DOI: 10.1111/pai.13436

EDITORIAL

WILEY

Risk factors for bronchiolitis and asthma, and COVID-19 symptoms in young children

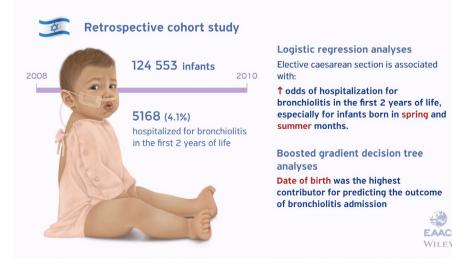
This issue opens with two educational articles destined to update the readers on current drug allergy and food allergy issues. In the first review article, Marina Atanaskovic Markovic, PAI Associate Editor for drug allergies, addresses key issues in this area.¹ In particular, she examines the overdiagnosis of beta-lactam allergy in young children with benign rashes, and the practical implications of unnecessary drug avoidance. Studies addressing this problem have been previously published in PAI.^{2,3} In the second review, Foong and Santos comment on the difficult task of assessing tolerance development in food allergic children with the help of biomarkers.⁴ In particular, they look at the validity of new tests, such as epitope mapping and the basophil and mast cell activation tests, currently emerging into clinical practice.



Lindsey Douglas

The first study I selected investigated a possible relationship between being born by cesarean section and hospital admission for bronchiolitis in the first two years of life. Lindsey Douglas and colleagues screened the medical record database of a large Israeli healthcare fund with over 4.5 million members.⁵ The two-year period investigated allowed recruitment of 124 553 infants of whom 5168 (4.1%) were hospitalized for bronchiolitis. They stratified their analysis by season and found the highest increased odds ratio for those born in the summer (35%; 95% CI: 1.18-1.60), and the lowest but still significant for those born in autumn (15%; 95% CI: 1.02-1.30). They concluded that while being born by cesarean section is a risk factor for the development of bronchiolitis in toddlers, the season of birth is a bigger influence on this. It is well known that babies born by cesarean section might have a modified microbiota, and this can influence the number of obstructive lung diseases in young children,⁶ similar to the use of antibiotics during pregnancy or early life, which also modifies the microbiota.⁷ Overall, the factors associated with pregnancy or early-life events of the development of bronchiolitis and asthma have been frequently studied recently⁸⁻¹¹ (Figure 1).

Elective caesarean section and bronchiolitis hospitalization



© 2021 EAACI and John Wiley and Sons A/S. Published by John Wiley and Sons Ltd.



Norbert Krautenbacher

The environment and heredity are the two well-known factors influencing the development of allergy diseases in general, and asthma in particular. Children born and growing up in a farming environment are a peculiarly interesting population to study with regard to the role of each of these factors. Norbert Krautenbacher et al. have studied over 1700 asthma patients and controls, including farm children, to see whether genetic and environmental factors interact for the development of asthma.¹² In prediction models, a predilection to asthma was driven in general by various environmental variables such as contact to cats, dogs, cows, straw, and hay, in addition to family history and gender, while candidate and genome-wide single nucleotide polymorphisms did not improve prediction. Only in farm children did genetic information contribute significantly to the prediction model, while environmental exposure did not add to prediction models in this group of children. They conclude by stating that "the potential of genome-wide data for the prediction of polygenic diseases might have been overrated, whereas the power of the environment merits a second look." While the farming environment provides a most interesting natural environment for such studies,¹³ recent studies have also explored environmental factors in relation to various socioeconomic regions for the development of allergies^{14,15} (Figure 2).

Asthma in farm children is more determined by genetic polymorphisms and in non-farm children by environmental factors





Char Leung

COVID-19 is a fascinating disease with many unanswered questions, in particular to us pediatricians. The severity of the disease in relation to age, with children being less but differently affected, has raised various hypotheses and clinical observations.¹⁶⁻¹⁸ In the third highlighted article in this issue, Char Leung has gathered publically available data from the Brazilian Ministry of Health including 3213 young patients diagnosed with COVID-19.¹⁹ Among these, 749 were neonates, and 2464 were infants. Neonates suffered significantly more frequently from dyspnoea, pharyngitis, and other various symptoms, but less from fever. Cough was reported similarly in both groups. While the interpretation of these data relies on the accuracy of the reporting health professionals, they suggest again that the immune system might be involved through either humoral or innate mechanisms, in relation to age. In addition, when some defenses are defective due to an immune deficiency, it might be compensated by other mechanisms ^{20,21} (Figure 3).



The editorial team hopes that the JMA article selection, as well as the other original articles and letters selected in this issue, will foster your continuous education and your interest in research in the field of pediatric allergy and immunology.

Philippe Eigenmann ២

Department of Women-Children-Teenagers, University Hospital of Geneva, Geneva, Switzerland Email: philippe.eigenmann@hcuge.ch

ORCID

Philippe Eigenmann 🕩 https://orcid.org/0000-0003-1738-1826

REFERENCES

- 1. Atanaskovic-Markovic M. What is new in beta-lactam allergy in children? Pediatr Allergy Immunol. 2021;32:219-222.
- Diaferio L, Chiriac AM, Leoni MC, et al. Skin tests are important in children with β-lactam hypersensitivity, but may be reduced in number. Pediatr Allergy Immunol. 2019;30:462-468.
- 3. Pouessel G, Winter N, Lejeune S, et al. Oral challenge without skin testing in children with suspected non-severe betalactam hypersensitivity. *Pediatr Allergy Immunol.* 2019;30:488-490.
- 4. Foong R-X, Santos AF. Biomarkers of diagnosis and resolution of food allergy. Pediatr Allergy Immunol. 2021;32:223-233.
- 5. Douglas LC, Leventer-Roberts M, Levinkron O, et al. Elective caesarean section and bronchiolitis hospitalization: A retrospective cohort study. *Pediatr Allergy Immunol.* 2021;32:280-287.
- 6. Zhang X, Zhang X, Zhang N, et al. Airway microbiome, host immune response and recurrent wheezing in infants with severe respiratory syncytial virus bronchiolitis. *Pediatr Allergy Immunol.* 2020;31:281-289.
- 7. Metzler S, Frei R, Schmaußer-Hechfellner E, et al. Association between antibiotic treatment during pregnancy and infancy and the development of allergic diseases. *Pediatr Allergy Immunol.* 2019;30:423-433.
- 8. Engelkes M, Baan EJ, de Ridder MAJ, et al. Incidence, risk factors and re-exacerbation rate of severe asthma exacerbations in a multinational, multidatabase pediatric cohort study. *Pediatr Allergy Immunol.* 2020;31:496-505.
- 9. Mejias A, Wu B, Tandon N, et al. Risk of childhood wheeze and asthma after respiratory syncytial virus infection in full-term infants. *Pediatr Allergy Immunol.* 2020;31:47-56.
- 10. Mitselou N, Hallberg J, Stephansson O, et al. Adverse pregnancy outcomes and risk of later allergic rhinitis—Nationwide Swedish cohort study. *Pediatr Allergy Immunol.* 2020;31:471-479.
- 11. Owora AH, Zhang Y. Childhood wheeze trajectory-specific risk factors: A systematic review and meta-analysis. *Pediatr Allergy Immunol.* 2021;32:34-50.
- 12. Krautenbacher N, Kabesch M, Horak E, et al. Asthma in farm children is more determined by genetic polymorphisms and in non-farm children by environmental factors. *Pediatr Allergy Immunol.* 2021;32:295-304.
- 13. Ojwang V, Nwaru BI, Takkinen H-M, et al. Early exposure to cats, dogs and farm animals and the risk of childhood asthma and allergy. *Pediatr Allergy Immunol.* 2020;31:265-272.
- 14. Le TTK, Nguyen DH, Vu ATL, et al. A cross-sectional, population-based study on the prevalence of food allergies among children in two different socio-economic regions of Vietnam. *Pediatr Allergy Immunol*. 2019;30:348-355.

²¹⁸ WILEY

- 15. Botha M, Basera W, Facey-Thomas HE, et al. Nutrition and allergic diseases in urban and rural communities from the South African Food Allergy cohort. *Pediatr Allergy Immunol.* 2019;30:511-521.
- 16. Matricardi PM, Negro RWD, Nisini R. The first, holistic immunological model of COVID-19: Implications for prevention, diagnosis, and public health measures. *Pediatr Allergy Immunol.* 2020;31:454-470.
- 17. Giacomet V, Stracuzzi M, Paradiso L, et al. Defining the clinical phenotype of COVID-19 in children. Pediatr Allergy Immunol. 2020;31:82-84.
- 18. Brough HA, Kalayci O, Sediva A, et al. Managing childhood allergies and immunodeficiencies during respiratory virus epidemics The 2020 COVID-19 pandemic: A statement from the EAACI-section on pediatrics. *Pediatr Allergy Immunol.* 2020;31:442-448.
- 19. Leung C. The younger the milder clinical course of COVID-19: Even in newborns? Pediatr Allergy Immunol. 2021;32:358-362.
- 20. Soresina A, Moratto D, Chiarini M, et al. Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover. Pediatr Allergy Immunol. 2020;31:565-569.
- 21. Castano-Jaramillo LM, Yamazaki-Nakashimada MA, Mendoza SCS, et al. A male infant with COVID-19 in the context of ARPC1B deficiency. *Pediatr Allergy Immunol.* 2021;32:199-201.