About the Authors

Jacob McCoy, MD

Dr. Jacob McCoy is a pediatric respirologist, currently completing further subspecialty training in severe asthma, and his PhD in Clinical Epidemiology and Health Care Research at the University of Toronto.

Affiliations: Division of Respiratory Medicine, The Hospital for Sick Children, University of Toronto, Toronto, Canada

Padmaja Subbarao, MD

Dr. Subbarao is a Clinician-Scientist in Pediatric Respiratory Medicine specializing clinically in severe asthma. She is the Director of the CHILD Study and holds a CRC Tier 1 Chair in Pediatric Asthma and Lung Health at the University of Toronto. She is also the Co-Lead of Precision Child Health and Associate Chief, Clinical Research at the RI. Trained in both Epidemiology and infant and preschool lung physiology, she holds appointments as a Senior Scientist in Translational Medicine and as a Professor in the Departments of Pediatrics, Physiology and in the Dalla Lana School of Public Health.

Affiliations: Division of Respiratory Medicine, The Hospital for Sick Children, University of Toronto, Toronto, Canada

doi.org/10.58931/cait.2025.5181

An Update on Biologics in Pediatric Asthma: A Canadian Perspective

Jacob McCoy, MD
Padmaja Subbarao, MD

Introduction

Asthma is one of the most common chronic diseases in Canada, affecting approximately 11% of Canadians.[1] Severe asthma, estimated to affect 5–10% of patients with asthma, is associated with a significant burden of disease-related morbidity.[2] In adults, typical management strategies include using combinations of inhaled corticosteroids, long-acting beta agonists, leukotriene receptor antagonists, long-acting muscarinic antagonists, and oral corticosteroids. However, in pediatric cases, particularly young children, our medication options are more limited. Although inhaled corticosteroids are effective for the majority of mild-to-moderate asthma cases, their efficacy in non-atopic asthma is limited. Furthermore, using inhaled corticosteroids at moderate-to-high doses can impair linear growth and lead to adrenal suppression. Given our growing recognition of asthma as a heterogenous disease, with multiple disease endotypes driven by distinct inflammatory pathways, there is an increasing demand for targeted therapies, particularly for patients with ongoing, uncontrolled disease (**Figure 1**). Type 2 (T2) high inflammation, characterized by elevated levels of IgE, interleukin (IL)-4, IL-5, and IL-13, alongside eosinophilia and atopy, remains the most well-defined endotype in school-age children and youth.[3] With the advent of biologic medications, targeting T2-high inflammatory pathways has become a critical component for managing uncontrolled, moderate-to-severe asthma in children. This approach aims to improve treatment response and reduce adverse effects. This review will explore the biologic therapies currently available in Canada for moderate-to-severe pediatric asthma, discuss key considerations in selecting the optimal biologic, and outline future research directions to inform the optimal timing for initiating and discontinuing biologic treatments.

Biologics in Canada

In Canada, four biologics are currently available for use in pediatric patients with asthma, as mentioned above, all are for T2 high asthma: omalizumab, dupilumab, mepolizumab, and tezepelumab (**Table 1**).

Omalizumab

Omalizumab is an anti-IgE monoclonal antibody that binds to free IgE, thereby preventing further interaction with mast cells, basophils, and eosinophils. It is approved for use in moderate-to-severe persistent asthma that remains uncontrolled despite inhaled corticosteroids. This approval is for children ≥6 years of age who have a positive skin prick test to a perennial aeroallergen and elevated IgE levels.

Several studies have demonstrated the clinical effectiveness of omalizumab in children. In the Inner-City Anti-IgE Therapy for Asthma study, which included children aged 6–20 years with persistent, allergic asthma, omalizumab led to a decrease in the number of participants with an asthma exacerbation by 40% (30% in the omalizumab arm versus 49% in the placebo arm). Additionally, there was a reduction in the mean number of days with symptoms per two-week period (1.48 days in the omalizumab arm versus 1.96 days in the placebo arm).[4] In the Preventative Omalizumab or Step-up Therapy for Fall Exacerbations study, children aged 6–17 years with asthma were randomized to receive omalizumab, placebo, or a doubled dose of inhaled corticosteroid (ICS).[5] Omalizumab led to a reduction in the fall season exacerbation rate compared with placebo (11% versus 21%), with an even more prominent effect in patients who had an exacerbation during the run-in period (6% versus 36%). Although there was no overall difference compared with the ICS 'boost' group, a significant reduction was observed in patients who had an exacerbation in the run-in

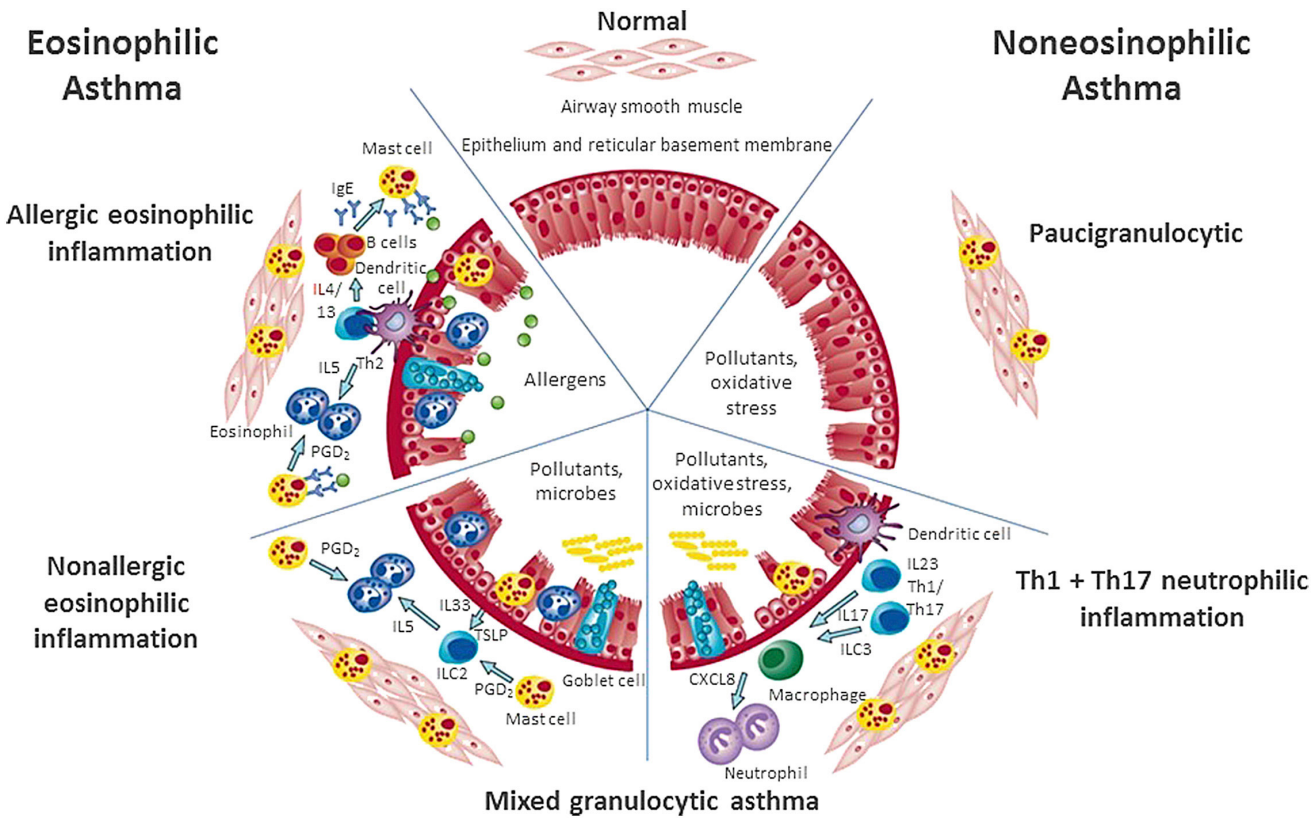

Figure 1. Inflammatory pathways involved in asthma immunopathology; *reproduced from William Busse, Biological treatments for severe Asthma: A major advance in asthma care, Allergology International, 2019, with permission from the Japanese Society of Allergology.*[20]

period (2% versus 28%). Additionally, omalizumab improved the mean asthma symptom days compared with placebo, but not compared to the ICS 'boost' group. A pooled *post hoc* analysis of these trials showed that the beneficial effect of omalizumab on exacerbations was higher in patients with frequent exacerbations, previous hospitalizations, lower baseline forced expiratory volume (FEV1) and a baseline blood eosinophil count ≥300 cells/uL.[6] Some trials have shown a reduction in ICS dose in patients on omalizumab compared with placebo, while others have not.[4,7] In adolescents, omalizumab has also been associated with a 12% increase in percent predicted FEV1.[8] Overall, these findings suggest that patients starting omalizumab may expect a reduction in asthma exacerbations, improved symptom control, and an improvement in FEV1.

In Canada, omalizumab is also approved for use in chronic idiopathic urticaria in patients ≥12 years of age, as well as chronic rhinosinusitis with nasal polyposis (CRSwNP) in patients ≥18 years of age. Recently, the Food and Drug Administration (FDA) in the United States has also approved omalizumab for IgE-mediated food allergies to reduce the risk of anaphylaxis. Patients with these comorbid conditions may be suitable candidates for omalizumab therapy.

Dupilumab

Dupilumab, an anti-IL-4 receptor alpha-subunit monoclonal antibody, is currently approved for treating severe asthma with a T2-high phenotype, or for asthma that is dependent on oral corticosteroids in children ≥6 years of age.

Dupilumab has been shown to improve asthma symptoms and FEV1 in children. In the Liberty Asthma VOYAGE trial, children aged 6-11 years with moderate-to-severe asthma were randomized to receive dupilumab or placebo.[9] Patients on dupilumab had a 59% relative risk reduction in the annualized rate of severe exacerbations, and a 5% higher increase in FEV1 percent predicted than those on placebo. Additionally, the Asthma Control Questionnaire

Biologic	Mechanism of Action	Age for Asthma Indication	Alternative Indications
Omalizumab	Anti-IgE	≥6 years	• CRSwNP (≥18 years) • CIU (≥12 years) • FDA: Food allergy (≥1 year)
Dupilumab	Anti-IL-4Ra	≥6 years	• AD (≥6 months) • EOE (≥6 year) • CRSwNP (≥18 years) • PR (≥18 years)
Mepolizumab	Anti-IL-5	≥6 years	• CRSwNP (≥18 years) • EGPA (≥18 years) • HE (≥18 years)
Tezepelumab	Anti-TSLP	≥12 years	

Table 1. Biologic agents approved by Health Canada for the treatment of severe asthma in children; *courtesy of Jacob McCoy, MD and Padmaja Subbarao, MD.*

Abbreviations: AD: Atopic dermatitis, **CRSwNP:** Chronic rhinosinusitis with nasal polyposis, **CIU:** Chronic idiopathic urticaria, **EGPA:** Eosinophilic granulomatosis with polyangiitis, **EOE:** Eosinophilic esophagitis, **HE:** Hypereosinophilic syndrome, **IL:** interleukin, **PR:** Prurigo nodularis, **TSLP:** thymic stromal lymphopoietin

(ACQ) score was statistically significantly lower in the dupilumab group. For patients aged ≥12 years, dupilumab led to a 47% relative risk reduction in the annualized rate of severe exacerbations compared to placebo, with a greater effect observed in patients with elevated blood eosinophil levels and fractional exhaled nitric oxide (FENO).[10] Dupilumab also led to an improvement in FEV1 of approximately 320-340 mL, which was a 130–140 mL greater improvement than that observed with placebo.

Considering that dupilumab is also approved for treating atopic dermatitis (for individuals ≥6 months of age), eosinophilic esophagitis (for those ≥12 months of age), and CRSwNP (for those ≥18 years of age), patients with asthma who have these comorbid conditions may experience additional benefit.

Mepolizumab

Mepolizumab is an anti-IL-5 monoclonal antibody that is currently approved for treating severe eosinophilic asthma, in children aged ≥6 years. It is indicated for patients with inadequate control despite moderate-to-high doses of ICS along with an additional controller, and is recommended for those with blood eosinophil levels of ≥150 cells/uL at initiation of treatment, or ≥300 cells/uL in the last year.

Mepolizumab has been shown to reduce severe exacerbations and improved FEV1 in children. In the MUPPITS-2 trial, mepolizumab led to a 27% relative risk reduction in the mean number of annual asthma exacerbations compared with placebo in children aged 6–17 years.[11] However, no difference was found in FEV1 or symptom scores between the groups.

For all patients aged ≥12 years in the MENSA trial (aged 12–82 years), mepolizumab reduced the rate of exacerbations by 53% compared with placebo. An even greater reduction of 61% was found for exacerbations requiring an ER visit or hospitalization.[12] Additionally, mepolizumab led to a 100 mL greater improvement in FEV1 compared with placebo, as well as improvements in asthma quality of life and symptom scores. Similar findings were uncovered in the MUSCA trial, which included patients aged ≥12 years. The trial reported improvements in quality of life scores, annual exacerbations requiring an ER visit or hospitalization, and in pre-bronchodilator FEV1.[13]

Overall, these findings suggest that children treated with mepolizumab may experience a reduction in asthma exacerbations. Further

research is needed to better determine whether symptoms and lung function may also improve.

Mepolizumab has also been approved for adults with CRSwNP, eosinophilic granulomatosis with polyangiitis, and hypereosinophilic syndrome. Patients who have eosinophil-predominant disease may be good candidates for mepolizumab.

Tezepelumab

Tezepelumab is a monoclonal antibody that targets thymic stromal lymphopoietin (TSLP), a cytokine positioned upstream in the inflammatory cascade, which may help disrupt airway inflammation. Tezepelumab is approved for treating severe asthma in children aged ≥12 years.

Tezepelumab has limited published evidence specifically for the pediatric population. However, in adult studies that included patients aged ≥12 years, tezepelumab has shown greater improvements in pre-FEV1, annualized rate of exacerbations (with a relative risk reduction of approximately 55%), asthma symptom scores, and quality of life scores than placebo.[14,15] These findings suggest potential benefits, however, they require further confirmation with studies specific to pediatric patients.

Selecting the Right Biologic

Comorbidities

Until further research is available to guide the selection of biologics based on patient clinical phenotype or biomarkers, providers should be keenly aware of patient comorbidities when selecting an appropriate biologic medication. **Table 1** shows current alternative indications for each biologic agent. Comorbidity-guided selection of biologics may provide an opportunity to improve patient quality of life and reduce symptom burden in addition to improving their asthma control.

Practical Considerations – Injections, Medication Coverage, and Early Initiation

All four biologic medications are administered via subcutaneous injection every 2 to 4 weeks, depending on the specific medication, the patient's weight, and/or biomarker levels. Pediatric providers should be aware of the frequency of medication administration and the number of injections required for each dose, as these may be important considerations for children and their families.

In Canada, public coverage for biologic therapies varies from province to province, which can significantly impact equitable access. Asthma providers should be familiar with their provincial access programs to ensure efficient initiation and ongoing, uninterrupted provision of medication.

Currently, biologics are reserved for pediatric patients with severe or difficult-to-treat asthma. However, as generic versions become available in the near future, the reduced costs may improve access and shift the focus of biologic treatments. Instead of being used only in the most severe patients with asthma refractory to all other therapeutic options, patients with active, ongoing eosinophilic inflammation, at higher risk for deterioration and long-term lung damage, may also be a target for treatment.

Until further research is available, providers may consider treatment with biologic agents for a period of 2–5 years. During this time, it is important to monitor treatment success by measuring rates of exacerbations, standardized symptom control scores, quality of life, lung function, FENO, and sputum cell counts.

Future Research Directions

Many questions remain unanswered regarding the use of biologic medications in children: How can we predict which patients will benefit most from which biologic? Does the earlier introduction of biologic therapy improve long-term outcomes? Additionally, how and when should biologics be discontinued? Finally, are there any patients that may benefit from dual-biologic therapy?

Head-to-head studies are needed to determine the relative efficacy of each biologic medication, particularly between subgroups of patients with various asthma phenotypes. Regarding the timing of initiation, adult patients with a longer duration since asthma diagnosis demonstrated lower odds of achieving asthma remission after biologic initiation.[16] This finding warrants further investigation in pediatric patients, but it may suggest that early use of biologics in high risk patients may improve the likelihood of treatment success. Studies investigating the discontinuation of biologics have shown varying results in adults, with many revealing an increase in significant exacerbations, and a worsening of asthma control.[17-19] Pediatric studies are needed that will assess outcomes after discontinuation, particularly among subgroups defined by duration

of treatment, degree of response, or biomarkers. Finally, further studies on biomarker-guided asthma treatment are necessary to identify symptomatic patients with ongoing, targetable airway inflammation despite using a single biologic agent. This could help inform which patients might benefit from dual-biologic therapy.

Conclusions

Biologic therapies have significantly advanced the treatment of children with severe asthma by improving our ability to directly target the underlying inflammatory pathways driving the disease. These medications have demonstrated improvements in reducing the rate of exacerbations, enhancing symptom control, and improving lung function in children with moderate-to-severe uncontrolled asthma. This progress has minimized our reliance on oral or high-dose inhaled steroids. Selecting the most appropriate biologic medication for patients requires thoughtful consideration of patient biomarkers, comorbidities, and practical factors, including coverage and patient preferences. Before initiating treatment, clinicians should establish goals for therapy and obtain measurable outcomes to determine treatment success. Further research in pediatrics is crucial to guide the optimal timing for biologic initiation and to develop evidence-based protocols for discontinuing therapy when appropriate.

Correspondence

Padmaja Subbarao, MD
Email: padmaja.subbarao@sickkids.ca

Financial Disclosures

J.M.: None declared.
P.S.: None declared.

References

1. Public Health Agency of Canada. Canadian Chronic Disease Surveillance System (CCDSS) — Canada.ca [Internet]. 2024 [cited 2025 Apr 13]. Available from: https://health-infobase.canada.ca/ccdss/data-tool/
2. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. [published correction appears in Eur Respir J. 2014;43(4):1216. Dosage error in article text] [published correction appears in Eur Respir J. 2018;52(1):1352020. doi: 10.1183/13993003.52020-2013.] [published correction appears in Eur Respir J. 2022;59(6):1362020. doi: 10.1183/13993003.62020-2013.]. Eur Respir J. 2014;43(2):343-373. doi:10.1183/09031936.00202013
3. Maison N, Omony J, Illi S, Thiele D, Skevaki C, Dittrich AM, et al. T2-high asthma phenotypes across lifespan. Eur Respir J. 2022;60(3):2102288. doi:10.1183/13993003.02288-2021
4. Busse WW, Morgan WJ, Gergen PJ, Mitchell HE, Gern JE, Liu AH, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. N Engl J Med. 2011;364(11):1005–1115. doi:10.1056/NEJMoa1009705
5. Teach SJ, Gill MA, Togias A, Sorkness CA, Arbes SJ, Calatroni A, et al. Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. J Allergy Clin Immunol. 2015;136(6):1476–1485. doi:10.1016/j.jaci.2015.09.008
6. Szefler SJ, Casale TB, Haselkorn T, Yoo B, Ortiz B, Kattan M, et al. Treatment Benefit with omalizumab in children by indicators of asthma severity. J Allergy Clin Immunol Pract. 2020;8(8):2673-2680.e3. doi:10.1016/j.jaip.2020.03.033
7. Lanier B, Bridges T, Kulus M, Taylor AF, Berhane I, Vidaurre CF. Omalizumab for the treatment of exacerbations in children with inadequately controlled allergic (IgE-mediated) asthma. J Allergy Clin Immunol . 2009;124(6):1210–1216. doi:10.1016/j.jaci.2009.09.021
8. Busse WW, Humbert M, Haselkorn T, Ortiz B, Trzaskoma BL, Stephenson P, et al. Effect of omalizumab on lung function and eosinophil levels in adolescents with moderate-to-severe allergic asthma. Ann Allergy Asthma Immunol . 2020;124(2):190–196. doi:10.1016/j.anai.2019.11.016
9. Bacharier LB, Maspero JF, Katelaris CH, Fiocchi AG, Gagnon R, de Mir I, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. N Engl J Med. 2021;385(24):2230–2240. doi:10.1056/NEJMoa2106567
10. Castro M, Corren J, Pavord ID, Maspero J, Wenzel S, Rabe KF, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med. 2018;378(26):2486–2496. doi:10.1056/NEJMoa1804092

11. Jackson DJ, Bacharier LB, Gergen PJ, Gagalis L, Calatroni A, Wellford S, et al. Mepolizumab for urban children with exacerbation-prone eosinophilic asthma in the USA (MUPPITS-2): a randomised, double-blind, placebo-controlled, parallel-group trial. Lancet. 2022;400(10351):502–511. doi:10.1016/S0140-6736(22)01198-9
12. Ortega HG, Liu MC, Pavord ID, Brusselle GG, FitzGerald JM, Chetta A, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014;371(13):1198–1207. doi:10.1056/NEJMoa1403290
13. Chupp GL, Bradford ES, Albers FC, Bratton DJ, Wang-Jairaj J, Nelsen LM, et al. Efficacy of mepolizumab add-on therapy on health-related quality of life and markers of asthma control in severe eosinophilic asthma (MUSCA): a randomised, double-blind, placebo-controlled, parallel-group, multicentre, phase 3b trial. Lancet Respir Med. 2017;5(5):390–400. doi:10.1016/S2213-2600(17)30125-X
14. Menzies-Gow A, Ambrose CS, Colice G, Hunter G, Cook B, Molfino NA, et al. Effect of Tezepelumab on Lung Function in Patients With Severe, Uncontrolled Asthma in the Phase 3 NAVIGATOR Study. Adv Ther. 2023;40(11):4957–71.
15. Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med. 2021;384(19):1800–1809. doi:10.1056/NEJMoa2034975
16. Perez-de-Llano L, Scelo G, Tran TN, Le TT, Fageråas M, Cosio BG, et al. Exploring definitions and predictors of severe asthma clinical remission after biologic treatment in adults. Am J Respir Crit Care Med. 2024;210(7):869–880. doi:10.1164/rccm.202311-2192OC
17. Ortega H, Lemiere C, Llanos JP, Forshag M, Price R, Albers F, et al. Outcomes following mepolizumab treatment discontinuation: real-world experience from an open-label trial. Allergy Asthma Clin Immunol. 2019;15(1):37. doi:10.1186/s13223-019-0348-z
18. Ledford D, Busse W, Trzaskoma B, Omachi TA, Rosén K, Chipps BE, et al. A randomized multicenter study evaluating Xolair persistence of response after long-term therapy. J Allergy Clin Immunol. 2017;140(1):162-169.e2. doi:10.1016/j.jaci.2016.08.054
19. Jeffery MM, Inselman JW, Maddux JT, Lam RW, Shah ND, Rank MA. Asthma patients who stop asthma biologics have a similar risk of asthma exacerbations as those who continue asthma biologics. J Allergy Clin Immunol Pract. 2021;9(7):2742-2750.e1. doi:10.1016/j.jaip.2021.02.031
20. Busse WW. Biological treatments for severe asthma: a major advance in asthma care. Allergol Int. 2019;68(2):158–166. doi:10.1016/j.alit.2019.01.004

Canadian Allergy & Immunology Today
Science for the Real World

canadianallergyandimmunologytoday.com

Canadian Allergy and Immunology Today is published three times per year in English. (ISSN 2818-1816) under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) license by Catalytic Health in Toronto, Ontario, Canada.