide Therapy

- Where does the headache begin?
- What is the frequency and duration of the headache?
- Where is the pain? Can you describe it?
  - Like an icepick? Stabbing? Throbbing? Pulsing? Pressure?
- Does the headache come with associated symptoms?
  - Sensitivity to light, noise, smell? Nausea or vomiting?
- Describe the level of disability?
  - Does it interfere with work? Home?
  - Is patient bedridden or able to function?
- Are there any red flags?
- How is headache treated now? What has patient already tried?  
For acute treatment, prevention or rescue?
- What is the monthly frequency of attacks and use of medications?

– Dr. Rose Giammarco



The headache phase can be considered in two parts, early, when pain is mild, and late when pain is moderate to severe. Regardless which medication is chosen, the most ideal time to treat a migraine is when the headache first begins and is mild.<sup>9,10</sup>

It has also been shown that if treatment is delayed and central sensitization has occurred (as evidenced for example by

allodynia) then treatment efficacy with triptans is reduced.<sup>10</sup>

Working with patients to help them understand the phases of their migraines and the ideal window in which to treat can help them achieve more effective control. Early treatment of migraine and associated symptoms may prevent allodynia and reduces the risk of recurrence and need for rescue medication.

### What is central sensitization?<sup>11,12</sup>

- When the brain's neurons become hyper-excitabile and once it has begun, it maintains itself without any input
- The main symptom is allodynia

### What is allodynia and how do I teach my patient to recognize it?

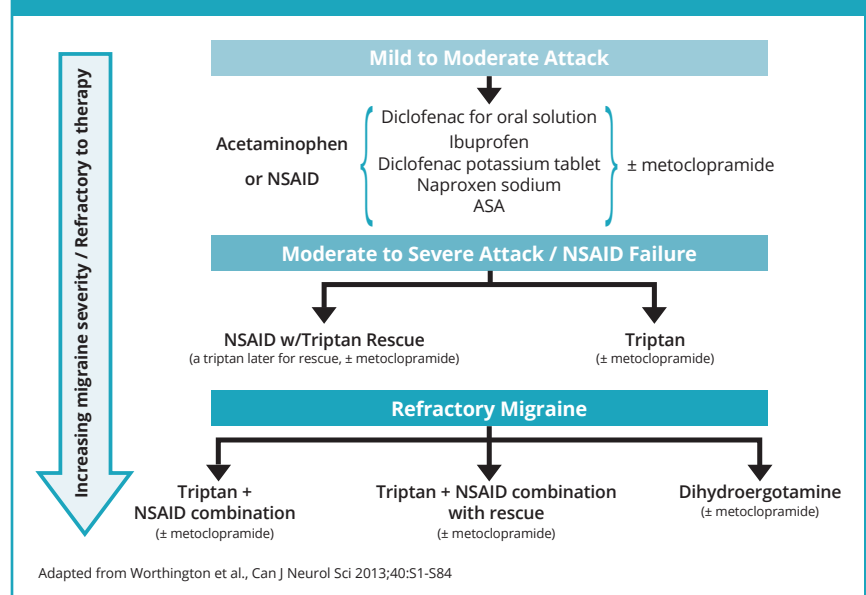
- Patient feels pain from something that normally should not cause pain
- The most common places to see cutaneous allodynia in migraineurs are the scalp, face and neck
- Examples of allodynia symptoms include feeling pain from wearing glasses, brushing hair, water on face from shower

## Migraines: How to treat

The Canadian Headache Society (CHS) offers guidelines on the treatment of acute migraines.<sup>10</sup> The CHS recommends acetaminophen or NSAIDs for mild to moderate migraine attacks. An NSAID with triptan rescue or a triptan is recommended for moderate to severe migraines or when NSAIDs alone have failed (Figure 1).

Medication recommendations for patients should be individualized, attending to both severity of episodes and previously trialed medications and responses.

Figure 1. CHS acute migraine treatment strategies



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# Acute Migraine Treatment: Recent Advance in Combination Therapy

Continued from page 7

When working with patients to determine the most effective medications for their migraine attacks the CHS suggests a “step care across attacks” approach, beginning with an NSAID, then moving to a triptan and then moving to a combination of the two.

## Role of combination therapy

Due to the multiple mechanisms at play in the pathophysiology of migraines, there is a role for combination therapy using both an NSAID and a triptan. The CHS recommends a triptan and NSAID combination with or without rescue or dihydroergotamine for refractory migraine.<sup>10</sup>

### Sumatriptan/naproxen fixed dose combination tablet (85/500 mg)

A fixed-dose, single tablet combination medication which contains the NSAID naproxen sodium and the triptan sumatriptan (Suvexx) is available in Canada as of September 2020. Despite being new to the Canadian market, Suvexx has been available and in use in the United States for over a decade under the brand name Treximet.

Brandes et al. conducted two parallel group randomized control trials comparing sumatriptan/naproxen single tablet (Suvexx) to naproxen alone, sumatriptan alone and placebo.<sup>13</sup> The fixed-dose single tablet sumatriptan/naproxen was more effective for headache relief at 2 hours (more than half of patients had pain relief at 2 hours) and for sustained 2-24 hours headache pain relief than either naproxen or sumatriptan alone.<sup>13</sup> The fixed-dose single tablet-treated patients also

“

The use of sumatriptan and naproxen sodium in a combination tablet “to treat migraine attacks is based on several randomized controlled trials which have shown that the combination is more effective than either drug used alone.” – CHS Guidelines

”

required significantly fewer rescue medications to treat their migraine attack and showed a higher percentage of patients who were pain-free post-treatment.<sup>13</sup>

As has been demonstrated in multiple studies, triptans are more effective when taken early in the migraine. Silberstein et al. conducted two double-blind, placebo controlled randomized control trials and found that the fixed-dose, single tablet sumatriptan/naproxen when taken within one hour of headache onset and while pain was still mild, was significantly more effective at providing 2-hour pain-free response

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# Acute Migraine Treatment: Recent Advance in Combination Therapy

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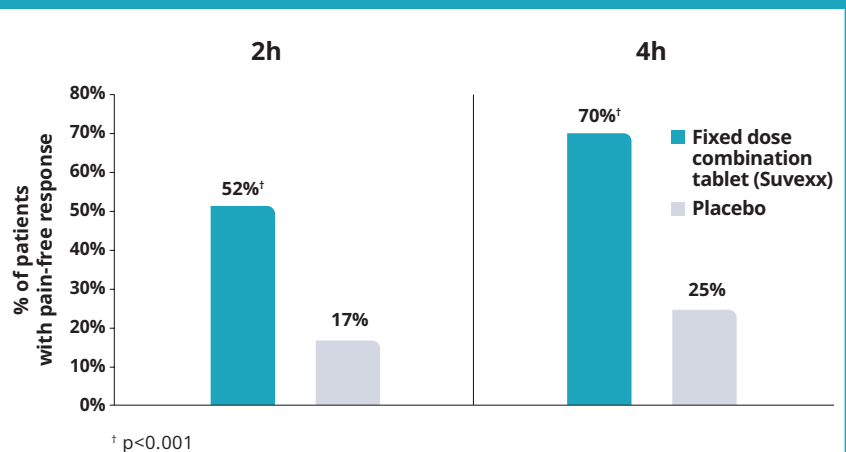
vs placebo (Figure 2). Furthermore, 86% of patients who were pain-free at 2 hours remained pain-free at 24 hours.<sup>14</sup>

In examining the pharmacokinetics, the fixed dose single tablet combination reveals differences. The maximal plasma concentration ( $T_{max}$ ) of sumatriptan is reached earlier than when given alone, and the  $T_{max}$  of naproxen is delayed by 5 hours than when components are taken individually (Figure 3).<sup>15,16</sup>

Two subsets of migraineurs may uniquely benefit from combination therapy: those who have had multiple triptan failures and those with menstrual migraines.

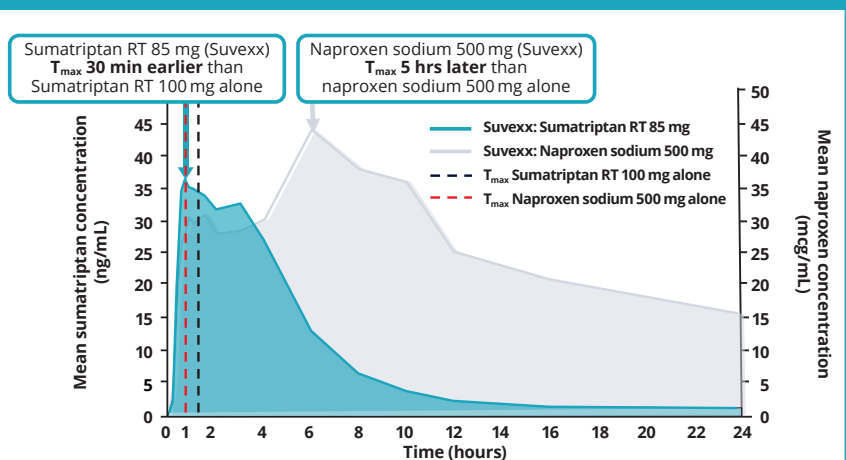
Mathew et al, undertook a multi-site double-blind placebo controlled RCT with patients who had trialed an average of 3.3 triptans and had discontinued them due to either ineffectiveness or intolerability.<sup>17</sup> Participants were again instructed to take the medication within 1 hour of headache onset when still mild. The authors found that compared to placebo, participants had improved pain-free response at both the 2hr and sustained pain-free response from 2-24 hours

**Figure 2. Early intervention with fixed-dose combination tablet: pain-free outcomes**



Silberstein S et al. Neurology 2008;71:114-121

**Figure 3. Earlier sumatriptan  $T_{max}$  and delayed naproxen  $T_{max}$  in combination tablet vs. the components taken alone**



Adapted from Haberler L et al. Headache 2010;Mar:357-373

(Figure 4).<sup>17</sup> This was very similar to outcomes seen in a less refractory population.

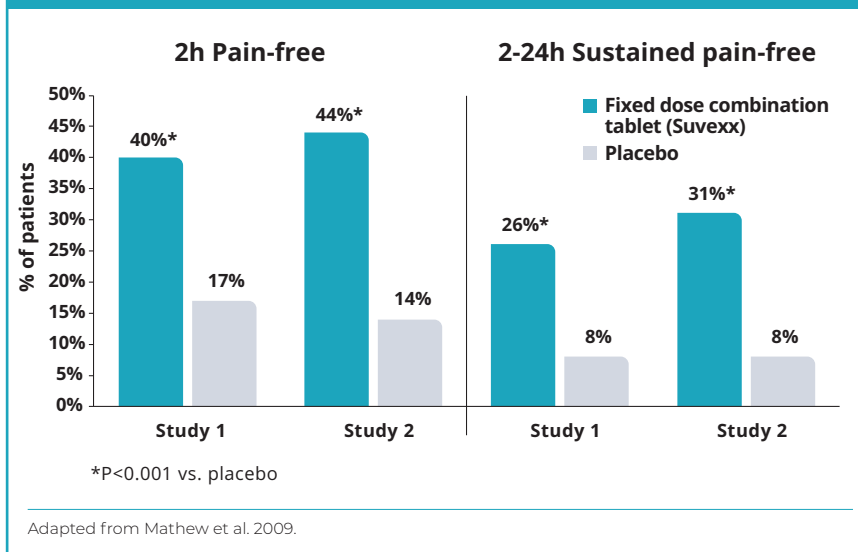
Menstrual migraines are defined as a migraine which occurs either 2 days prior to or 3 days following the onset of menses. Migraines associated with menses are typically harder to treat and longer lasting.<sup>10</sup> Mannix et al, undertook 2 replicate double-blind placebo controlled RCTs to evaluate sumatriptan/naproxen single tablet combination therapy in women who suffer menstrual-related migraines.<sup>18</sup> Patients were more likely to be pain-free at 2 hours and most patients treated with the fixed dose combination tablets continued to be pain-free through 24 hours compared to placebo (Figure 5). The fixed dose combination tablet also significantly decreased non-painful menstrual symptoms of bloating, tiredness and irritability versus placebo.

## Side effects/compliance

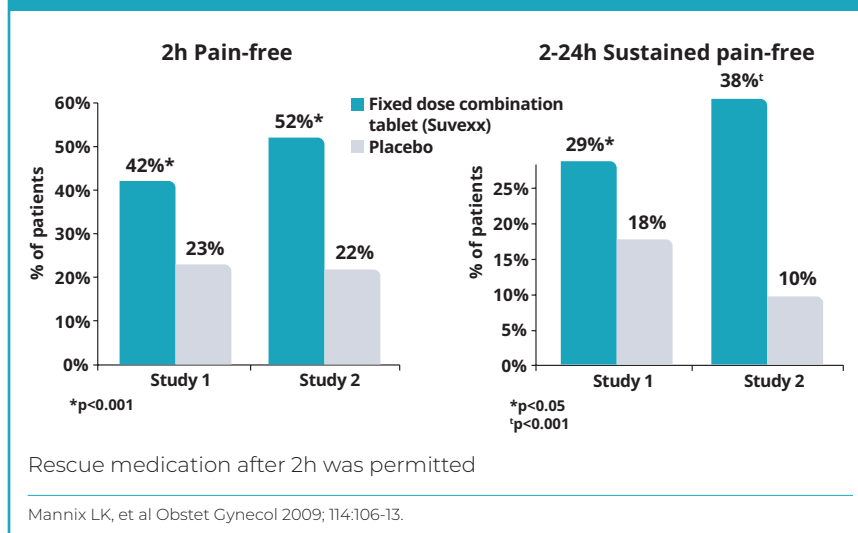
The safety profile of the single tablet sumatriptan/naproxen is similar to both drugs alone and the side effect profile is similar as when used in monotherapy. Adverse events seen with the fixed dose combination tablet treatment did not differ meaningfully from those seen with sumatriptan or naproxen monotherapy in controlled trials.<sup>16</sup>

Compliance is likely to be enhanced by a single tablet combination therapy over combination therapy using each component individually.

**Figure 4. Efficacy of fixed dose combination tablet in triptan poor responders**



**Figure 5. Menstrual migraine and dysmenorrhea 2h and sustained pain-free response**



Patients prescribed both an NSAID and triptan to use in combination were found to vary their medication use with only 10% using their NSAID and triptan in their next attack at the same time.<sup>19</sup>

Being able to prescribe combination therapy in a single tablet offers an opportunity to mediate these obstacles and increase compliance in the effort to help patients achieve better migraine control and more pain-free days.

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# Acute Migraine Treatment: Recent Advance in Combination Therapy

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## Summary

Migraine is a commonly encountered clinical problem that greatly impacts patients' quality of life. Accurate diagnosis of migraine is essential for directing therapeutic choices and educating patients on how best to manage their migraines. The Canadian Headache Society guidelines provide evidence-based direction on therapeutic choice. A fixed-dose, single tablet NSAID/triptan combination medication of naproxen sodium and sumatriptan (Suvexx) is now available in Canada. Patients who could benefit from this treatment combination include those with moderate to severe migraines, menstrual migraine, triptan poor responders, those patients who experience a recurrence of migraine within the first 24 hours.

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# Asthma Management: An Update

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## Introduction

Independent clinicians such as physicians and nurse practitioners are expected to draw on evidence-based information to guide their treatment of various disorders in a safe and effective manner.<sup>1</sup> In disorders such as asthma, clinicians are expected to diagnose the patient based on a cluster of symptoms they present, categorize the severity of their condition, and decide on a treatment plan.<sup>2</sup>

The authors of this article will present an overview of asthma, and provide an outline for treatment based on different levels of asthma severity. This will assist NPs in the process of prescribing asthmatic treatment.

## Pathophysiology

Asthma is a chronic respiratory condition that affects more than 300 million people across the globe.<sup>3</sup> It is a challenging syndrome due to its vague and complex pathogenesis and while there are several approaches to controlling

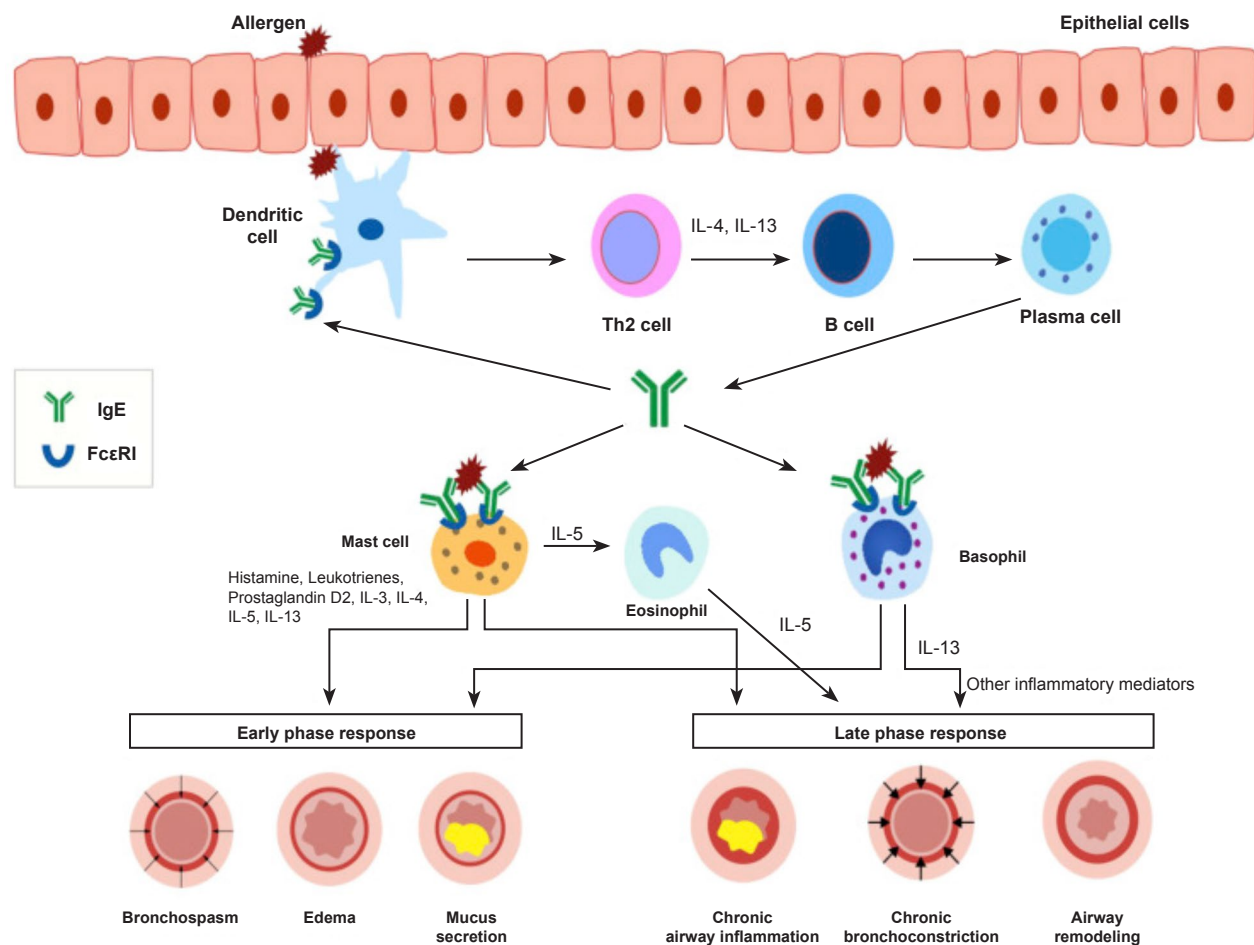
asthma, there is no cure.<sup>4</sup> Asthma continues to be a burden not only for the patients, but also the healthcare system, and there is a continued need for better management of this syndrome.<sup>4</sup>

Asthma has been described as a heterogenous disorder as it involves a collection of various symptoms such as wheezing, coughing, chest tightness, and shortness of breath.<sup>4</sup> The complexity of asthma is due to its various clinical phenotypes whose expression is influenced by environmental factors and gene susceptibility.<sup>3</sup> Asthma phenotypes are defined as recognizable combinations of clinical and/or pathophysiological characteristics.<sup>2</sup> Some phenotypes identified by the Global Initiative for Asthma (GINA)<sup>2</sup> include allergic asthma, non-allergic asthma, adult-onset, asthma with persistent airflow limitation, and asthma with obesity.

Asthma is initiated when a certain trigger, such as a pollutant or other risk factor, enters the body and triggers the immunoglobulin E (IgE) antibodies which are sensitized and released

**Figure 1. Shows the pathophysiology as an allergen which triggers dendritic cells, which then triggers plasma cells to release immunoglobulin E antibody (IgE). The IgE attaches to mast cells to result in bronchospasm, edema, and mucus secretion, along with the help of interleukins. In severe cases, The IgE will attach to basophils which will result in chronic inflammation and bronchoconstriction, along with airway remodeling.**

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Adapted from Humbert et al., 2019, p. 1420

by plasma cells.<sup>5</sup> The IgE antibodies bind to mast cells in the body which causes the mast cells to release cytokines and degranulate.<sup>5</sup> The degranulation of mast cells releases histamine, prostaglandins, and leukotrienes which cause reversible inflammation and bronchoconstriction.<sup>5</sup>

In severe cases, airway remodeling also takes place which results in the thickening of the mucosal cells in the airway.<sup>6</sup> Airway remodeling paired with bronchoconstriction can result in excessive airway narrowing which can be fatal in some patients.<sup>6</sup>

## Diagnosis

Asthma is a general term that encompasses a variety of pulmonary disorders who all share the characteristic of having reversible airway obstruction.<sup>7</sup> Patients with asthma display clinical symptoms such as chest tightness, wheezing, cough, and dyspnea.<sup>7</sup> According to GINA patients diagnosed with asthma have confirmed variable expiratory airflow limitations, altering their forced expiratory volume in one second (FEV<sub>1</sub>) and peak expiratory flow (PEF) scores. The

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# Asthma Management: An Update

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definition of airway obstruction is a spirometry measurement of FEV<sub>1</sub> less than 0.8. As the FEV<sub>1</sub> score decreases asthma patients tend to deteriorate and their management becomes challenging.<sup>5</sup> Asthma can be classified into four different groups depending on spirometry and/or clinical indications: intermittent, mild, moderate, and severe.<sup>5</sup> Intermittent asthma is when the patient experiences symptoms less than two days a week, and nighttime awakenings less than two times a month.<sup>5</sup> Mild asthma is classified as experiencing symptoms more than two times a week, with nighttime awakenings averaging three to four times per month.<sup>5</sup> Those with moderate asthma experience symptoms daily, and have nighttime awakenings greater than once a week. Lastly, severe asthma is where the patient is symptomatic throughout the day and can have more than seven nighttime awakenings per week.<sup>5</sup>

Chronic obstructive pulmonary disease (COPD) adds to the difficulty of diagnosing asthma as the two conditions have similar symptoms such as wheezing, coughing, and dyspnea.<sup>7</sup> However, the distinguishing feature between the two is the irreversible damage of the lung parenchyma and limited response to therapy in patients with COPD.<sup>7</sup> COPD is also highly associated with the inhalation of cigarette smoke whereas asthma has many different triggers and, in most cases, begins at a young age.<sup>7</sup>

## Pharmacological management

Corticosteroids are known as the controller medication for asthma as they are used to reduce airway inflammation, prevent

exacerbations, and generally control symptoms.<sup>2</sup> Overall, their effect is to suppress activated inflammatory genes, and increase transcription of anti-inflammatory genes in order to reduce airway hyperresponsiveness.<sup>8</sup> The following outline provides an overview of the common drugs used to manage asthma and will guide NPs when deciding the proper treatment plan for different severity levels of asthma. It also includes information on the use of desensitization therapy, which is used for allergen specific asthma.

## Mild asthma

GINA recommended that patients with mild asthma be prescribed a controller medication such as an ICS, especially if the main concern is symptom control.

In addition to ICS, GINA recommended that NPs also prescribe patients with mild asthma, a short-acting beta agonist inhaler for as needed symptom relief. Beta agonist medications work on beta-adrenergic receptors within the bronchioles which are coupled with G protein receptors. The medication will activate the neurotransmitter cyclic adenosine monophosphate (cAMP) which will activate smooth muscle relaxation resulting in bronchodilation.<sup>9</sup> Before 2019, GINA supported the use of Short-Acting Beta-Agonists (SABA) alone for the as needed treatment of asthma. However, with the evidence emerging from current literature, GINA updated its recommendation to include regular daily dose of ICS with as needed SABA to avoid over-reliance on SABA medications.<sup>2</sup>



Recently, researchers started exploring the efficacy of taking an inhaled combination of ICS/fast-onset long-acting beta-agonists (LABAs) as reliever therapy for patients with mild asthma, as an alternative to regular maintenance dose ICS with as needed SABA. In Canada, O'Byrne et al.<sup>10</sup> conducted a randomized controlled trial (RCT) (n=3836) to explore the efficacy of combined ICS/fast-onset LABA where budesonide-formoterol, a common ICS/fast-onset LABA was administered to patients with mild asthma. Participants were split into three different groups: maintenance dose placebo with as needed terbutaline (SABA) (n=1280), maintenance dose placebo with as needed budesonide-formoterol (n=1279), and maintenance dose budesonide with as needed terbutaline (n=1290).<sup>10</sup> O'Byrne et al.<sup>10</sup> established that the duration of asthma symptoms control with the as needed budesonide-formoterol was longer in comparison to the as needed terbutaline alone (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% CI, 1.00 to 1.30; P=0.046). However, as needed budesonide-formoterol was shown to be inferior to maintenance budesonide and as needed terbutaline with regards to recorded weeks with well-controlled asthma (34.4% of 1279 participants vs. 44.4% of 1290 participants; odds ratio, 0.64; 95% CI, 0.57 to 0.73).<sup>10</sup> O'Byrne et al.<sup>10</sup> also demonstrated that budesonide-formoterol used as needed resulted in a 64% decrease in severe exacerbations (annualized exacerbation rate, 0.07 vs. 0.20; rate ratio, 0.36; 95% CI, 0.27 to 0.49), but that the rates of severe exacerbations between the budesonide-formoterol as needed, and the budesonide maintenance/terbutaline as needed group did not differ significantly (annualized exacerbation rate, 0.07 and 0.09, respectively; rate ratio, 0.83; 95% CI, 0.59 to 1.16).<sup>10</sup> The researchers concluded that patients who adhere to the twice daily budesonide and use terbutaline as needed, would achieve effective daily asthma control and decrease the odds of severe exacerbations.<sup>10</sup>

In South Africa, Bateman et al.<sup>11</sup> conducted an RCT (n=4176) where they separated their participants into two groups; budesonide-formoterol as needed or budesonide as a maintenance medication with as needed terbutaline. Bateman et al.<sup>11</sup> demonstrated that as needed budesonide-formoterol was equal to maintenance budesonide with terbutaline with regards to limiting or decreasing the rate of severe exacerbation (0.11 vs. 0.12, 95% CI, 0.10-0.135). However, the results also showed that the budesonide maintenance with terbutaline as needed therapy resulted in better control of asthma symptoms (asthma control questionnaire-5 [ACQ-5]; 40.3% vs 44.3%; odds ratio, 0.86; 95% CI, 0.75 to 0.99) and quality of life (asthma quality of life questionnaire [AQLQ]; mean difference, -0.10; 95% CI, -0.14 to -0.05).<sup>11</sup>

Given the evidence provided by Bateman et al.<sup>12</sup> and O'Byrne et al.,<sup>10</sup> NPs should prescribe patients with mild asthma, an ICS maintenance drug along with a separate, as needed, SABA.

## Moderate asthma

Similar to patients with mild asthma, GINA recommended that patients with moderate-severe asthma should be initiated on an ICS for symptom control.<sup>2</sup> However, for patients with moderate to severe asthma, who are not achieving the desired symptom control with the base ICS dose, GINA recommended increasing the dose of ICS.<sup>12</sup>

Zhang et al.<sup>13</sup> performed a systematic review of 8 RCTs (n=3866) at University in Sichuan, China to evaluate the efficacy and safety of increasing the dose of ICS. Zhang et al.<sup>13</sup> focused on the efficacy and safety of increasing ICS doses concluding that, increasing that dose of ICS was associated with lower risk of treatment failure (OR 0.82, 95% CI 0.70-0.97, P = 0.02). However, there was an association between increasing the dose of ICS and non-serious adverse events

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# Asthma Management: An Update

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(OR 3.50, 95% CI 1.93-6.35). Zhang et al.<sup>13</sup> added that increasing the dose of ICS will reduce the odds of requiring systemic corticosteroids.

Chipps et al.<sup>14</sup> in an RCT studied the effect of different dosages of ICS on nighttime symptom score, nighttime rescue medication usage, FEV<sub>1</sub>, and adverse events that led to withdrawals from the study. Based on these results, Chipps et al.<sup>14</sup> concluded that there was no significant difference between starting with low, moderate, and high doses of various ICS, and that all doses were seen equivalent with regards to the aforementioned outcomes. While administering moderate-to-high dose of ICS did show significant improvement in morning peak expiratory flow (PEF), it failed to establish improvement in other lung functions. Starting high-initial doses of ICS, were also linked to side effects associated with long-term use of high-dose corticosteroids.<sup>13</sup> Chipps et al.<sup>13</sup> also compared ICS alone with ICS/LABA. Chipps et al.<sup>13</sup> revealed that there was no significant difference between low or moderate doses of ICS/LABA (raw mean difference, 25; 95% credible intervals [CrI], 6.1-45.0; raw mean difference, 23; 95% CrI, 9.0-39.0; respectively) compared to the high doses of ICS with regards to improvement of morning PEF values.

GINA recommends that NPs start their patients on a maintenance dose of ICS. However, if the symptoms are not well controlled with the maintenance dose of ICS doubling or quadrupling the dose is recommended for further symptom control. The risks and potential adverse events such as stomatitis, pharyngitis, bitter taste in mouth, and sore throat must be taken into consideration. Therefore, replacing the ICS with an ICS/LABA such as fluticasone propionate with salmeterol

combination, could also be beneficial as it would provide better symptom control without the need to increase the dose of corticosteroids, thus limiting the adverse effects from high-dose corticosteroids.

After four weeks of no progress from the ICS/LABA inhaler, it is suggested that NPs prescribe their patients an additional short-acting muscarinic antagonist (SAMA) or short-acting beta agonist (SABA) inhaler and/or switch the ICS/LABA medication to an ICS/LAMA (long-acting muscarinic antagonist medication).

Anticholinergic drugs such as SAMA and LAMA, act on muscarinic receptors on bronchial smooth muscle to inhibit bronchoconstriction and mucus secretion from hyperplastic goblet cells, which is usually caused by acetylcholine release; their main goal is to induce bronchodilation.<sup>14</sup> SAMA medications are an example of a reliever medication for asthma as they will have a fast onset of action providing quick relief of breakthrough symptoms.<sup>2</sup> This is why they are beneficial for additive treatment, when SABA alone is not enough.

## Allergen-specific asthma

Another treatment that can be used for adjunct therapy for those who experience allergen-specific asthma is desensitization therapy also called immunotherapy. Desensitization therapy is used for patients with allergic asthma, and while there are many different phenotypes for asthma, allergic asthma is one of the best described phenotypes.<sup>14</sup> There are two different types of allergen immunotherapy (AIT) for asthma: subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT).<sup>2</sup>

NPs should refer patients to an allergist for AIT assessment if they suspect an allergic component. Examples of allergen extracts that could be used are grass, cat, dog, trees, moulds, latex, and weeds.<sup>15</sup>

## Conclusion

This article presented an overview of the management of asthma, using an outline that uses severity levels of asthma as a framework. We have used data from rigorous and well-designed studies to support our recommendations. We were also intentional about including guideline driven intervention such as those highlighted by the Global Initiative for Asthma.<sup>2</sup> We believe that this manuscript has potential to be used as a knowledge translation vehicle to improve adherence to best practices.

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# The Role of the Multiple Sclerosis Nurse Practitioner

Colleen Harris, Shantha George, Chantal Kahovec,  
Margaret Prociuk and Alexandra Roll, Lynn McEwan

## Introduction

Multiple sclerosis (MS) is a chronic, neurological disease with diverse manifestations and responses to treatment (Leahy & Counihan, 2018). With an increasing number of disease-modifying therapies (DMTs) available for the treatment of MS, comes an increase in the complexity of treatment and care of MS patients (Leahy & Counihan, 2018). Nurse practitioners (NPs) provide a dynamic contribution to the care of MS patients and work collaboratively with neurologists, family physicians, registered nurses (RNs) and other members of the healthcare team. The MS NP is a growing profession in MS clinics, and more awareness and recognition of their valuable position in MS care is needed.

The goals of this whitepaper are to provide a clear understanding of the NP role in MS care, describe the complementary roles that NPs are able to fulfil within the comprehensive MS care teams as well as to offer an understanding of the value NPs bring to the field of MS and how this value can be maximized. This whitepaper is the collaboration of six MS NPs from clinics across Canada and will highlight the growing need for MS NPs in the current landscape of MS care.

## The role of the MS NP

The NP profession was established in Canada during the 1960s and encompasses

experienced registered nurses who have completed a master's program and have an advanced scope of practice (Delvin, Braithwaite, & Camargo Plazas, 2018). The NP practice is grounded in the knowledge, values and theories of the nursing profession and incorporates knowledge and theories traditionally associated with physicians (Canadian Nurses Association, 2016).

Beginning in the 1980s, the Canadian government decreased medical school admission and active training positions, which led to a shortage in the number of physicians trained in certain specialties (Jiang, 2016). According to the 2012 Canadian Neurological Society Manpower Survey, wait-times for neurologists still exceeded international standards despite physicians working an average of 57 hours/week (Kirby, Weston, Barton, Buske, & Chauhan, 2016). Half of survey respondents reported a shortage of neurologists in their community and this situation is anticipated to worsen in the coming years as experienced neurologists retire (Kirby et al., 2016). Multiple sclerosis NPs can help fill the care gap in MS as a result of the neurologist shortage.

The MS NP has a dynamic role that supports patient care across the lifespan from the time of diagnosis, to planning for pregnancy, to dealing with the management of relapses and disability progression. The MS NP plays many roles, including administrator, educator,

collaborator, consultant, researcher, advocate and expert clinician (Costello & Halper, 2010). The MS NP is able to complement the care of the neurologist by managing neurological symptoms, monitoring ongoing blood work and liaising with other specialties and agencies when patients require additional assistance. Nurse practitioners offer support, help improve medication compliance and manage care in a cost-effective manner (Canadian Nurses Association, 2006). Multiple sclerosis NPs are often a bridge between neurology and family practice; helping to ensure patients have improved access in a timely manner.

### Maximizing the value of NPs in an MS practice

Maximizing the value of NPs in the care of MS patients is imperative due to the complex nature of the disease. There are several areas in MS care that can be optimized by the NP including: acute relapse management, symptom management, yearly follow-up visits and ongoing management of the intricate needs of patients with MS.

Acute relapse management provided by the NP has been shown to be an effective measure to ensure patients are seen within the recommended guidelines of 14 days since acute relapse onset (Leahy & Counihan, 2018). The advanced knowledge of the NP allows a detailed history to be taken and pertinent assessments to be ordered, with the ability to interpret the results, develop and implement a treatment plan for acute relapses. MS management decision-making by NPs is comparable to that of neurologists for patients with potential relapses and/or treatment escalation (Leahy & Counihan, 2018).

Common symptoms of MS managed by NPs include: fatigue, spasticity, sphincteric dysfunction, pain, motor and sensory symptoms (Oliver, 2009). The expertise of the NP allows them to understand the

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MS management decision-making by NPs is comparable to that of neurologists for patients with potential relapses and/or treatment escalation.

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complex treatments that MS patients receive, including symptomatic management. The time they are able to spend with the patient during each visit allows not only for the formation of a management plan, but also for building a trusting relationship. Patient adherence to the proposed treatment and symptomatic management plan is fostered by the relationship NPs are able to establish. The NP is vital in collaborating with the interdisciplinary care team, the patient and caregivers, to improve quality of life for patients with MS. As key members of the healthcare team, NPs promote the continuity of care; meeting the complex care needs of patients, including patients who are at risk of repeat hospital admissions and those requiring longer visits to manage psychosocial needs such as increased anxiety.

Multiple sclerosis NPs also play key roles in annual DMT follow-up and ongoing patient education to ensure adherence to the prescribed treatment plans. Nurse practitioners have the ability to recognize treatment failure and to independently manage sequencing of medications. Nurse practitioners excel in their ability to provide patient education, enabling patients to understand their treatment and

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# The Role of the Multiple Sclerosis Nurse Practitioner

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“

Nurse practitioners play a key role in mitigating unnecessary emergency department visits...

”

the possible side effects. Through consistent monitoring and follow-up, NPs successfully promote adherence.

## Role of the NPs in improving health outcomes

With the growing number of patients with chronic illnesses, healthcare systems are increasingly challenged in providing necessary care and encouraging patients to participate in their care (Watts et al., 2009). Nurse practitioners are an important factor in overcoming these challenges (Watts et al., 2009). Engaging patients to participate in their care can empower patients and improve health outcomes. This involves a multidisciplinary approach, a trusting relationship with their healthcare provider and shared decision-making.

In addition to the high cost of DMTs and routine imaging, hospital admissions due to MS relapses contribute to the cost of managing MS (Abboud et al., 2017). Patients with MS

visit the emergency department for several reasons, including: relapses, pseudo-relapses (temporary worsening of preexisting deficits), other medical complications and treatment-related adverse effects (Abboud et al., 2017; Farber, Hannigan, Alcauskas, & Krieger, 2014) (Oynhausen et al., 2014). In our experience management of these patients can differ greatly across hospitals. Patients with MS can receive unnecessary admissions, tests and treatments (Abboud et al., 2017). Nurse practitioners play a key role in mitigating these unnecessary emergency department visits by providing patient education, encouraging communication with the MS care team and ensuring each patient has an optimal and tailored treatment strategy. Furthermore, NPs also assess the patients' support system to ensure their care plan is manageable and sustainable while identifying obstacles to patient participation (Roman & Menning, 2017).

As MS therapies evolve, there has been a growing need for competent and reliable MS nurses to provide proper counselling and management of patient expectations. We believe the MS NP can provide leadership and education to the MS nurse, preparing them for successful patient encounters to promote treatment adherence and improve patient outcomes (Burke, Dishon, McEwan, & Smrtka, 2011).

Nurse practitioners improve access to healthcare for a chronic disease population and increase patient satisfaction (Thotam & Buhse, 2020). Satisfied patients are more likely to comply with treatment regimens and participate in their own care (Fan, Burman, McDonnell, & Fihn, 2005). When compared to



physicians, NPs were found to have longer consultation times, providing more information and education to patients and families (Newhouse et al., 2011). Nurse practitioners demonstrated a higher likelihood of having more frequent follow-ups with the patient and providing a greater degree of education and teaching around health promotion (Newhouse et al., 2011). Empowering patients to take control of their disease, readying them with the necessary education and facilitating access to healthcare can improve their overall outcomes when managing MS.

## Future directions

Nurse Practitioners directly involved in the care of MS patients have demonstrated positive outcomes. A cost effectiveness review revealed that NPs in ambulatory care roles have equivalent or better patient outcomes than comparators and are potentially cost-saving (Martin-Misener et al., 2015). There is no available research on MS NPs and their effect on decreasing emergency department visits for patients with MS. Future research displaying a reduction in emergency department visits by MS patients when seen by MS NPs would be instrumental in highlighting the ability of the expert MS NPs to manage symptoms and efficiently treat ongoing concerns of patients. These outcomes could be tracked through electronic health records or patient logs indicating when the patient had attended the emergency department due to an inability to contact the NP. Barriers to care could be identified and removed appropriately to facilitate workflows in clinics.

Potential research assessing the development and implementation of the NP role in clinics across Canada would assist for current clinics that do not have an NP to understand the potential value of an NP. Sangster-Gormley, Martin-Misener, Downe-Wamboldt, and Dicenso (2011) reviewed the importance of discussions leading up to the decision to

incorporate an NP into a practice as well as mentoring and role expectations. As MS has a very specific disease process and there are limited numbers of MS NPs in Canada, it would be prudent to consider a retrospective review assessing how MS NP positions were developed and the ways in which the role is currently being leveraged in Canada.

## Conclusions

Multiple sclerosis is a complex and serious neurological condition. Multiple sclerosis NP's have the advanced education and skill set to meet the diverse needs of those living with MS throughout the disease trajectory. Unfortunately, patients are facing greater challenges in accessing MS specialist care due to fewer available MS neurologists and longer wait-times for consultations and follow-ups (Kirby et al., 2016). Nurse practitioners play a key role in improving access to care and enhancing patient outcomes.

It is important to recognize that NP's are autonomous in their role and that building relationships with the neurologist and healthcare team members is vital for the success of the MS NP (Côté, Freeman, Jean, & Denis, 2019). Rather than determining how an MS NP could "fit in," MS NPs should be provided the opportunity to define their own practice and outline the expertise they bring to the role (Delvin et al., 2018). Multiple sclerosis NP roles may also differ between MS clinics. Evaluation, defining meaningful outcome measures and collaborative research will be important for success in implementing and sustaining the MS NP role.

## Acknowledgements

Editorial assistance was provided by MEDUCOM Health Inc. and supported by Sanofi-Genzyme.



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# SARS-CoV-2 in Children:

## What symptoms are most predictive of a positive SARS-CoV-2 test?

King JA, Whitten TA, Bakal JA and McAlister FA, Symptoms associated with a positive result for a swab for SARS-CoV-2 infection among children in Alberta, CMAJ 2021 January 4;193:E1-9. doi: 10.1503/cmaj.202065; early-released November 24, 2020

Available online at: <https://www.cmaj.ca/content/cmaj/193/1/E1.full.pdf>

### What was studied?

The study goal was to determine, in a community-setting, what symptoms were most commonly associated with testing positive for SARS-CoV-2 in children.

### How was this studied?

An observational study was undertaken between April and September 2020 in Alberta of children tested for SARS-CoV-2. Positive likelihood ratios (LR) were calculated based on the children's self-reported symptoms and positive SARS-CoV-2 test.

### Who was included?

All children (<18 years old) who had a positive SARS-CoV-2 test result or who were tested because they were a high-risk contact, either through close contact with a positive case or an outbreak.



### What did they find?

A total of 2463 children were included in the analysis; 1987 with a positive test result and 476 with a negative result. Approximately one-third (35.9%) of children who tested positive were asymptomatic. The most common

symptoms reported were cough (24.5%) and rhinorrhea (19.3%). However, these symptoms were also common in children who were negative for SARS-CoV-2 and were not useful as predictors of positivity.

The symptoms that were most strongly predictive of a positive SARS-CoV-2 test result were anosmia/ageusia (positive LR 7.33), nausea/vomiting (positive LR 5.51), headache (positive LR 2.49) and fever (positive LR 1.68).

### Community-based symptom patterns of SARS-CoV-2 in children in Alberta

- 35.9% of children with a positive SARS-CoV-2 test were asymptomatic
- The 4 symptoms most commonly associated with being SARS-CoV-2 positive were:
  - Anosmia/ageusia
  - Nausea/vomiting
  - Headache
  - Fever

# In the News

## Current healthcare research

### International study shows polypill along with aspirin cuts heart attacks and strokes by up to 40%

Findings recently published in the *New England Journal of Medicine* have shown that a polypill combining three blood pressure medications and one lipid-lowering medication may reduce cardiovascular incidents, including heart attacks and strokes, by 20% when taken alone and by 40% when taken with aspirin.

The study randomly sorted over 5,700 participants with elevated risk of myocardial infarction into several treatment groups, following them for 4.6 years on average. Serious cardiovascular incidents occurred in 4.4% of the polypill-only group and 5.5% of the matching placebo group, 4.1% of the aspirin-only group and 4.7% of the matching placebo group, and in 4.1% of the polypill-and-aspirin group, compared to 5.8% of the double-placebo group.

Presently, over 80% of cardiovascular disease-related deaths occur in low- and middle-income countries. The convenience and cost-effectiveness of the polypill make it greatly promising as a primary preventive intervention to reduce the risk of cardiovascular events worldwide.

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Yusuf, S. et al. (2020). Polypill with or without Aspirin in Persons without Cardiovascular Disease. *New England Journal of Medicine*. doi:10.1056/nejmoa2028220



### Sleep apnea treatment reduces heart problems in patients with prediabetes, a new study finds

A study published in the *Journal of the American Heart Association* found that nighttime continuous positive airway pressure (CPAP) treatment can reduce resting daytime heart rate in patients with obstructive sleep apnea and prediabetes, reducing cardiovascular risk.

Thirty-nine participants were randomly assigned to receive either optimal in-laboratory CPAP for 8 hours per night on average or a placebo for two weeks, continuing routine daytime activities. The treatment group showed a mean daytime resting heart rate decrease of 4.1 bpm compared to placebo; the effect appeared to be cumulative. Each 1 bpm resting heart rate increase has been linked to a 3% mortality rise in middle age.



Approximately 50-70% of individuals with prediabetes or diabetes have sleep apnea. Prior studies have not established a connection between CPAP and cardiovascular outcomes; the research team posits that their new findings may support increasing the current recommended CPAP duration of 4 hours per night.

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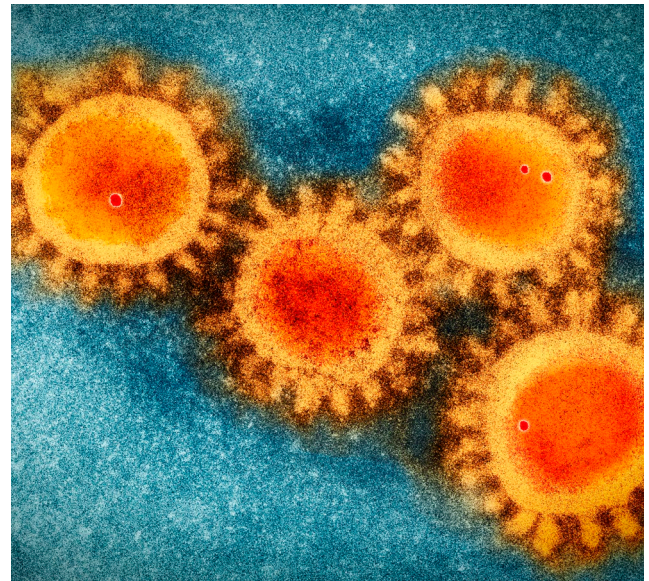
Pamidi, S. et al. (2020). Optimal Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea Reduces Daytime Resting Heart Rate in Prediabetes: A Randomized Controlled Study. *Journal of the American Heart Association*, 9(19). doi:10.1161/JAHA.120.016871

## Canadian study looks at treatment with ciclesonide for mild COVID-19 cases

An ongoing trial at the Research Institute of the McGill University Health Centre is investigating whether the steroid ciclesonide could alleviate shortness of breath and decrease the need for oxygen or hospitalization in mild symptomatic cases of COVID-19.

Studies have already shown that ciclesonide can reduce the viral replication of SARS-Cov-2. The virus begins replication in the nose and airways, causing damage to lung tissue, which results in difficulty breathing. Ciclesonide, administered via inhaler and nasal spray, may therefore potentially be able to minimize replication where it begins, preventing further deterioration in the early stages.

Presently, participants must be Québec residents over the age of 18 that have been diagnosed with and experiencing symptoms of COVID-19 within 5 days of enrollment. Upon confirmation of eligibility, participants will be randomly assigned to receive either ciclesonide or a placebo by courier. Recruitment in Ontario and British Columbia is expected to begin soon.




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Nip it in the bud: New study will attack SARS-Cov-2 where it multiplies. (2020, September). Retrieved December 06, 2020, from <https://publications.mcgill.ca/medenews/2020/09/17/nip-it-in-the-bud-new-study-will-attack-sars-cov2-where-it-multiplies/>

## McMaster study links early menopause and depression

A study published in *Menopause* has established a connection between premature menopause occurring before age 40 and an elevated risk of depression.

Researchers examined data from over 13,000 female participants aged 45-64 in the Canadian Longitudinal Study on Aging (CSLA). Depressive symptoms were self-reported using the Center for Epidemiologic Studies Short Depression Scale-10 (CESD-10), on which a score of 10 or higher indicates depression. Variables such as current stage of menopause, age at onset, and time since onset were also considered in the analysis.

Of the study population, 18.4% met the CESD-10 criteria for depression. Women

Continued on page 31

# FINANCIAL LITERACY: Empower Your Future Self

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**SPEAKER:**  
**Dr. Vu Kiet Tran**

On June 4 Dr. Tran will be hosting a day-long workshop for healthcare professionals on Financial Literacy. This is an opportunity for healthcare professionals from across Ontario to gather for the purpose of continuing professional and personal education on basic financial concepts, risk management and investment. As we reflect on this past year, we look to the future and discuss the changing trends and issues that will affect how Ontarians manage their finances.

Be sure to check out Dr. Tran's pod cast at <https://financialhealthdoc.com/podcast/>

For more information visit  
<http://beautifultimesinc.ca/conference-and-workshops>

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# In the News

## Current healthcare research

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disclosing premature menopause and post-menopausal women using hormone therapy (HT) at time of study were both more likely to experience depression. HT is not believed to be the cause, but rather an indicator of severe menopausal symptoms, an established risk factor for depression. Understanding these risk factors could help clinicians evaluate patients' mental health.

Shea, A. K. (2020). Depression, hormone therapy, and the menopausal transition among women aged 45 to 64 years using Canadian Longitudinal Study on aging baseline data. *Menopause*, 27(7), 763-770. doi:10.1097/GME.0000000000001540

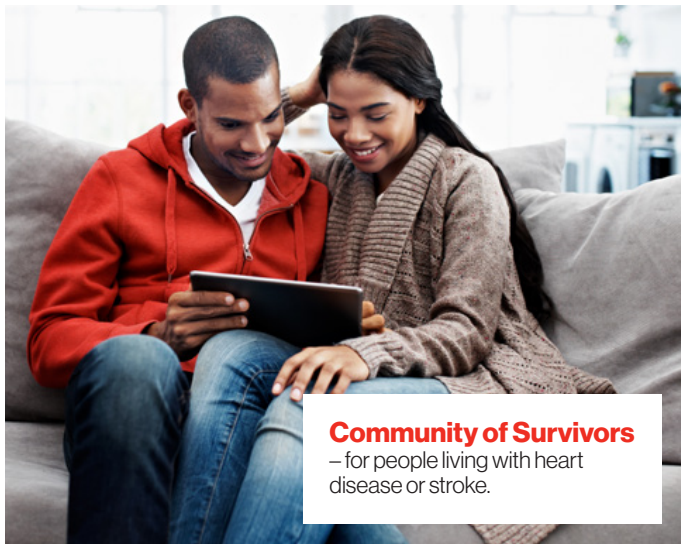


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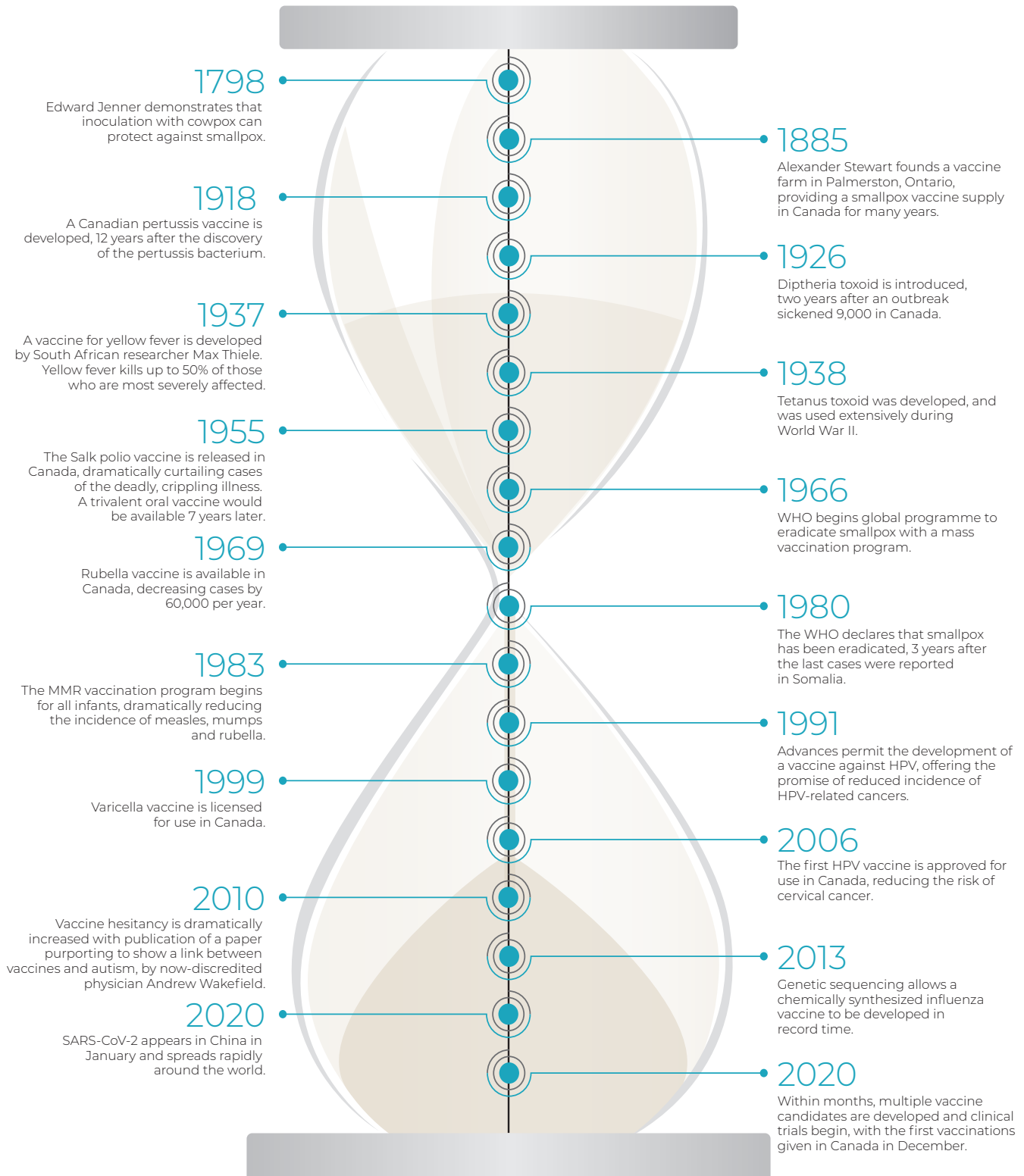


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# Milestones: Vaccines that have changed our world





A study was performed to assess the effects of BLEXTEN<sup>®</sup> and bilastine 40 mg on real time driving performance compared to placebo and hydroxyzine 50 mg. Bilastine did not affect driving performance differently than placebo following day one or after one week of treatment. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.<sup>1</sup> BLEXTEN<sup>®</sup> is only indicated for use at 20 mg once daily.<sup>1\*</sup> Note: Hydroxyzine is not indicated for the treatment of allergic rhinitis.

**Indication**

BLEXTEN<sup>®</sup> (bilastine) is indicated for the symptomatic relief of nasal and non-nasal symptoms of seasonal allergic rhinitis (SAR) in patients 12 years of age and older and for the relief of the symptoms associated with chronic spontaneous urticaria (CSU) (e.g. pruritus and hives), in patients 18 years of age and older.

**Contraindication**

- History of QT prolongation and/or torsade de pointes, including congenital long QT syndromes

**Relevant warnings and precautions**

- QTc interval prolongation, which may increase the risk of torsade de pointes
- Use with caution in patients with a history of cardiac arrhythmias; hypokalemia, hypomagnesaemia; significant

bradycardia; family history of sudden cardiac death; concomitant use of other QT/QTc-prolonging drugs

- P-glycoprotein inhibitors may increase plasma levels of BLEXTEN<sup>®</sup> in patients with moderate or severe renal impairment; co-administration should be avoided
- BLEXTEN<sup>®</sup> should be avoided during pregnancy unless advised otherwise by a physician

**For more information**

Please consult the product monograph at <https://www.miravohealthcare.com/wp-content/uploads/2020/11/Blexten-PM-ENG-Dec-2018.pdf> for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The product monograph is also available by calling 1-866-391-4503.

<sup>2</sup> As of March 2018, the estimate of patient exposure is based on units sold, the defined daily dose (DDD) of 20 mg for bilastine and the mean treatment duration of 3 weeks.

\* Clinical significance has not been established.

**Reference:**

1. Blexten<sup>®</sup> Product Monograph. Aralez Pharmaceuticals Canada Inc. December 13, 2018.



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## ONLINE SURVEY



# Education and Intervention for Childhood Asthma

Complete a brief NP Current online survey and share your perspectives on managing childhood asthma. We are seeking your input to help in the planning and implementation of an education and intervention program to improve the management of childhood asthma.

This information is being collected on behalf of a leading respiratory care company that is committed to improving the lives of people living with chronic respiratory conditions. They are looking for input from nurse practitioners as key pillars of diverse healthcare communities in Canada. The information collected from this survey is anonymous and you will not be contacted for follow-up.

*Complete the survey at:*

**[www.npcurrent.ca/asthmasurvey](http://www.npcurrent.ca/asthmasurvey)**

