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# Pediatric Respirology and Critical Care Medicine

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## Contents

# Pediatric Respiratory Issues in Asia: A Mélange

The current issue of *Pediatric Respirology and Critical Care Medicine* features three compelling articles, each representing a distinct aspect of the specialty.

We begin with a narrative review of the changes observed in pediatric critical care in the post-coronavirus disease 2019 (COVID-19) era.[1] This review examines the evolving disease patterns during and after the peak of the COVID-19 pandemic. In many countries, respiratory illnesses unrelated to COVID-19, particularly severe infections, saw a significant decline during the peak of restrictions and the implementation of public health measures related to the pandemic. The psychosocial impact of these restrictions was evidenced by an increase in PICU admissions for self-harm. This was followed by a return to pre-COVID-19 illness patterns in most countries,[2-4] and within a few months, a resurgence in influenza and RSV infections was reported,[5] particularly in Australia. The author also discusses the impact of the pandemic on the workforce, including the loss of trained professionals, and the response of the healthcare sector in creating more resources and adapting technologies and strategies to maintain the productivity of critical healthcare staff.

Although the pandemic's impact on global preparedness for managing severe respiratory illnesses has not been extensively documented, it is fair to say that most nations are now better equipped to face future challenges due to enhanced physical and institutional capacities. The pandemic also highlighted the importance of caring for healthcare workers, with an increased focus on resilience training and burnout prevention.[6,7] The heightened public awareness regarding hygiene measures for infection control, telemedicine, remote monitoring, and personal healthcare devices is likely to have lasting benefits, though these effects have not yet been fully documented.

In terms of our understanding of respiratory viruses, there is an ever-growing body of work documenting new viruses or their strains affecting children. Rhinovirus C has been implicated in severe acute respiratory infections (ARIs) and asthma exacerbations. Wang *et al.* from Taiwan presented a small study on the clinical characterization of human rhinovirus in hospitalized children with acute lower respiratory tract infections, comparing the features of HRV-C with those of non-HRV-C illnesses.[8] Although the study is somewhat dated, the findings remain relevant, and similar results have been reported by others.[9,10]

The evolution of health science is breaking new frontiers, covering everything from acute to chronic conditions and from pandemics to rare diseases like mucopolysaccharidosis (MPS). Many systemic diseases manifest in diverse ways, often leading affected children to seek help from various specialties. For example, a child with short stature might visit a general pediatric or endocrinology clinic, while those with a typical phenotype may be seen in a genetics clinic. Respiratory involvement in MPS is common and can result from several factors, including airway obstruction (both upper and lower) due to GAG deposition and/or facial and spinal deformities; restrictive lung disease due to a small thoracic cage and/or weak diaphragm. Sleep-disordered breathing may often lead these patients to consult otolaryngologists.[11] Lee *et al.*[12] presented the otorhinolaryngological perspective on the management of mucopolysaccharidosis in this issue. The impact of enzyme replacement therapy for mucopolysaccharidosis is an area of growing experience, and it remains to be seen how effectively it can improve respiratory problems.

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## Conflicts of interest

There are no conflicts of interest.

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## References

1. Oberende F. The greatest challenges of pediatric critical care pulmonology in the after-COVID era: A narrative review. Respirol Crit Care Med 2024;8:49-52.
2. Yang Y, He Y, Huang J, Yan H, Zhang X, Xiao Z, *et al*. Characteristics and spectrum changes of PICU cases during the COVID-19 pandemic: A retrospective analysis. Front Pediatr 2024;12:1325471.
3. Xin MY, Wu JF, Wang XS, Han L. Changes in the disease spectrum in the pediatric intensive care units within 2 years before and after the outbreak of coronavirus disease 2019. Zhongguo Dang Dai Er Ke Za Zhi 2022;24:1098-103.

4. Breinig S, Mortamet G, Brossier D, Amadieu R, Claudet I, Javouhey E, *et al*. Impact of the French national lockdown on admissions to 14 pediatric intensive care units during the 2020 COVID-19 pandemic-A retrospective multicenter study. Front Pediatr 2021;9:764583.
5. Sachdeva R, Soto-Campos G, Brundage N, Rice T, Wetzel R. Pre-Covid, Covid, and Post-Covid trends of RSV and Influenza across geographic regions in the USA. Critical Care Med 2023;51:285.
6. Cutler DM. Health system change in the wake of COVID-19. JAMA Health Forum 2023;4:e234355.
7. Arabi YM, Azoulay E, Al-Dorzi HM, Phua J, Salluh J, Binnie A, *et al*. How the COVID-19 pandemic will change the future of critical care. Intensive Care Med 2021;47:282-91.
8. Wang H-C, Yong S-B, Lin T-I, Chen Y-S, Tsai C-C, Huang Y-L, *et al*. Prevalence and clinical characterization of human rhinovirus in hospitalized children with acute lower respiratory tract infection in Taiwan. Respirol Crit Care Med 2024;8:60-6.
9. Cox DW, Khoo SK, Zhang G, Lindsay K, Keil AD, Knight G, *et al*. Rhinovirus is the most common virus and rhinovirus-C is the most common species in paediatric intensive care respiratory admissions. Eur Respir J 2018;52:1800207.
10. Sayama A, Okamoto M, Tamaki R, Saito-Obata M, Saito M, Kamigaki T, *et al*. Comparison of Rhinovirus A–, B–, and C–associated respiratory tract illness severity based on the 5′-untranslated region among children younger than 5 years. Open Forum Infect Dis 9:ofac387.
11. Berger KI, Fagondes SC, Giugliani R, Hardy KA, Lee KS, McArdle C, *et al*. Respiratory and sleep disorders in mucopolysaccharidosis. J Inherit Metab Dis 2013;36:201-10.
12. Lee C-L, Lee K-S, Chuang C-K, Cu C-H, Chiu H-C, Chang Y-H, *et al*. Advancements in otorhinolaryngological management of mucopolysaccharidosis: A comprehensive review. Respirol Crit Care Med 2024;8:53-9.



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# The Greatest Challenges of Pediatric Critical Care Pulmonology in the After-COVID Era: A Narrative Review

**Felix Oberender**[1,2]

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## Abstract

The COVID pandemic has had a profound effect on pediatric intensive care and especially on pediatric critical care pulmonology. The indirect impacts caused by the most profound global healthcare challenge in a generation continue to define the current post-COVID era. This era is characterized by postpandemic surges in acute pediatric respiratory illness, disruption of seasonal disease patterns, and an apparent increase in disease severity with a rise in complicated pneumonia as well as associated severe sepsis and septic shock. The consequent demand is met by pediatric intensive care units that are recovering from the strain of the pandemic but also building on progress made during a time of great challenges.

**Keywords:** Critical care, pediatric, pulmonology

## Introduction

Clinicians and parents alike were given some relief when, even at the height of the global pandemic, the direct impact of COVID on children was comparatively small. Australia recorded 226 COVID-related admissions to pediatric intensive care units (PICUs) between 2020 and 2022 with less than a third requiring invasive ventilation.[1] By comparison, COVID led to over two thousand adults needing intensive care with 50% requiring mechanical ventilation within little over a year of the coronavirus reaching the country.[2] However, not only did the virus not completely spare the pediatric population but children were also subject to a range of indirect impacts of the pandemic. The consequences of what was one of the most profoundly disruptive events in recent medical history reach well into the current post-COVID era. In this context, few fields are affected more than pediatric critical care pulmonology: the seasonal pattern of acute respiratory disease seems to have disappeared, at least temporarily while critical pulmonary illness has returned with a vengeance, and the PICU, though superficially the same, is a changed place.

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## What happened to the seasons?

Concerns about indirect impacts of the COVID pandemic were first raised in the field of pediatric and adolescent mental health in early 2020 and later confirmed in a number of qualitative and quantitative studies.[3-5] At the severe end of this spectrum, we saw a significant rise of admissions of children and adolescents with deliberate self-harm to intensive care in Australia.[6] At the same time, our data also showed that this occurred on a background of a steep decline in the overall number of PICU admissions [Figure 1]. The strong public health measures put in place to control COVID had led to a near elimination of acute pediatric infectious diseases responsible for a large proportion of pediatric intensive care admissions. However, following the onset of the pandemic, it became evident that not only had there been an unprecedented trough, but also the well-established pattern of peaks

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of nonelective PICU admissions during the winter months had disappeared. In 2020, PICU admissions in Australia were highest around October to December, the southern hemisphere spring and early summer. 2021 saw a big rise in April, corresponding to early autumn.[7] The seasonal pattern of acute critical pediatric disease—well-established over decades with most being respiratory—seemed to have vanished. It is only now, in early 2024, that there are early, tentative signs that the seasons of pediatric respiratory illness may be resuming.

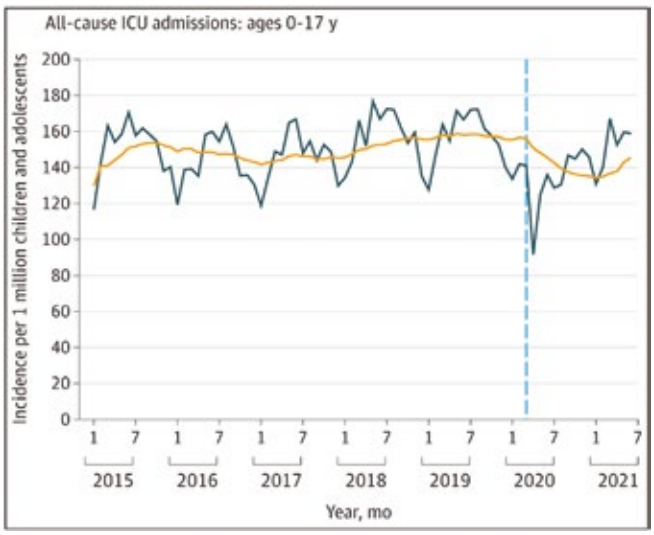


**Figure 1:** Temporal trend in all-cause Australian PICU admissions of children of all ages (0 to 17 years). Reprinted from Admissions of Children and Adolescents With Deliberate Self-harm to Intensive Care During the SARS-CoV-2 Outbreak in Australia, by C. Corrigan *et al*. JAMA Network Open 2022; 5(5). Copyright license CC-BY

## The return of severe respiratory disease

The loss of seasonality was most impressively illustrated by the near disappearance of bronchiolitis in 2020.[8,9] By 2021, however, this common cause of PICU admission in infants had returned, if not to its rolling pattern but to prepandemic levels, and in 2022 Australia found itself in a veritable bronchiolitis epidemic, placing enormous pressure on pediatric pulmonology and critical care resources, a phenomenon replicated in several countries around the world.[10-12] Importantly, the severity of the illness was greater, reflected in increased hospital length of stay and increased admissions to intensive care.[13] The reasons for these changes are unclear and remain under intense debate.[14-16] More concerningly still, there has been a concomitant significant rise in severe bacterial pneumonia, including an increase in thoracic empyema with more frequent need for chest drainage, an experience also reported from other countries [Figure 2].[17-19]

Most worryingly, these increases in upper and lower respiratory tract infections were followed closely by an ongoing surge of children presenting with rapid-onset sepsis and septic shock. In August 2023, news outlets reported that 'cases of flesh-eating invasive strep A bacteria surge in Australian children.[20] This trend had first been seen in Melbourne in 2022.[21] It was subsequently confirmed nationwide, mirroring the epidemiology in Europe.[22-25] The figures were nothing short of extraordinary with the state of Victoria recording a 50% rise in the number of invasive group A streptococcal (iGAS) diseases in the first 6 months of 2023 compared with all of 2022, while cases in New South Wales more than doubled during the same time.[26] Severe pneumonia complicated by rapid-onset septic shock with multi-organ failure has since become a

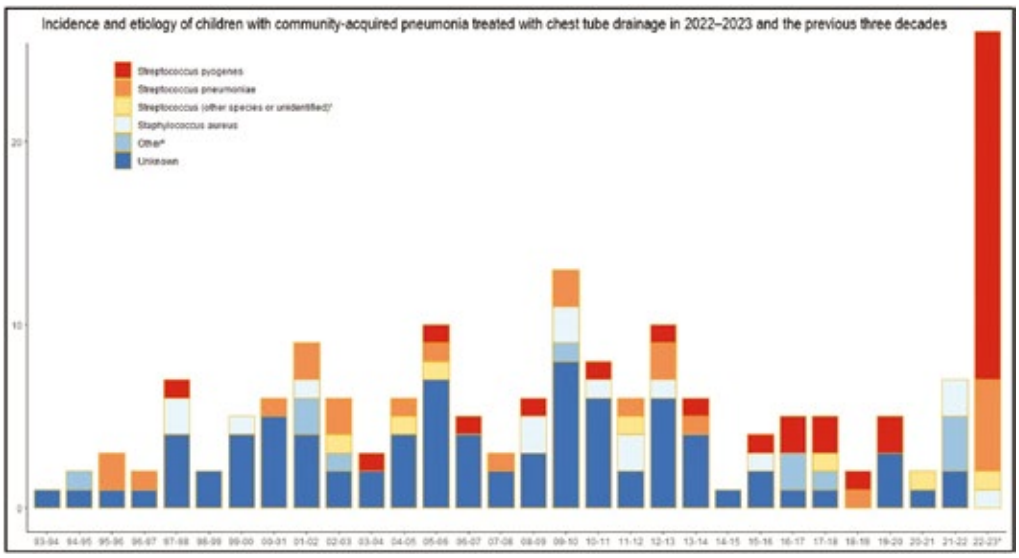


**Figure 2:** Incidence and etiology of children with community-acquired pneumonia treated with chest tube drainage in 2022–2023 and the previous three decades, by U. Nygaard *et al*. Arch Dis Child 2023; 108(11). Copyright license CC-BY-NC 4.0

common scenario and iGAS is now an urgent notifiable disease across Australia.[27]

### Pediatric intensive care—A new space

If pediatric intensive care looks very much the same as it did before the pandemic, appearances can be deceiving. It is a mature specialty that in high-income countries provides children with the full range of life-support technologies from high-flow oxygen therapy to extracorporeal membrane oxygenation.[23] The most important constituent of any unit, however, is not technology but its staff. It is here that the pandemic took its toll. The extraordinary pressures on frontline professionals in both adult and pediatric intensive care were well recognized at the start of the COVID pandemic.[28] This affected all levels of staff but none more so than the ICU nursing workforce.[29-31] As a consequence, intensive care nurses left the profession in large numbers, exacerbating prepandemic staffing challenges.[32] The impact on the PICU in the current post-COVID era is not only quantitative but also qualitative. As health services across the world are working hard to re-recruit and rebuild, the pediatric intensive care nursing workforce of 2024 is considerably younger and less experienced than its prepandemic counterpart.[33,34] This places a heavy burden of responsibility on the remaining senior nursing leaders as well as on nursing educators. It also shines a bright light on the strengths and weaknesses of the mutual support network that exists between doctors and nurses in their daily work on the PICU floor where professionals complement each other with their respective experience and situational awareness, delivering complex care and protecting vulnerable young patients.[35]

While these challenges are real and ongoing, there has also been exceptional growth and progress in the PICU space, particularly with respect to pediatric critical care pulmonology. In contrast to Hong Kong, Singapore, or Canada where health care systems were exposed to and learned from the SARS-CoV-1 outbreak in the early 2000s, other jurisdictions, including Australia, were ill-equipped to deal with airborne infection in 2020.[36,37] Four years on, the admission of a COVID patient—or, more commonly, a child with symptoms that require COVID be ruled out—is routine in an Australian PICU. Teamwork is well-honed and processes are well-tuned. Personal protective equipment that had been haphazard and untested is now standardized and fitted. Ventilation systems and administrative measures of infection control, once the niche of building engineers and hospital managers, have become central to critical care.[38] Intensive care resources, including PICU beds, are monitored and tracked in near real-time.[39,40] The flow-on effects of these changes in the PICU stand to benefit pediatric critical care and critical care pulmonology overall.

## Conclusion

The COVID pandemic has left an indelible mark on pediatric critical care pulmonology and continues to impact the field in important ways in this current post-COVID era. Pediatric respiratory disease has surged and previously well-established seasonal patterns disappeared. The severity of respiratory illness has increased and this is accompanied by a rise in complicated pneumonia as well as in severe sepsis and septic shock. The consequent growth in demand as well as in complexity is met by PICUs that are recovering from the severe strain of the pandemic years, but are also leveraging the progress made during times of extraordinary challenges.

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### Conflicts of interest

There are no conflicts of interest.

## References

1. Otto M, Britton PN, Serpa Neto A, Erickson S, Festa M, Crawford NW, *et al*.; SPRINT-SARI Australia Investigators. COVID-19 related ICU admissions in paediatric and young adult patients in Australia: A national case series 2020–2022. Lancet Reg Health West Pac 2023;36:100763.
2. Begum H, Neto AS, Alliegro P, Broadley T, Trapani T, Campbell LT, *et al*. People in intensive care with COVID-19: Demographic and clinical features during the first, second, and third pandemic waves in Australia. Med J Aust 2022;217:352-60.
3. Reachout.com Online mental health service for young people and their parents in Australia. Mental health concerns as thousands of young people seek help for loneliness during COVID-19. Published on 21 May 2020. [Last accessed on 16 Jun 2020]. https://www.medianet.com.au/releases/187521/
4. Racine N, McArthur BA, Cooke JE, Eirich R, Zhu J, Madigan S. Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: A meta-analysis. JAMA Pediatr 2021;175:1142-50.
5. Li W, Zhang Y, Wang J, Ozaki A, Wang Q, Chen Y, *et al*. Association of home quarantine and mental health among teenagers in Wuhan, China, during the COVID-19 pandemic. JAMA Pediatr 2021;175:313-6.
6. Corrigan C, Duke G, Millar J, Paul E, Butt W, Gordon M, *et al*.; Australian and New Zealand Intensive Care Society Pediatric Study Group (ANZICS PSG) and the ANZICS Center for Outcome and Resource Evaluation (ANZICS CORE). Admissions of children and adolescents with deliberate self-harm to intensive care during the SARS-CoV-2 outbreak in Australia. JAMA Netw Open 2022;5:e2211692.
7. Eden JS, Sikazwe C, Xie R, Deng Y-M, Sullivan SG, Michie A, *et al*.; Australian RSV study group. Off-season RSV epidemics in Australia after easing of COVID-19 restrictions. Nat Commun 2022;13:2884.
8. Yeoh DK, Foley DA, Minney-Smith CA, Martin AC, Mace AO, Sikazwe CT, *et al*. Impact of coronavirus disease 2019 public health measures on detections of influenza and respiratory syncytial virus in children during the 2020 Australian Winter. Clin Infect Dis 2021;72:2199-202.
9. Bourdeau M, Vadlamudi NK, Bastien N, Embree J, Halperin SA, Jadavji T, *et al*.; Canadian Immunization Monitoring Program Active (IMPACT) Investigators. Pediatric RSV-associated hospitalizations

before and during the COVID-19 pandemic. JAMA Netw Open 2023;6:e2336863.
10. Bardsley M, Morbey RA, Hughes HE, Beck CR, Watson CH, Zhao H, *et al*. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: A retrospective observational study. Lancet Infect Dis 2023;23:56-66.
11. Chuang YC, Lin KP, Wang LA, Yeh TK, Liu PY. The impact of the COVID-19 pandemic on respiratory syncytial virus infection: A narrative review. Infect Drug Resist 2023;16:661-75.
12. Ujiie M, Tsuzuki S, Nakamoto T, Iwamoto N. Resurgence of respiratory syncytial virus infections during COVID-19 pandemic. Emerg Infect Dis 2021;27:2969-70.
13. Remien KA, Amarin JZ, Horvat CM, Nofziger RA, Page-Goertz CK, Besunder JB, *et al*. Admissions for bronchiolitis at children's hospitals before and during the COVID-19 pandemic. JAMA Netw Open 2023;6:e2339884.
14. Abu-Raya B, Paramo MV, Reicherz F, Lavoie PM. Why has the epidemiology of RSV changed during the COVID-19 pandemic? eClinicalMedicine 2023;61:102089.
15. Ang HJ, Menegale F, Preziosi G, Pariani E, Migliari M, Pellegrinelli L, *et al*. Reconstructing the impact of COVID-19 on the immunity gap and transmission of respiratory syncytial virus in Lombardy, Italy. eBioMedicine 2023;95:104745.
16. Messacar K, Baker RE, Park SW, Nguyen-Tran H, Cataldi JR, Grenfell B. Preparing for uncertainty: Endemic paediatric viral illnesses after COVID-19 pandemic disruption. Lancet (London, England) 2022;400:1663-5.
17. Nygaard U, Bloch J, Dungu KHS, Vollmond C, Buchvald FF, Nielsen KG, *et al*. Incidence and aetiology of Danish children with community-acquired pneumonia treated with chest tube drainage in 2022–2023 versus the previous three decades. Arch Dis Child 2023;108:945-6.
18. Ouldali N, Deceuninck G, Lefebvre B, Gilca R, Quach C, Brousseau N, *et al*. Increase of invasive pneumococcal disease in children temporally associated with RSV outbreak in Quebec: A time-series analysis. Lancet Reg Health Am 2023;19:100448.
19. Parums DV. Editorial: Outbreaks of Post-Pandemic Childhood Pneumonia and the Re-Emergence of Endemic Respiratory Infections. Med Sci Monit 2023;29:e943312.
20. Davey M, editor MDM. Cases of flesh-eating invasive strep A bacteria surge in Australian children. Guardian. https://www.theguardian.com/australia-news/2023/aug/23/cases-of-flesh-eating-invasive-strep-a-bacteria-surge-in-australian-children. 2023. [Last Accessed on 5 Mar 2024].
21. MacPhail A, Lee WJI, Kotsanas D, Korman TM, Graham M. A rise in invasive and non-invasive group A streptococcal disease case numbers in Melbourne in late 2022. Med J Aust 2023;218:378-9.
22. Abo YN, Oliver J, McMinn A, Osowicki J, Baker C, Clark JE, *et al*. Increase in invasive group A streptococcal disease among Australian children coinciding with northern hemisphere surges. Lancet Reg Health West Pac 2023;41:100873.
23. Lassoued Y, Assad Z, Ouldali N, Caseris M, Mariani P, Birgy A, *et al*. Unexpected Increase in Invasive group A streptococcal infections in children after respiratory viruses outbreak in France: A 15-year time-series analysis. Open Forum Infect Dis 2023;10:ofad188.
24. Johannesen TB, Munkstrup C, Edslev SM, Baig S, Nielsen S, Funk T, *et al*. Increase in invasive group A streptococcal infections and emergence of novel, rapidly expanding sub-lineage of the virulent Streptococcus pyogenes M1 clone, Denmark, 2023. Euro Surveill 2023;28:2300291.
25. Wolters M, Berinson B, Degel-Brossmann N, Hoffmann A, Bluszis R, Aepfelbacher M, *et al*. Population of invasive group A streptococci isolates from a German tertiary care center is dominated by the hypertoxigenic virulent M1UK genotype. Infection 2023;52:667-71.
26. Hla TK, Cannon JW, Bowen AC, Wyber R. Getting to grips with invasive group A streptococcal infection surveillance in Australia: Are we experiencing an epidemic? Med J Aust 2023;219:242-5.
27. Australian Government Department of Health and Aged Care. Invasive Group A Streptococcal (iGAS) Disease – CDNA National guidelines for Public Health Units. Australian Government Department of Health and Aged Care. 2024. Available from: https://www.health.gov.au/resources/publications/invasive-group-a-streptococcal-igas-disease-cdna-national-guidelines-for-public-health-units?language=en. [Last accessed on 5th Mar 2024].
28. Ffrench-O'Carroll R, Feeley T, Tan MH, Magner C, L'Estrange K, Efrimescu C-I, *et al*; Collaborators. Psychological impact of COVID-19 on staff working in paediatric and adult critical care. Br J Anaesth 2021;126:e39-41.
29. Topple M, Jaspers R, Watterson J, McClure J, Rosenow M, Pollock W, *et al*. Nursing workforce deployment and intensive care unit strain during the COVID-19 pandemic in Victoria, Australia. Austral Crit Care 2023;36:84-91.
30. Guttormson JL, Calkins K, McAndrew N, Fitzgerald J, Losurdo H, Loonsfoot D. Critical care nurse burnout, moral distress, and mental health during the COVID-19 pandemic: A United States survey. Heart Lung 2022;55:127-33.
31. Miller M. An impossible job: What it's like to work in a pediatric ICU. Macleans.ca. 2023. [Last accessed on 5 Mar 2024]. https://macleans.ca/society/health/healthcare-pandemic-pediatric-icu-what-its-like/
32. Gibney RTN, Blackman C, Gauthier M, *et al*. COVID-19 pandemic: The impact on Canada's intensive care units. FACETS 2022;7:1411-72.
33. Sustain and Retain in 2022 and Beyond. ICN – International Council of Nurses. [Last accessed on 5 Mar 2024]. https://www.icn.ch/resources/publications-and-reports/sustain-and-retain-2022-and-beyond
34. SCCM | SCCM Critical Care Workforce Update 2023. Society of Critical Care Medicine (SCCM). [Last accessed on 5 Mar 2024]. https://sccm.org/Blog/February-2024/SCCM-Critical-Care-Workforce-Update-2023
35. Taylor W, Pelletier J, Heneghan J, Ramgopal S, Woeltje M, Prout A, *et al*. 11: Association between nursing workforce and agency use on pediatric intensive care outcomes. Crit Care Med 2024;52:S6-S6.
36. MacIntyre CR, Ananda-Rajah M, Nicholls M, Quigley AL. Current COVID-19 guidelines for respiratory protection of health care workers are inadequate. Med J Aust 2020;213:251-2.
37. Broom J, Broom A, Williams Veazey L, Burns P, Degeling C, Hor S, *et al*. "One minute it's an airborne virus, then it's a droplet virus, and then it's like nobody really knows…": Experiences of pandemic PPE amongst Australian healthcare workers. Infect Dis Health 2022;27:71-80.
38. Providing a Safe Working Environment – Engineering Controls. ANZICS. [Last accessed on 5 Mar 2024]. https://www.anzics.com.au/providing-a-safe-working-environment-engineering-controls/
39. Pilcher D, Coatsworth NR, Rosenow M, McClure J. A national system for monitoring intensive care unit demand and capacity: The Critical Health Resources Information System (CHRIS). Med J Aust 2021;214:297-8.e1.
40. Introducing the statewide paediatric critical health resource information system | Safer Care Victoria. [Last accessed on 5 Mar 2024]. https://www.safercare.vic.gov.au/news/introducing-the-statewide-paediatric-critical-health-resource-information-system

Review Article

# Advancements in Otorhinolaryngological Management of Mucopolysaccharidosis: A Comprehensive Review

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## Abstract

Mucopolysaccharidosis (MPS) is a group of rare lysosomal storage disorders caused by a lack of specific lysosomal enzymes, resulting in the accumulation of glycosaminoglycans in various tissues and organs. Ear, nose, and throat disorders are frequently present as early and common symptoms in MPS patients, particularly in types I, II, and VI. These conditions include recurrent otitis media with effusion, hearing loss, chronic rhinosinusitis, nasal obstruction, adenotonsillar hypertrophy, and upper airway obstruction, which results in obstructive sleep apnea syndrome. Pediatric otolaryngologists are critical in enabling early diagnosis, initiating multidisciplinary treatment, and providing optimal perioperative care to MPS patients. This review examines the pediatric otolaryngologists' involvement and role in managing MPS, respiratory complications that come with it, potential treatment options, such as novel surgical techniques and enzyme replacement therapy, and the significance of hearing impairment as a critical diagnostic indicator for MPS. Furthermore, it emphasizes the importance of a smooth transition from pediatric to adult care for MPS patients.

**Keywords:** Enzyme replacement therapy, mucopolysaccharidosis, otorhinolaryngological manifestations, respiratory complications, transition of care

## Role of Pediatric Otolaryngologists in the Management of Mucopolysaccharidosis (MPS)

MPS is a rare lysosomal storage disorder caused by a lack of enzymes needed to break down glycosaminoglycans (GAGs), resulting in their accumulation in various organs and tissues.[1,2] This accumulation leads to a variety of progressive systemic dysfunctions and manifestations.

Ear, nose, and throat (ENT) complications are early and common clinical symptoms in MPS patients, particularly in types I, II, and VI.[2-6] This includes the following: (1) recurrent otitis media with effusion and resulting hearing loss; (2) chronic rhinosinusitis and nasal obstruction; (3) adenotonsillar enlargement; and (4) upper airway obstruction causes obstructive sleep apnea (OSA) syndrome. These ENT issues are typically the first symptoms that cause MPS patients to seek medical attention, often before the MPS diagnosis is confirmed.[5-8]

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Otolaryngologists play a crucial role in identifying diseases early and initiating comprehensive management,[8,9] particularly types I and II. Many cases of MPS I/II are initially identified during routine tonsillectomy procedures. The tonsils of MPS patients are often exceptionally large for the patient's age, and these children may present with OSA earlier than their peers with similar living conditions.[6,10]

Otolaryngologists must remain vigilant when encountering cases of unusual snoring or exceptionally enlarged tonsils in children. In such cases, sending tonsillar specimens for histopathological examination is of utmost importance. The histopathological findings, such as the presence of foam cells or increased glycosaminoglycan deposits, can provide valuable clues for the diagnosis of MPS.[10]

This practice of routine histopathological examination of tonsil specimens in unusual cases can significantly contribute to the early detection of MPS, allowing for timely intervention and management of the disease.[10]

Early and accurate diagnosis is critical, as treatments like enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation are most effective when started early before irreversible organ damage occurs.[11,12] Any delay in diagnosis can have serious consequences for the patient's prognosis and quality of life.

Furthermore, managing MPS necessitates several ENT surgical interventions, which present significant anesthetic challenges due to the complexities of airway management.[13] Knowing the underlying MPS condition allows otolaryngologists to anticipate better and manage potential complications.

In conclusion, the prevalence and early onset of ENT symptoms in MPS necessitates that otolaryngologists be familiar with these manifestations. They play an essential role in prompt diagnosis, effective treatment management, and providing the best perioperative care through a multidisciplinary approach, ultimately improving outcomes for MPS patients.

## Respiratory Complications in MPS

Respiratory complications are common with all types of MPS. These issues arise due to GAG accumulation, which causes anatomical distortions and functional impairments in the airways.[1,14-20] Individuals with MPS frequently have specific anatomical characteristics predisposing them to respiratory dysfunction.[21] As GAGs accumulate throughout the respiratory system, they cause extensive damage at all levels of the airway, from the lips to the lungs.[22,23]

OSA, recurrent respiratory infections, and structural abnormalities, such as adenoid and tonsillar hypertrophy

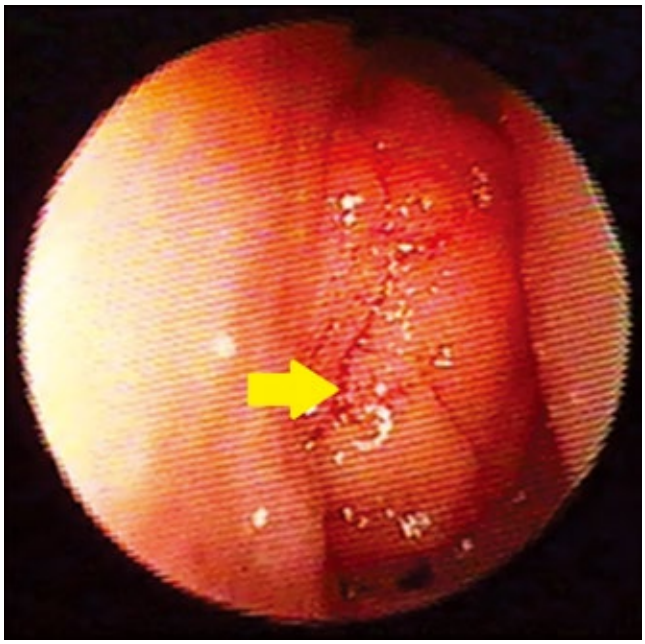

**Figure 1:** Adenoid hypertrophy in a patient with mucopolysaccharidosis. Nasopharyngeal endoscopic view showing enlarged adenoid tissue (marked with arrow) obstructing the posterior choanae. This hypertrophy can lead to nasal obstruction and contribute to sleep-disordered breathing in MPS patients

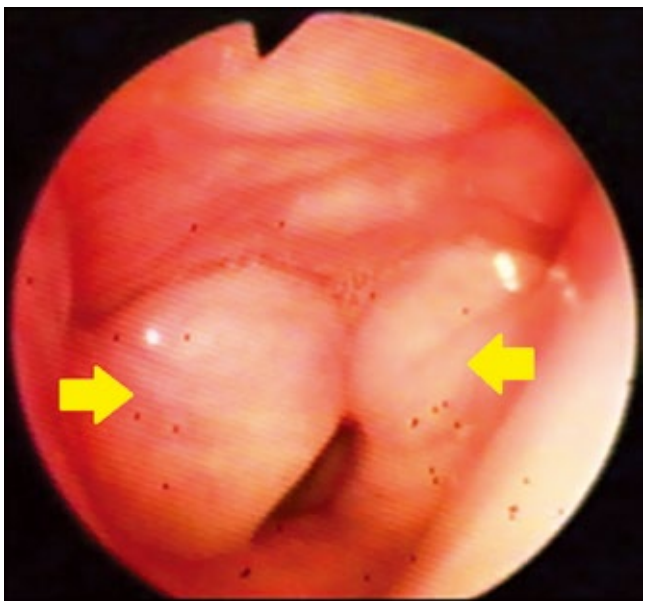

**Figure 2:** Tonsillar hypertrophy in a patient with mucopolysaccharidosis. Oropharyngeal view demonstrating significantly enlarged palatine tonsils (arrows), characteristic of MPS. Grade 3+ tonsillar hypertrophy is shown, nearly meeting at midline and potentially causing upper airway obstruction

[Figures 1 and 2], nasal septum irregularities, turbinate hypertrophy, and macroglossia [Figure 3] are among the respiratory problems seen in MPS. Additional complications include a thickened pharyngeal wall, laryngeal anomalies, tracheomalacia, tracheal stenosis, a

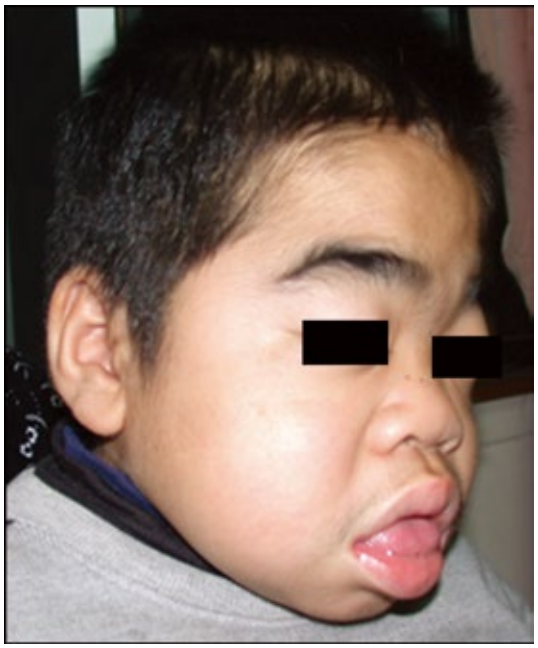

**Figure 3:** Macroglossia in a patient with mucopolysaccharidosis. Clinical photograph showing an enlarged tongue (macroglossia) characteristic of MPS. Note how the tongue protrudes beyond the dental arch, potentially causing difficulties with speech, eating, and airway management. *Note.* Copyright: ©2024 Lee *et al.* Used with permission

short neck, dyspnea, limited joint mobility, and skeletal deformities, as well as increased mucus production in both the upper and lower airways.[3,24-27] These structural changes can cause chronic rhinosinusitis and otitis media, resulting in hearing loss.[1,14,15] Excessive tissue growth on the arytenoid cartilages and aryepiglottic folds can cause prolapse into the laryngeal inlet, resulting in stridor, and severe airway obstruction.[3]

Hepatosplenomegaly can limit diaphragmatic movement, and GAG deposits in the lungs may impair gas exchange, resulting in diffusion abnormalities.[16] Thick, copious secretions throughout the respiratory tract are common, as are frequent infections in the upper and lower respiratory systems, with more than half of patients suffering from recurring throat and ear infections.[28] However, the rarity of MPS makes it challenging to draw definitive conclusions about the prevalence and severity of respiratory complications in each subtype.[22]

## Potential Treatment Approaches for Respiratory Conditions in MPS

The treatment of airway obstruction in MPS patients remains contentious, with only moderate success.[3] The therapeutic strategy frequently begins with surgical interventions to remove obstructions caused by GAG accumulation in the adenoids and tonsils, which leads to hypertrophy. These structures are frequently targeted for surgical removal in cases exhibiting upper airway obstruction symptoms, with varying rates of adenoidectomy and/or tonsillectomy reported in the literature.[3-6,8,15,23]

When simpler airway procedures are insufficient or there are significant tracheobronchial complications, continuous positive airway pressure (CPAP) is sometimes used while sleeping.[23] Although CPAP can provide temporary relief, it is frequently poorly tolerated in patients with behavioral issues and may become less effective as the airway condition deteriorates.[3,13]

If less invasive measures fail to effectively manage upper airway obstruction, a tracheotomy may be necessary. This procedure is used for severe and persistent upper airway blockages to help with difficult airway management before other non-ENT surgical procedures in an emergency. Tracheotomy is reported in approximately 11% of cases, which is consistent with data from studies.[3,8,14,15,23,28] Before surgery, a computed tomography scan of the chest and airway is recommended to determine the extent of airway narrowing.[28]

Furthermore, tracheostomy is essential in managing complex cases of MPS II (Hunter's syndrome), particularly when simpler treatments fail. Challenges and complications associated with tracheostomy in this patient population have been documented, emphasizing the importance of skilled multidisciplinary care and thorough preoperative discussions about the procedure's implications.[29]

Recently, innovative surgical methods such as tracheal resection have been investigated for severe cases, such as in Morquio A syndrome (MPS IVA), where traditional methods are infective. A notable case involved a successful tracheal resection without cardiopulmonary bypass, which resulted in promising postoperative improvements in respiratory and overall health after 1 year.[30]

Tracheal resection is a complex surgical procedure that may be considered for severe cases of airway obstruction in MPS patients, particularly when other less invasive methods have failed.[31] Indications include severe and persistent upper airway obstruction, failure of conservative management and less invasive surgical interventions, and progressive tracheal stenosis unresponsive to other treatments. Potential complications include anastomotic dehiscence, restenosis, voice changes, tracheomalacia, and infection. The decision to perform a tracheal resection should be made by a multidisciplinary team, considering the patient's overall health status, the extent of airway involvement, and the potential risks and benefits of the procedure. Close postoperative monitoring and long-term follow-up are essential to manage potential complications and ensure optimal outcomes.

(ERT is a newer treatment option that has shown significant benefits in alleviating respiratory symptoms

in MPS II and VI patients. ERT has been particularly effective in improving the sleep-disordered breathing conditions observed in these patients.[31,32] However, the efficacy of ERT varies by MPS type, with MPS III patients showing less respiratory improvement than those with MPS I, II, and VI.[33]

Given these findings, while ERT can alleviate many MPS symptoms, its application may be limited to certain types of the condition. It is still critical to assess the efficacy of ERT across different MPS types and consider alternative treatment options for patients who do not respond well to ERT.

## Hearing Impairment as a Diagnostic Indicator for MPS

Hearing impairment is a critical symptom in the diagnosis of MPS, and it is nearly universally among affected children, making early detection and intervention critical.[1-4] Hearing loss in MPS usually involves both conductive and sensorineural mechanisms.[5]

Conductive hearing loss in MPS patients is frequently caused by seromucous otitis media [Figure 4][6] or ossicular chain deformities,[7] which are caused by the accumulation of GAGs in middle ear structures, such as the mucosa, tympanic membrane, and ossicles.[1,8] Although surgical interventions, such as adenoidectomy and ventilation tubes, can help with conductive hearing loss, hearing aids are frequently required to treat residual sensorineural hearing loss.[5,6]

The sensorineural hearing loss component is thought to be caused by GAG deposition in the cochlea, auditory nerve, and brainstem,[5,7] which may be exacerbated by a reduction in cochlear hair cells.[9] Patients frequently exhibit mixed-type hearing loss that includes both conductive and sensorineural elements.[5]

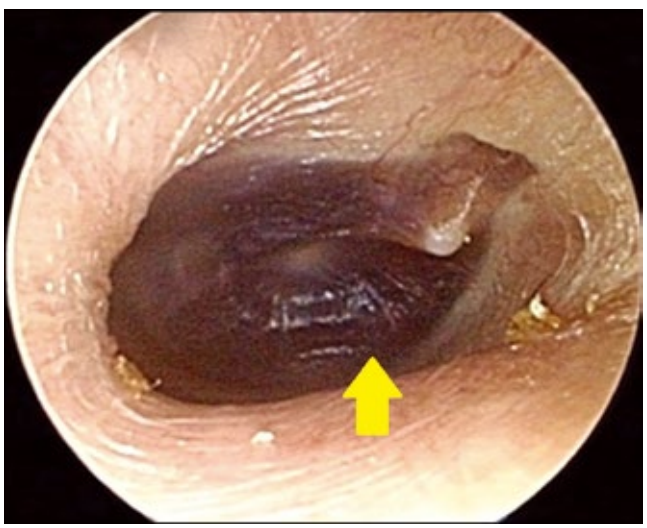

**Figure 4:** Seromucous otitis media in a patient with mucopolysaccharidosis. Otoscopic view of the tympanic membrane showing a cloudy, amber-colored appearance (arrow) indicative of middle ear effusion. This condition is common in MPS patients and can lead to conductive hearing loss if left untreated

Hearing loss occurs early in the course of MPS, particularly in types I, II, and VI, and has significant diagnostic implications.[3,11] According to the Hunter Outcome Survey, approximately 67% of people with MPS II have experienced hearing loss, with half of these cases necessitating the installation of ventilation tubes.[13] Because of the significant impact on language development and overall quality of life, early and proactive otolaryngological evaluations are strongly advocated and recommended.[6,14]

Furthermore, a recent study found that hearing loss is often the first symptom in MPS II patients, appearing around the age of 6 months.[34] This emphasizes the importance of early detection and treatment of hearing impairment in MPS patients to allow for timely management and better outcomes.

## Early Symptoms of MPS and the Importance of Prompt Diagnosis

Recognizing MPS in its early stages necessitates careful observation of a variety of symptoms, many of which can be mistaken for common childhood illnesses.[2] Notably, hearing loss appears as an early and significant symptom in children with MPS, necessitating prompt otolaryngological evaluations and interventions.[21] Distinct clusters of symptoms, which are uncommon in unaffected children but appear together in those with MPS II [Table 1], can help raise clinical suspicion for the disorder.[7]

The size and appearance of tonsils can serve as an early diagnostic indicator for MPS. Exceptionally enlarged tonsils, especially when accompanied by early-onset OSA, should raise suspicion for MPS. Otolaryngologists should consider the possibility of MPS when encountering

**Table 1: Clinical features that may suggest a diagnosis of mucopolysaccharidosis II**

| Clinical Features |
|---|
| Coarse facial features |
| Macrocephaly |
| Macroglossia |
| Short stature |
| Joint stiffness/contractures |
| Hernias |
| Hepatosplenomegaly |
| Recurrent ENT infections |
| Loud snoring/sleep apnea |
| Progressive cognitive impairment |

such cases, particularly if the child's tonsils are disproportionately large compared to their age and if OSA symptoms appear earlier than expected.[20]

In cases of unusual snoring or enlarged tonsils in children, it is recommended to perform a histopathological examination of tonsillar specimens following tonsillectomy. This practice can lead to early diagnosis of MPS, even in cases where the condition was not initially suspected.[20]

Aside from hearing loss, early symptoms of MPS include recurrent upper respiratory infections, chronic rhinosinusitis, nasal blockages, and adenotonsillar enlargement.[3,4,6] The coexistence of these symptoms should raise the possibility of MPS.[7,8] Early and proactive engagement by otolaryngologists is critical, as early diagnosis and treatment significantly improve life quality and slow disease progression.[8,9] Furthermore, ERT is effective in managing these early symptoms when initiated early.[30,33] Early detection and diagnosis by otolaryngologists are critical because they allow for more effective multidisciplinary management, ensuring that affected children receive the comprehensive care necessary for the best possible outcomes.[8,9]

## Treatment Options for Auditory and Otologic Issues in MPS Patients

Sensorineural and mixed conductive-sensorineural hearing loss are common in MPS patients, particularly in the first decade of life.[3,9] Ventilation tubes are commonly used to treat conductive hearing loss, which is often caused by persistent middle ear fluid. Long-lasting tympanostomy tubes are recommended for initial use to reduce anesthetic risks and the possibility of recurring middle ear effusions.[3] If the hearing loss is progressive and neurosensory, postaural hearing aids may be the best option.[9] However, normalization of hearing following the insertion of transtympanic drainage tubes does not eliminate the need for regular audiological evaluation.[3,5]

Using hearing aids and transtympanic ventilation tubes has been shown to improve language development in children with moderate cognitive impairments.[6,9] As a result of the ongoing impact of hearing loss on their development and overall quality of life, these patients require routine follow-up assessments.[3,9] Management of auditory and otologic issues in MPS patients requires a comprehensive approach, taking into account the specific subtype of MPS and the individual patient's needs.[35]

## Navigating the Transition from Pediatric to Adult Care for MPS Patients

As more MPS patients live into adulthood thanks to advances in diagnostic and therapeutic techniques, it is critical to ensure a smooth transition from pediatric to adult care. Lampe *et al.*[36] investigate the critical considerations required to develop an effective transition strategy for patients with severe and progressive MPS symptoms. The study emphasizes the importance of starting transition planning early, giving patients and their families enough time in the adult care environment, and building rapport with the new medical team. It is critical to actively involve both patients and caregivers in educational activities to improve their understanding of the transition process and promote the development of self-care skills. The use of transition documents and checklists aids in assessing the patient's readiness for the transition and identifying any potential obstacles. Furthermore, the participation of a well-coordinated multidisciplinary team with expertise in MPS is critical to ensure continuity of care and meeting these individuals' complex health needs. The authors argue that transition plans should be detailed and tailored to each patient's medical, social, and emotional needs.[35] By incorporating these critical components, healthcare providers can ensure a smooth and effective transition from pediatric to adult care for MPS patients, improving their overall disease management and quality of life.

## Conclusion

The prevalence and early presentation of ENT symptoms in MPS conditions emphasize the need for otolaryngologists to be well-versed in these disorders to facilitate quick diagnosis, initiate appropriate management, and provide the best perioperative care through a team-based approach. Recent research studies have reaffirmed the importance of pulmonary function and hearing loss as early diagnostics indicators for MPS. Innovative surgical methods, such as tracheal resection in severe airway blockages in MPS IVA cases, have produced promising results for carefully chosen patients. ERT has demonstrated varying degrees of success in relieving respiratory symptoms across MPS types, emphasizing the importance of individual treatment protocols. As MPS patients' life expectancy increases, otolaryngologists and pulmonologists play increasingly important roles in the early detection and ongoing management of these conditions. Additionally, a smooth transition from pediatric to adult care is critical for MPS patients' health and quality of life. Medical professionals can improve patient outcomes and disease management by developing and implementing comprehensive, tailored transition strategies. Otolaryngologists play a critical role in improving the quality of care for MPS patients, and working with a multidisciplinary team is essential to providing the best possible care. Furthermore, the importance of histopathological examination of tonsillar specimens in cases of unusual snoring or enlarged tonsils in children cannot be overstated, as it can lead to early diagnosis of MPS and timely intervention.

## Declaration of patient consent

Informed consent was obtained from the patient (or legal guardian) for the publication of the image.


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## Author contributions

C.-L.L. was the primary author of the manuscript. S.-P.L., K.-S.L., C.-H.S., and H.-Y.L. contributed to patient follow-up and provided valuable input during the manuscript preparation process. C.-K.C., J.-L.L., and R.-Y.T. were responsible for conducting biochemical analyses and critically revising the manuscript. Y.-T.L., Y.-H.C., and H.-C.C. assisted with patient screening and offered crucial revisions to the manuscript. All authors thoroughly reviewed the final version of the manuscript and gave their approval for submission.

## Data availability statement

This comprehensive review article does not report original research data. All information analyzed and discussed in this review is based on previously published studies, which are properly cited throughout the manuscript. The data supporting the findings of this study are available from the corresponding authors of the original research articles cited. Any inquiries regarding the data discussed in this review should be directed to the original authors or the journals in which the primary studies were published.

## Statement from the Institutional Review Board

Not applicable.


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## Conflicts of interest

There are no conflicts of interest.

## Abbreviations

CPAP: Continuous positive airway pressure
CT: Computed tomography
ENT: Ear, nose, and throat
ERT: Enzyme replacement therapy
GAGs: Glycosaminoglycans
MPS: Mucopolysaccharidosis
OSA: Obstructive sleep apnea

## References


1. Muenzer J. Overview of the mucopolysaccharidoses. Rheumatology 2011;50:v4-12.
2. Zhou J, Lin J, Leung WT, Wang L. A basic understanding of mucopolysaccharidosis: Incidence, clinical features, diagnosis, and management. Intractable Rare Dis Res 2020;9:1-9.
3. Simmons MA, Bruce IA, Penney S, Wraith E, Rothera MP. Otorhinolaryngological manifestations of the mucopolysaccharidoses. Int J Pediatr Otorhinolaryngol 2005;69:589-95.
4. Arn P, Bruce IA, Wraith JE, Travers H, Fallet S. Airway-related symptoms and surgeries in patients with mucopolysaccharidosis I. Ann Otol Rhinol Laryngol 2015;124:198-205.
5. Mesolella M, Cimmino M, Cantone E, Marino A, Cozzolino M, Della Casa R, *et al*. Management of otolaryngological manifestations in mucopolysaccharidoses: Our experience. Acta Otorhinolaryngol Ital 2013;33:267-72.
6. Gönüldaş B, Yılmaz T, Sivri HS, Güçer KS, Kılınç K, Genç GA, *et al*. Mucopolysaccharidosis: Otolaryngologic findings, obstructive sleep apnea and accumulation of glucosaminoglycans in lymphatic tissue of the upper airway. Int J Pediatr Otorhinolaryngol 2014;78:944-9.
7. Wold SM, Derkay CS, Darrow DH, Proud V. Role of the pediatric otolaryngologist in diagnosis and management of children with mucopolysaccharidoses. Int J Pediatr Otorhinolaryngol 2010;74:27-31.
8. Torres DA, Barth AL, Valente MPM, Mello PP, Horovitz DDG. Otolaryngologists and the early diagnosis of mucopolysaccharidoses: A cross-sectional study. Diagnostics 2019;9:187.
9. Vargas-Gamarra MF, de Paula-Vernetta C, Vitoria Miñana I, Ibañez-Alcañiz I, Cavallé-Garrido L, Alamar-Velazquez A. Audiological findings in children with mucopolysaccharidoses type I-IV. Hallazgos audiológicos en niños con mucopolisacaridosis tipos i-iv. Acta Otorrinolaringol Esp 2017;68:262-8.
10. Arn P, Wraith JE, Underhill L. Characterization of surgical procedures in patients with mucopolysaccharidosis type I: Findings from the MPS I Registry. J Pediatr 2009;154:859-64.e3.
11. Valayannopoulos V, Wijburg FA. Therapy for the mucopolysaccharidoses. Rheumatology 2011;50:v49-59.
12. Lehman TJ, Miller N, Norquist B, Underhill L, Keutzer J. Diagnosis of the mucopolysaccharidoses. Rheumatology 2011;50:v41-8.
13. Walker R, Belani KG, Braunlin EA, Bruce IA, Hack H, Harmatz PR, *et al*. Anaesthesia and airway management in mucopolysaccharidosis. J Inherit Metab Dis 2013;36:211-9.
14. Yeung AH, Cowan MJ, Horn B, Rosbe KW. Airway management in children with mucopolysaccharidoses. Arch Otolaryngol Head Neck Surg 2009;135:73-9.
15. John A, Fagondes S, Schwartz I, Azevedo AC, Barrios P, Dalcin P, *et al*. Sleep abnormalities in untreated patients with mucopolysaccharidosis type VI. Am J Med Genet A 2011;155A:1546-51.
16. Leighton SE, Papsin B, Vellodi A, Dinwiddie R, Lane R. Disordered breathing during sleep in patients with mucopolysaccharidoses. Int J Pediatr Otorhinolaryngol 2001;58:127-38.
17. Lin HY, Chen MR, Lin CC, Chen C-P, Lin D-S, Chuang C-K, *et al*. Polysomnographic characteristics in patients with mucopolysaccharidoses. Pediatr Pulmonol 2010;45:1205-12.

18. Nashed A, Al-Saleh S, Gibbons J, MacLusky I, MacFarlane J, Riekstins A, *et al*. Sleep-related breathing in children with mucopolysaccharidosis. J Inherit Metab Dis 2009;32:544-50.
19. Santamaria F, Andreucci MV, Parenti G, Polverino M, Viggiano D, Montella S, *et al*. Upper airway obstructive disease in mucopolysaccharidoses: Polysomnography, computed tomography and nasal endoscopy findings. J Inherit Metab Dis 2007;30:743-9.
20. Muhlebach MS, Wooten W, Muenzer J. Respiratory manifestations in mucopolysaccharidoses. Paediatr Respir Rev 2011;12:133-8.
21. Semenza GL, Pyeritz RE. Respiratory complications of mucopolysaccharide storage disorders. Medicine 1988;67:209-19.
22. Berger KI, Fagondes SC, Giugliani R, Hardy KA, Lee KS, McArdle C, *et al*. Respiratory and sleep disorders in mucopolysaccharidosis. J Inherit Metab Dis 2013;36:201-10.
23. Steven Sims H, Kempiners JJ. Special airway concerns in patients with mucopolysaccharidoses. Respir Med 2007;101:1779-82.
24. Kamin W. Diagnosis and management of respiratory involvement in Hunter syndrome. Acta Paediatr 2008;97:57-60.
25. Nagano R, Takizawa S, Hayama N, Umemura S, Uesugi T, Nakagawa S, *et al*. Three-dimensional CT and histopathological findings of airway malacia in Hunter syndrome. Tokai J Exp Clin Med 2007;32:59-61.
26. Pelley CJ, Kwo J, Hess DR. Tracheomalacia in an adult with respiratory failure and Morquio syndrome. Respir Care 2007;52:278-82.
27. Shih SL, Lee YJ, Lin SP, Sheu CY, Blickman JG. Airway changes in children with mucopolysaccharidoses. Acta Radiol 2002;43:40-3.
28. Shapiro J, Strome M, Crocker AC. Airway obstruction and sleep apnea in Hurler and Hunter syndromes. Ann Otol Rhinol Laryngol 1985;94:458-61.
29. Malik V, Nichani J, Rothera MP, Wraith JE, Jones SA, Walker R, *et al*. Tracheostomy in mucopolysaccharidosis type II (Hunter's syndrome). Int J Pediatr Otorhinolaryngol 2013;77:1204-8.
30. Frauenfelder C, Maughan E, Kenth J, Nandi R, Jones S, Walker R, *et al*. Tracheal resection for critical airway obstruction in Morquio A syndrome. Case Rep Pediatr 2023;2023:7976780.
31. Solano M, Fainboim A, Politei J, Porras-Hurtado GL, Martins AM, Souza CFM, *et al*. Enzyme replacement therapy interruption in patients with mucopolysaccharidoses: Recommendations for distinct scenarios in Latin America. Mol Genet Metab Rep 2020;23:100572.
32. Kampmann C, Lampe C, Whybra-Trümpler C, Wiethoff CM, Mengel E, Arash L, *et al*. Mucopolysaccharidosis VI: cardiac involvement and the impact of enzyme replacement therapy. J Inherit Metab Dis 2014;37:269-76.
33. Muenzer J. Early initiation of enzyme replacement therapy for the mucopolysaccharidoses. Mol Genet Metab 2014;111:63-72.
34. Wolfberg J, Chintalapati K, Tomatsu S, Nagao K. Hearing loss in mucopolysaccharidoses: Current knowledge and future directions. Diagnostics 2020;10:554.
35. AlSayed M, Arafa D, Al-Khawajha H, Afqi M, Al-Sanna'a N, Sunbul R, *et al*. Consensus-based expert recommendations on the management of MPS IVa and VI in Saudi Arabia. Orphanet J Rare Dis 2024;19:269.
36. Lampe C, McNelly B, Gevorkian AK, Hendriksz CJ, Lobzhanidze TV, Pérez-López J, *et al*. Transition of patients with mucopolysaccharidosis from paediatric to adult care. Mol Genet Metab Rep 2019;21:100508.

# Prevalence and Clinical Characterization of Human Rhinovirus in Hospitalized Children with Acute Lower Respiratory Tract Infection in Taiwan

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## Abstract

**Background:** Human rhinovirus (HRV) and its species are the predominant viruses contributing to acute lower respiratory tract infection (ALRTI) in several countries. We explored their prevalence and clinical implications in hospitalized children with ALRTI in southern Taiwan. **Materials and Methods:** From 2011 to 2013, children with ALRTI younger than or 13 years admitted to the hospital were enrolled. Nasopharyngeal swab samples were collected to detect HRV, HRV species, and other common respiratory viruses. Participants were then categorized into HRV and non-HRV groups according to their virus test results. **Results:** A total of 55 children were enrolled: 21 in the HRV group and 34 in the non-HRV group. Respiratory viruses were found in 76.4% of the cases, including HRV (38.2%), enterovirus (18.2%), adenovirus (16.4%), and respiratory syncytial virus (7.3%). In the HRV group, HRV-C (57.1%) was predominant over HRV-A (23.8%) and HRV-B (19.0%). HRV and HRV-C were more common in spring and winter ($P < 0.05$). The diagnosis of bronchitis or bronchiolitis was significantly higher in the HRV group (52.4%) compared with the non-HRV group (17.6%, $P = 0.009$). The proportion of patients with comorbid asthma attack was higher in the HRV group than in the non-HRV group and higher in the HRV-C group than in the HRV-B or HRV-C group. **Conclusions:** HRV is the most predominant virus in hospitalized children because of ALRTI in southern Taiwan, and HRV-C is the predominant species. HRV and HRV-C are more common in spring and winter and are associated with asthma attacks in hospitalized children with ALRTI.

**Keywords:** Asthma exacerbation, children, respiratory airway infection, rhinovirus, rhinovirus C

## Introduction

Acute respiratory tract infections significantly contribute to morbidity and mortality among children.[1] Human rhinovirus (HRV), respiratory syncytial virus (RSV), influenza virus, enterovirus, human metapneumovirus, and parainfluenza virus are the most common viruses.[2,3] Research indicates that HRV significantly contributes to various clinical presentations in children, ranging from symptomless upper airway illness to serious lower respiratory tract infections. These include conditions such as the common cold, bronchiolitis/bronchitis, pneumonia, and asthma exacerbations (AEs).[3-5] Despite new developments in asthma treatment, managing

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environmental triggers and maintaining regular low-dose medication are essential for most children with asthma.[6] Studies show that HRV leads to more severe symptoms than other viruses, particularly asthma attack, in countries such as Japan, Hong Kong, China, Korea, Thailand, Australia, and Canada.[4,5,7-13]

HRV, a member of the *Picornaviridae* family and enterovirus genus, is a nonenveloped virus with a single-stranded ribonucleic acid (RNA) genome. Its viral capsid is composed of four viral proteins, VP1 to VP4.[14] More than 100 serotypes of HRV exist and are categorized into three species in accordance with their genetic classification: HRV-A, HRV-B, and HRV-C.[14] Different species of HRV are associated with differing severity of respiratory diseases.[15] HRV-C is associated with more severe conditions, including acute lower respiratory tract infections (ALRTIs) and AEs.[7,9,10] Iwane *et al*. and Xen *et al*.[12,16] suggested that the clinical manifestations of the three HRV species do not differ other than in the aforementioned manners. The relationship between clinical presentations and HRV species in children remains controversial and warrants investigation.

We hypothesized that HRV and various respiratory viruses cause ALRTIs with differing clinical severity. Consequently, this prospective study was undertaken to examine the prevalence and clinical manifestations of HRV and other respiratory viruses among hospitalized children with ALRTI. We also evaluated the clinical significance of the three HRV species in southern Taiwan by examining their prevalence and clinical manifestations.

## Materials and Methods

### Patients

This was a prospective study. Children younger than 13 years hospitalized with ALRTI at a medical center between 2011 and 2013 were enrolled [Figure 1]. ALRTI was diagnosed when the patient exhibited respiratory symptoms with abnormal lung sounds (e.g., wheezing, rales, or rhonchi), including bronchiolitis, bronchitis, bronchopneumonia, or pneumonia. When the chest X-ray (CXR) exclusively showed an infiltration pattern, bronchiolitis (<2 years old) or bronchitis (≥2 years old) was diagnosed. If the CXR revealed an alveolar pattern, the diagnosis was bronchopneumonia or pneumonia. An AE was defined as bilateral wheeze that responds well to bronchodilator or corticosteroid, coupled with a prior asthma diagnosis. Nasopharyngeal swabs were collected and tested to determine the viruses. Participants were then classified into the HRV group if their viral tests were positive for HRV and into the non-HRV group if their tests were negative for HRV. Informed consent was obtained from the parents or guardians of all children. The Hospital Ethical Review Committee approved this study protocol.

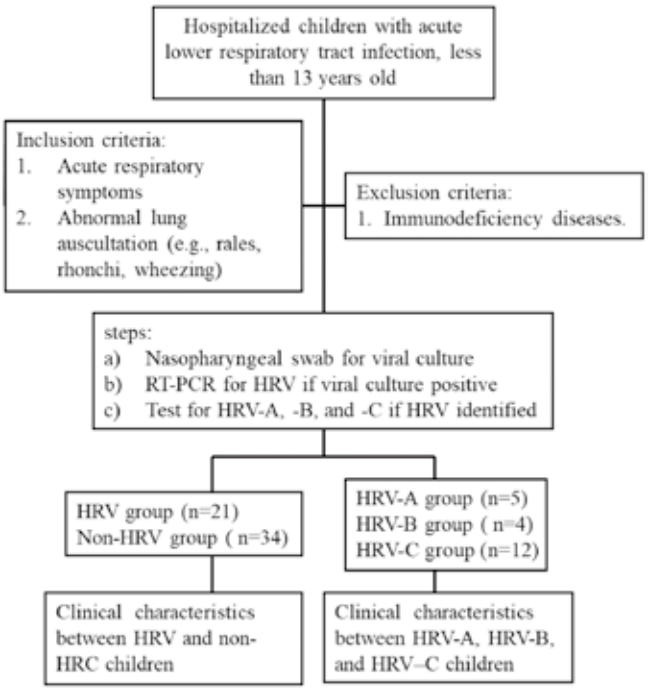


**Figure 1:** Study flowchart. HRV, human rhinovirus

### Viral culture

Samples were tested for respiratory viruses using conventional viral culture with MDCK, A549, LLC-MK2, and MRC-5 cell lines. Upon cytopathic effect observation, cells were stained for respiratory viruses, herpes simplex virus 1, pan enteroviruses, and cytomegalovirus, with HRV detection via real-time reverse transcription–polymerase chain reaction (RT-PCR).

### One-step RT-PCR technique for HRV detection

RNA was extracted using a MagCore Viral Nucleic Acid Kit. HRV detection employed a one-step RT-PCR targeting the 5′ noncoding region with the AgPath-ID kit,[17] analyzed by using Bio-Rad CFX96 for threshold cycles.

### VP4/VP2 sequencing for typing the HRV genome

The SuperScript III system was used for RT-PCR first-strand synthesis, followed by VP4/VP2 amplification and seminested PCR, as previously described.[17] An ABI 3130xl analyzer was used to analyze PCR products, with the Basic Local Alignment Search Tool for sequence analysis. HRV classification used the neighbor-joining method in MEGA version 5.0.

### Statistical analysis

The features of both the HRV and non-HRV groups, as well as the HRV-A, HRV-B, and HRV-C groups, are presented as mean ± standard deviation (SD). To compare variables across the HRV and non-HRV groups and among the HRV-A, HRV-B, and HRV-C groups, we used

two-sample *t* tests, chi-square tests, and the Fisher's exact test. Data were analyzed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). A *P* value of <0.05 was used to establish statistical significance.

## Results

### Patient characteristics

From 2011 to 2013, 55 children were recruited for the study, distributed into two groups: 21 in the HRV group and 34 in the non-HRV group, as detailed in [Table 1]. The average ages (mean ± SD) of the overall, HRV, and non-HRV groups were 3.1 ± 3.1, 2.8 ± 3.5, and 3.3 ± 2.9 years, respectively. The proportion of boys in each group was 63.6%, 71.4%, and 58.8%, respectively.

### Detection of HRV and other respiratory viruses

The respiratory viruses detected in our patients are detailed in [Table 2]. Overall, the prevalence of the identified respiratory viruses was 76.4%. The most common virus was HRV (38.2%), followed by enterovirus (18.2%), adenovirus (16.4%), and RSV (7.3%). In the HRV group, the rate of single virus infection stood at 66.7%, compared with 50.0% in the non-HRV group. Among the HRV group, the most common comorbid virus was enterovirus (23.8%). In the non-HRV group, the most common viruses were adenovirus (23.8%), enterovirus (14.7%), and RSV (11.8%).

### Epidemiology of HRV infection

As shown in [Table 1 and Figure 2], the majority of HRV samples were detected during cold seasons (spring and winter; $P < 0.05$). The proportion of HRV among ALRTI cases also peaked during winter (66.7%; Figure 3].

### Clinical manifestations of HRV and non-HRV infection

The clinical presentations in the children in the HRV and non-HRV groups are listed in [Table 1]. The extents of comorbid asthma attack and corticosteroid use were higher in the HRV group than in the non-HRV group (28.6% vs 11.8% and 33.3% vs 11.8%, $P = 0.156$ and 0.082, respectively). The length of hospital stay was similar in the groups (5.2 vs 4.9 days, $P = 0.520$). Of diagnoses, 52.4% were of bronchitis/bronchiolitis in the HRV group, which was higher than the 17.6% rate in the non-HRV group ($P = 0.009$).

**Table 1: Demographic and clinical features of HRV versus non-HRV infections in hospitalized children with acute lower respiratory tract infections**

| | All patients ($n = 55$) | HRV group ($n = 21$) | Non-HRV group ($n = 34$) | *P* value |
|---|---|---|---|---|
| Male sex, *n* (%) | 35 (63.6) | 15 (71.4) | 20 (58.8) | 0.399[a] |
| Age in years, mean ± SD, median (min, max) | 3.1 ± 3.1<br>1.8 (0.1, 13.8) | 2.8 ± 3.5<br>1.3 (0.1, 13.8) | 3.3 ± 2.9<br>2.0 (0.1, 11.0) | 0.284[c] |
| <3 years, *n* (%) | 37 (67.3) | 16 (76.2) | 21 (61.8) | 0.318[b] |
| 3–6 years, *n* (%) | 12 (21.8) | 3 (14.3) | 9 (26.5) | |
| 7–13 years, *n* (%) | 6 (10.9) | 2 (9.5) | 4 (11.8) | |
| Length of hospitalization in days, mean ± SD, median (min, max) | 5.0 ± 2.3<br>4.0 (2.0, 13.0) | 5.2 ± 2.4<br>5.0 (2.0, 11.0) | 4.9 ± 2.3<br>4.0 (3.0, 13.0) | 0.520[c] |
| Asthma attack, *n* (%) | 10 (18.2) | 6 (28.6) | 4 (11.8) | 0.156[b] |
| Corticosteroids, *n* (%) | 11 (20.0) | 7 (33.3) | 4 (11.8) | 0.082[b] |
| Diagnosis, *n* (%) | | | | 0.009 [a*] |
| Bronchitis or bronchiolitis | 17 (30.9) | 11 (52.4) | 6 (17.6) | |
| Bronchopneumonia or pneumonia | 38 (69.1) | 10 (47.6) | 28 (82.4) | |
| Symptoms and signs, *n* (%) | | | | |
| Fever | 45 (81.8) | 15 (71.4) | 30 (88.2) | 0.156[b] |
| Dyspnea or tachypnea | 30 (54.5) | 14 (66.7) | 16 (47.1) | 0.177[a] |
| Supplemental oxygen | 16 (29.1) | 8 (38.1) | 8 (23.5) | 0.360[a] |
| Season, *n* (%) | | | | 0.025[a*] |
| Spring or winter | 25 (45.5) | 14 (66.7) | 11 (32.4) | |
| Summer or autumn | 30 (54.5) | 7 (33.3) | 23 (67.6) | |

HRV, human rhinovirus

Data are represented as number (percentage). The *P* values are for comparing the HRV group versus the non-HRV group

[*] $P < 0.05$

[a]Pearson's chi-squared test with Yates' continuity correction

[b]Fisher's exact test

[c]Mann–Whitney *U* test

**Table 2: Distribution of respiratory viruses in HRV and non-HRV groups in hospitalized children with acute lower respiratory tract infections**

| Viral result | All patients ($n$ = 55) | HRV ($n$ = 21) | Non-HRV ($n$ = 34) | $P$ value |
|---|---|---|---|---|
| Positive | 42 (76.4) | 21 (100) | 21 (61.8) | 0.001[b*] |
| Single infection | 31 (56.4) | 14 (66.7) | 17 (50.0) | 0.272[a] |
| HRV | 21 (38.2) | 21 (100) | 0 (0.0) | 0.001[b*] |
| Enterovirus | 10 (18.2) | 5 (23.8) | 5 (14.7) | 0.480[a] |
| Adenovirus | 9 (16.4) | 1 (4.8) | 8 (23.5) | 0.131[b] |
| RSV | 4 (7.3) | 0 (0.0) | 4 (11.8) | 0.286[b] |
| Influenza B | 2 (3.6) | 0 (0.0) | 2 (5.9) | 0.519[b] |
| Parainfluenza | 3 (5.5) | 1 (4.8) | 2 (5.9) | 1.000[b] |
| CMV | 3 (5.5) | 0 (0.0) | 3 (8.8) | 0.279[b] |
| HSV-1 | 1 (1.8) | 0 (0.0) | 1 (2.9) | 1.000[b] |

HRV, human rhinovirus; RSV, respiratory syncytial virus; CMV, cytomegalovirus; HSV, herpes simplex virus

Data are represented as number (percentage). The $P$ values are for comparing the HRV group versus the non-HRV group

[*] $P < 0.05$

[a] Pearson's chi-squared test with Yates' continuity correction

[b] Fisher's exact test

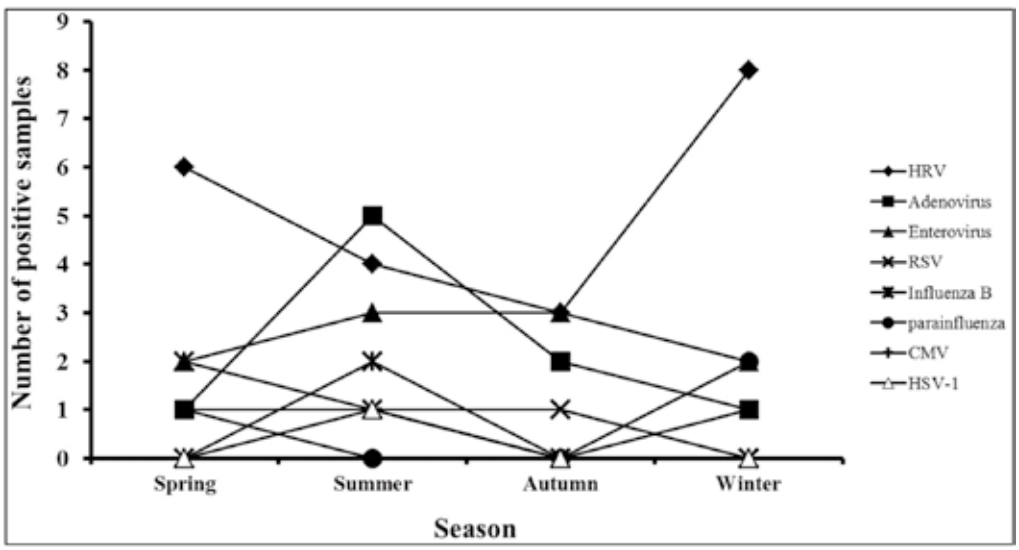


**Figure 2:** Seasonal distribution of HRV and other respiratory viruses. HRV, human rhinovirus; RSV, respiratory syncytial virus; CMV, cytomegalovirus; HSV, herpes simplex virus

### Prevalence and clinical manifestations of HRV-A, HRV-B, and HRV-C infection

As shown in [Table 3 and Figure 3], the number of cases of each HRV species identified was 5 for HRV-A, 4 for HRV-B, and 12 for HRV-C. The prevalence of HRV-A, HRV-B, and HRV-C was 23.8%, 19.0%, and 57.1%, respectively. The length of hospital stay was similar for HRV-A (4.6 days), HRV-B (5.5 days), and HRV-C infection (5.4 days). Comorbid asthma attack and corticosteroid use were more prevalent for HRV-C (41.7%, 50.0%) than for HRV-A (20.0%, 20.0%) or HRV-B (0.0%, 0.0%).

## Discussion

Our prospective study investigated the clinical implication of HRV and other viruses on hospitalized children with ALRTI in southern Taiwan, and the clinical symptoms linked to various HRV species. We found that HRV was the most common virus, particularly in winter and spring. Moreover, HRV infection, especially those caused by HRV-C, tends to induce comorbid asthma attacks in hospitalized children with ALRTI.

Respiratory viruses cause various respiratory disorders. HRV infection vary from asymptomatic to severe respiratory distress. Our findings align with Daniel's study,[13] which identified HRV as the predominant respiratory virus between September and February among hospitalized children with acute respiratory infections in Hong Kong. In Changsha, China, Zeng *et al.*[12] reported HRV to be the leading virus between September and December in hospitalized children with ALRTI.

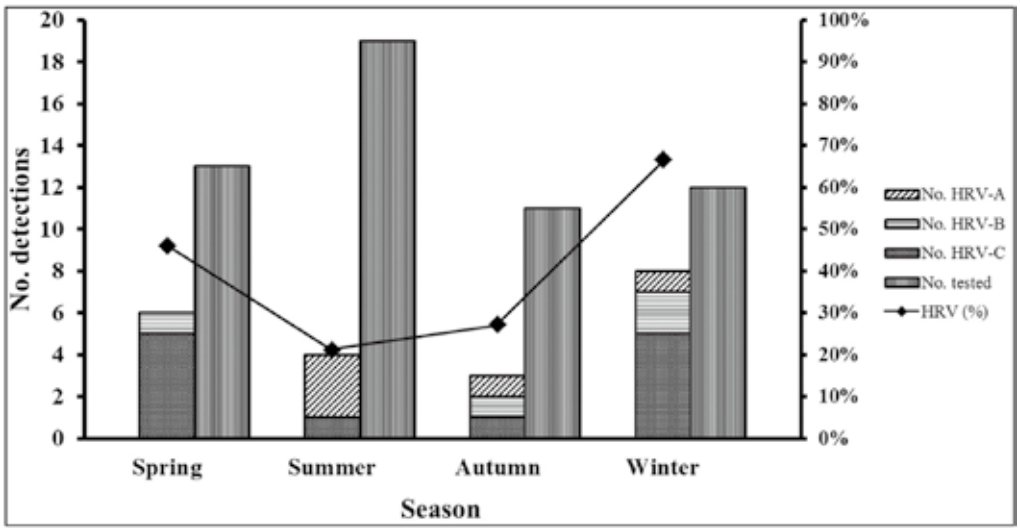


**Figure 3:** Percentage of HRV infection and case numbers of HRV species in hospitalized children with acute lower respiratory tract infections over four seasons. HRV, human rhinovirus

**Table 3: Demographic and clinical features of HRV-A, HRV-B, and HRV-C subgroups in hospitalized children with acute lower respiratory tract infections**

| | HRV-A | HRV-B | HRV-C | *p* value |
|---|---|---|---|---|
| Case number, *n* (%) | 5 (23.8) | 4 (19.0) | 12 (57.1) | |
| Male sex, *n* (%) | 4 (80.0) | 3 (75.0) | 8 (66.7) | 1.000[b] |
| Age in years, mean ± SD,<br>median (min, max) | 3.2 ± 5.9<br>0.7 (0.1, 13.8) | 1.2 ± 0.9<br>1.1 (0.3, 2.4) | 3.1 ± 2.8<br>2.3 (0.4, 10.2) | 0.175[c] |
| Length of hospitalization in days, mean ± SD, median (min, max) | 4.6 ± 2.4<br>4.0 (2.0, 8.0) | 5.5 ± 1.9<br>6.0 (3.0, 7.0) | 5.4 ± 2.7<br>5.0 (2.0, 11.0) | 0.770[c] |
| Asthma attack, *n* (%) | 1 (20.0) | 0 (0.0) | 5 (41.7) | 0.443[b] |
| Corticosteroids, *n* (%) | 1 (20.0) | 0 (0.0) | 6 (50.0) | 0.225[b] |
| Diagnosis, *n* (%) | | | | 0.708[b] |
| Bronchitis or bronchiolitis | 2 (40.0) | 3 (75.0) | 6 (50.0) | |
| Bronchopneumonia or pneumonia | 3 (60.0) | 1 (25.0) | 6 (50.0) | |
| Symptoms and signs, *n* (%) | | | | |
| Fever | 4 (80.0) | 3 (75.0) | 8 (66.7) | 1.000[b] |
| Dyspnea or tachypnea | 2 (40.0) | 3 (75.0) | 9 (75.0) | 0.452[b] |
| Supplemental oxygen | 1 (20.0) | 1 (25.0) | 6 (50.0) | 0.484[b] |
| Season, *n* (%) | | | | 0.042[b]* |
| Spring or winter | 1 (20.0) | 3 (75.0) | 10 (83.3) | |
| Summer or autumn | 4 (80.0) | 1 (25.0) | 2 (16.7) | |

HRV, human rhinovirus

Data are represented as number (percentage) unless specified otherwise

[b] Fisher's exact test

[c] Kruskal–Wallis test

In hospitalized children with ALRTI, the diagnosis of bronchitis/bronchiolitis was significantly predominant in the HRV group of this study, whereas the diagnosis of bronchopneumonia/pneumonia was predominant in the non-HRV group. Although the groups had similar lengths of hospital stay, the prevalence of comorbid asthma attack and corticosteroid use in the HRV group was more than twice that in the non-HRV group. Johnston *et al*. reported that viral infection contributed to AEs in approximately 85% of children and that approximately 65% of AEs linked to viruses were due to rhinovirus in the United Kingdom.[18] In Japan, among children with a history of asthma or wheezing and undergoing acute wheezing episodes, 61.5% were found to be positive for HRV infection.[8] Gern *et al*.[19] reported that HRV was present in 48%–57% of children with asthma, versus 24%–45% of those with bronchiolitis and pneumonia. Th1 response, innate immune response, and viral load play important roles in patients with HRV-related AEs.[20-22] The close relationship between HRV and asthma attack in children

has been addressed globally, and relevant findings were obtained in this study.

In the 21 children with HRV infection, HRV-C was more prevalent than was HRV-A or HRV-B (57.1% vs 23.8% vs 19.0%, respectively). In Hong Kong, HRV-C constituted 80.8% of HRV-related acute respiratory illness in children,[23] and HRV-C also accounted for 55% of hospitalizations due to respiratory distress in American children with asthma who are younger than 5 years.[24] Bizzintino *et al*.[7] detected HRV in 87.5% of children with AEs and found that HRV-C contributed to the majority (59.4%) in Australia. Iwasaki *et al*.[25] studied the antibodies in children with AEs and found that the titers against HRV-C were lower than those against HRV-A or HRV-B. Our study found that a larger percentage of patients infected with HRV-C experienced dyspnea compared with those with HRV-A or HRV-B (50% vs 20% vs 25%, respectively).

This is the first evaluation of the epidemiology and clinical implications of HRV species in hospitalized children with ALRTI in southern Taiwan. However, this study has some limitations. First, we investigated the epidemiology of respiratory viruses in severe clinical cases of ALRTI requiring hospitalization; thus, the results do not represent the prevalence of the virus generally among all respiratory diseases. Second, it lacks testing for total or specific immunoglobulin E for allergens, omitting correlations between viral infection, allergic status, and clinical manifestation. Further studies should investigate these topics.

In conclusion, HRV was the most predominant virus in children admitted to hospital with ALRTI and was most common during spring and winter in southern Taiwan. HRV-C is more likely to induce an asthma attack in children with ALRTI than is HRV-B or HRV-C. Developing preventive and therapeutic strategies for HRV, especially HRV-C, may contribute to reducing the clinical impact of hospitalization of children with ALRTI.

## Data availability statement

The patients' data were collected during the presence at E-Da hospital. According to the regulation of E-Da Hospital Ethical Review Committee and the "Personal Information Protection Act" in Taiwan, patients' raw data cannot be made public. The interpretation of the analyzed results acquired from medical records been unlinked to patients' identification and is available from the corresponding author upon request of the editorial staff.

## Author contributions

Hsiu-Chuan Wang, Yu-Tsun Su, and Su-Boon Yong conceptualized the study, collected grants, and wrote the initial paper; Ching-Chung Tsai, Ting-I Lin, and Yu-Shen Chen contributed to data collection and data analysis; Ya-Ling Huang and Yi-Feng Su analyzed the blood and nasopharyngeal samples; and Jiu-Yao Wang and Yu-Tsun Su contributed to the study design, interpreted data, and edited the paper. All authors approved the final paper as submitted.

## Ethics approval

The study was approved by the ethics committee/ Institutional Review Board of E-DA Hospital (IRB No.: EMRP-099-072).

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## References

1. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis 2002;2:25-32.
2. Nathan AM QY, Jafar FL, Chan YF, Eg KP, Thavagnanam S, *et al*. Viruses and hospitalization for childhood lower respiratory tract infection in Malaysia - A prospective study. Pediatr Respirol Crit Care Med 2017;1:46-51.
3. Nguyen TVT, Tran TA, Le VT, To KG. Virus infection and severe asthma exacerbations: A cross-sectional study in Children's Hospital 1, Ho Chi Minh City, Vietnam. Pediatr Respirol Crit Care Med 2023;7:20-5.
4. Kwon JM, Shim JW, Kim DS, Jung HL, Park MS, Shim JY. Prevalence of respiratory viral infection in children hospitalized for acute lower respiratory tract diseases, and association of rhinovirus and influenza virus with asthma exacerbations. Korean J Pediatr 2014;57:29-34.
5. Johnston NW, Johnston SL, Duncan JM, Greene JM, Kebadze T, Keith PK, *et al*. The September epidemic of asthma exacerbations in children: a search for etiology. J Allergy Clin Immunol 2005;115:132-8.
6. Bush A. Update in paediatric asthma 2024. Pediatr Respirol Critical Care Med 2024;8:3-10.
7. Bizzintino J, Lee W-M, Laing IA, Vang F, Pappas T, Zhang G, *et al*. Association between human rhinovirus C and severity of acute asthma in children. Eur Respir J 2011;37:1037-42.
8. Fujitsuka A, Tsukagoshi H, Arakawa M, Goto-Sugai K, Ryo A, Okayama Y, *et al*. A molecular epidemiological study of respiratory viruses detected in Japanese children with acute wheezing illness. BMC Infect Dis 2011;11:168.
9. Mak RK, Tse LY, Lam WY, Wong GWK, Chan PKS, Leung TF. Clinical spectrum of human rhinovirus infections in hospitalized Hong Kong children. Pediatr Infect Dis J 2011;30:749-53.
10. Linsuwanon P, Payungporn S, Samransamruajkit R, Posuwan N, Makkoch J, Theanboonlers A, *et al*. High prevalence of human rhinovirus C infection in Thai children with acute lower respiratory tract disease. J Infect 2009;59:115-21.

11. Xiao Q, Zheng S, Zhou L, Ren L, Xie X, Deng Y, *et al*. Impact of human rhinovirus types and viral load on the severity of illness in hospitalized children with lower respiratory tract infections. Pediatr Infect Dis J 2015;34:1187-92.
12. Zeng SZ, Xiao N-G, Xie Z-P, Xie G-C, Zhong L-L, Wang J, *et al*. Prevalence of human rhinovirus in children admitted to hospital with acute lower respiratory tract infections in Changsha, China. J Med Virol 2014;86:1983-9.
13. Cheuk DK, Tang IWH, Chan KH, Woo PCY, Peiris MJS, Chiu SS. Rhinovirus infection in hospitalized children in Hong Kong: A prospective study. Pediatr Infect Dis J 2007;26:995-1000.
14. Turner RB. Rhinovirus: more than just a common cold virus. J Infect Dis 2007;195:765-6.
15. Calvo C, Casas I, García-García ML, Pozo F, Reyes N, Cruz N, *et al*. Role of rhinovirus C respiratory infections in sick and healthy children in Spain. Pediatr Infect Dis J 2010;29:717-20.
16. Iwane MK, Prill MM, Lu X, Miller EK, Edwards KM, Hall CB, *et al*. Human rhinovirus species associated with hospitalizations for acute respiratory illness in young US children. J Infect Dis 2011;204:1702-10.
17. Lu X, Holloway B, Dare RK, Kuypers J, Yagi S, Williams JV, *et al*. Real-time reverse transcription-PCR assay for comprehensive detection of human rhinoviruses. J Clin Microbiol 2008;46:533-9.
18. Johnston SL, Pattemore PK, Sanderson G, Smith S, Lampe F, Josephs L, *et al*. Community study of role of viral infections in exacerbations of asthma in 9-11 year old children. BMJ 1995;310:1225-9.
19. Gern JE. The ABCs of rhinoviruses, wheezing, and asthma. J Virol 2010;84:7418-26.
20. Wark PA, Johnston SL, Bucchieri F, Powell R, Puddicombe S, Laza-Stanca V, *et al*. Asthmatic bronchial epithelial cells have a deficient innate immune response to infection with rhinovirus. J Exp Med 2005;201:937-47.
21. Papadopoulos NG, Stanciu LA, Papi A, Holgate ST, Johnston SL. A defective type 1 response to rhinovirus in atopic asthma. Thorax 2002;57:328-32.
22. Message SD, Laza-Stanca V, Mallia P, Parker HL, Zhu J, Kebadze T, *et al*. Rhinovirus-induced lower respiratory illness is increased in asthma and related to virus load and Th1/2 cytokine and IL-10 production. Proc Natl Acad Sci U S A 2008;105:13562-7.
23. Lau SK, Yip CCY, Tsoi H-W, Lee RA, So L-Y, Lau Y-L, *et al*. Clinical features and complete genome characterization of a distinct human rhinovirus (HRV) genetic cluster, probably representing a previously undetected HRV species, HRV-C, associated with acute respiratory illness in children. J Clin Microbiol 2007;45:3655-64.
24. Miller EK, Edwards KM, Weinberg GA, Iwane MK, Griffin MR, Hall CB, *et al*; New Vaccine Surveillance Network. A novel group of rhinoviruses is associated with asthma hospitalizations. J Allergy Clin Immunol 2009;123:98-104.e1.
25. Iwasaki J, Smith W-A, Khoo S-K, Bizzintino J, Zhang G, Cox DW, *et al*. Comparison of rhinovirus antibody titers in children with asthma exacerbations and species-specific rhinovirus infection. J Allergy Clin Immunol 2014;134:25-32.

The **FIRST AND ONLY** asthma biologic to inhibit IL-4 and IL-13 signaling


AN ADD-ON MAINTENANCE TREATMENT FOR PATIENTS **(6+ YEARS)** WITH **INADEQUATELY CONTROLLED SEVERE ASTHMA** WITH TYPE 2 INFLAMMATION[1]

# A CLEAR PATH TO ASTHMA CONTROL

## NOW AVAILABLE

## UP TO 72% REDUCTION
### SIGNIFICANT EXACERBATION REDUCTION
**in annualized severe exacerbations at Week 24** with DUPIXENT 200 mg Q2W + SOC vs placebo + SOC ($P$=0.0003)[3]

## 86% OF PATIENTS
### REDUCED OR NO INCREASE IN THEIR OCS DOSE
**by Week 24** with DUPIXENT 300 mg Q2W + SOC vs 68% with placebo + SOC (P<0.001)[2]

## 200 mL IMPROVEMENT
### RAPID AND SUSTAINED IMPROVEMENT IN LUNG FUNCTION
**at Week 52** with DUPIXENT 200 mg Q2W + SOC vs placebo + SOC ($P$<0.001)[3]

## UP TO 75% OF PATIENTS
### HIGH RESPONDER RATE
in Asthma Control Questionnaire measures of **sleep, activity limitations, and breathing**[1]

### SELF-INJECTABLE
Convenient subcutaneous injection[1]

LIBERTY ASTHMA VENTURE Study Design[3]: 210 patients were randomly assigned with oral glucocorticoid-treated asthma to receive add-on DUPIXENT (at a dose of 300 mg) or placebo every 2 weeks for 24 weeks. After a glucocorticoid dose-adjustment period before randomization, glucocorticoid doses were adjusted in a downward trend from week 4 to week 20 and then maintained at a stable dose for 4 weeks. The primary end point was the percentage reduction in the glucocorticoid dose at week 24. Key secondary end points were the proportion of patients at week 24 with a reduction of at least 50% in the glucocorticoid dose and the proportion of patients with a reduction to a glucocorticoid dose of less the 5 mg per day. Severe exacerbation rates and the forced expiratory volume in 1 second ($FEV_1$) before bronchodilator use were also assessed.

LIBERTY ASTHMA QUEST Study design[2]: 1902 patients who were 12 years of age or older with uncontrolled asthma were randomly assigned in a 2:2:1:1 ratio to received add-on subcutaneous DUPIXENT at a dose of 200 or 300 mg every 2 weeks or mated volume placebos for 52 weeks. The primary end points were the annualized rate of severe asthma exacerbations and the absolute change from baseline to week 12 in the forced expiratory volume in 1 second (FEV1) before bronchodilator use in the overall trial population. Secondary endpoints included the exacerbation rate and FEV, in patients with a blood eosinophil count of 300 or more per cubic millimetre. Asthma control and DUPIXENT safety were also assessed.

EOS, eosinophils; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; OCS, oral corticosteroid; Q2W, every 2 weeks; SOC, standard of care.

**References: 1.** DUPIXENT Hong Kong prescribing information. **2.** Rabe KF, et al. N Engl J Med. 2018 Jun 28;378(26):2475-2485. **3.** Castro M, et al. N Engl J Med. 2018;378(26):2486-2496.

**Presentation:** Dupilumab solution for injection in a pre-filled syringe with needle shield. **Indications:** Atopic Dermatitis (AD): Moderate-to-severe AD in adults and adolescents ≥12 years who are candidates for systemic therapy; severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy. Asthma: In adults and adolescents ≥12 years as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment. In children 6 to 11 years old as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with medium to high dose ICS plus another medicinal product for maintenance treatment. For 300 mg only – Chronic rhinosinusitis with nasal polyposis (CRSwNP): As an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control. Prurigo Nodularis (PN): Moderate-to-severe PN in adults who are candidates for systemic therapy. Eosinophilic esophagitis (EoE): In adults and adolescents ≥12 years, weighing ≥40 kg, who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy. **Dosage & Administration:** Subcutaneous injection. AD adults: Initial dose of 600 mg (two 300 mg injections), followed by 300 mg Q2W. AD adolescents (12-17y/o): Body weight <60 kg- initial dose of 400 mg (two 200 mg injections), followed by 200 mg Q2W. Body weight ≥60 kg- same dosage as adults. AD children (6-11y/o): Body weight 15kg-<60 kg- initial dose of 300 mg on Day 1 follow by 300 mg on Day 15, then 300mg Q4W. Body weight ≥60 kg- same dosage as adults. * The dose may be increased to 200 mg Q2W in patients with body weight of 15 kg-< 60 kg based on physician's assessment. AD children (6 months-5y/o): Body weight 5kg-<15 kg- initial dose of 200 mg, then 200 mg Q4W. Body weight 15kg-<30 kg- initial dose of 300 mg, then 300 mg Q4W. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, e.g. face, neck, intertriginous and genital areas. Consider discontinuing treatment in patients who have shown no response after 16 weeks. Asthma adults and adolescents: Initial dose of 400 mg, followed by 200 mg Q2W. For patients with severe asthma and on oral corticosteroids or with severe asthma and co-morbid moderate-to-severe AD or adults with co-morbid severe CRSwNP- initial dose of 600 mg, followed by 300 mg Q2W. Asthma children (6-11y/o): Body weight 15kg-<30 kg- 300 mg Q4W. Body weight 30kg-<60 kg- 200 mg Q2W; or 300 mg Q4W. Body weight ≥60 kg- 200 mg Q2W. For paediatric patients (6-11y/o) with asthma and co-morbid severe atopic dermatitis, as per approved indication, the recommended dose should follow AD children (6-11y/o). Patients receiving concomitant oral corticosteroids may reduce steroid dose gradually once clinical improvement with dupilumab has occurred. The need for continued dupilumab therapy should be considered at least annually as determined by a physician. CRSwNP: Initial dose of 300 mg, followed by 300 mg Q2W. Consider discontinuing treatment in patients who have shown no response after 24 weeks. PN: Initial dose of 600 mg (two 300 mg injections), followed by 300 mg Q2W. Dupilumab can be used with or without topical corticosteroids. Consider discontinuing treatment in patients who have shown no response after 24 weeks. EoE: 300 mg QW. Dupilumab 300 mg QW has not been studied in patients with EoE weighing <40 kg. Dosing beyond 52 weeks has not been studied. For Missed dose instructions, please refer to the full prescribing information. **Contraindications:** Hypersensitivity to dupilumab or any of the excipients. **Precautions:** Not be used to treat acute asthma symptoms, acute exacerbations, acute bronchospasm or status asthmaticus. Do not discontinue corticosteroids abruptly upon start of dupilumab. Reduction should be gradual and performed under supervision of a physician; it may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. Biomarkers of type 2 inflammation may be suppressed by systemic corticosteroid use. If systemic hypersensitivity reaction occurs, discontinue dupilumab and initiate appropriate therapy. Be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in patients with eosinophilia. Treat pre-existing helminth infections before initiating dupilumab. If patients become infected while receiving dupilumab and do not respond to anti-helminth treatment, discontinue dupilumab until infection resolves. Cases of enterobiasis were reported in children 6 to 11 years old in the paediatric asthma development program. Advise patients to promptly report new onset or worsening eye symptoms. Patients who develop conjunctivitis, dry eye and keratitis that does not resolve following standard treatment should undergo ophthalmological examination. Sudden changes in vision or significant eye pain that does not settle warrant urgent review. Patients with comorbid asthma should not adjust or stop asthma treatments without consultation with physicians. Carefully monitor patients after discontinuation of dupilumab. Avoid using live and live attenuated vaccines concurrently with dupilumab. Patients should be brought up to date with immunisations before starting dupilumab. **Drug Interactions:** Immune responses to Tdap vaccine and meningococcal polysaccharide vaccine were assessed. Patients receiving dupilumab may receive concurrent inactivated or non-live vaccinations. **Pregnancy and lactation:** Should be used during pregnancy only if potential benefit justifies potential risk to foetus. Unknown whether dupilumab is excreted in human milk or absorbed systemically after ingestion. Decision must be made whether to discontinue breast-feeding or dupilumab taking into account benefit of breast feeding for the child and benefit of therapy for the woman. **Undesirable effects:** Most common adverse reactions reported- injection site reactions, conjunctivitis, conjunctivitis allergic, arthralgia, oral herpes, eosinophilia and injection site bruising. Safety profile observed in adolescents and children 6 months to 11 years old consistent with that seen in adults. For other undesirable effects, please refer to the full prescribing information. **Preparation:** 2 x 300mg/2ml in pre-filled syringe with needle shield, 2 x 200mg/1.14ml in pre-filled syringe with needle shield. **Legal Classification:** Part 1, First & Third Schedules Poison **Full prescribing information is available upon request.** API-HK-DUP-23.10

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## Certificate Course in

# Paediatric Respirology and Allergy 2024 *(Video Lectures)*

**Jointly organised by**

The Federation of Medical Societies of Hong Kong

Hong Kong Society of Paediatric Respirology and Allergy

**Objectives:**

The course aims to provide a comprehensive update on important topics of paediatric respiratory medicine. After attending the course, the attendees should be able to provide an up-to-date management to children with respiratory diseases and know when to refer patients to PRM specialists.

| Date | Topics | Speakers |
|---|---|---|
| 31 Oct 2024 | Allergic Rhinitis – A Comprehensive Management | Dr. Daniel Kwok-keung NG<br>Specialist in Paediatric Respiratory Medicine |
| 7 Nov 2024 | Chronic Cough in Children | Dr. Alfred Yat-cheung TAM<br>Specialist in Paediatric Respiratory Medicine |
| 14 Nov 2024 | OSAS – The Importance of Early Intervention | Dr. Daniel Kwok-keung NG<br>Specialist in Paediatric Respiratory Medicine |
| 21 Nov 2024 | Understanding Paediatric Asthma Guidelines | Professor Ellis Kam-lun HON<br>Professor (by courtesy)<br>Department of Paediatrics & The Jockey Club School of Public Health and Primary Care<br>The Chinese University of Hong Kong |
| 28 Nov 2024 | Recurrent Preschool Wheeze: An Update | Dr. Wa-keung CHIU<br>Consultant<br>Department of Paediatrics and Adolescent Medicine<br>United Christian Hospital |
| 5 Dec 2024 | Childhood Pneumonia | Dr. Ka-ka SIU<br>Clinical Associate Professor of Practice<br>Department of Paediatrics and Adolescent Medicine<br>The University of Hong Kong |

**Date :** 31 October, 7, 14, 21, 28 November & 5 December 2024 (Thursday)
**Duration of Session :** 1.5 hours (6 sessions)
**Time :** 7:00 pm – 8:30 pm
**Course Feature :** Video lectures (with Q&A platform for participants to post the questions)
**Language Media :** Cantonese (Supplemented with English)
**Quiz for doctors :** DOCTORS are required to complete a quiz after the completion of each lecture
**Course Fee :** HK$1,200
**Certificate :** Awarded to participants with a minimum attendance of 70% (4 out of 6 sessions)
**Deadline :** **24 October 2024**
**Enquiry :** The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax : 2865 0345 Email : toto.chan@fmshk.org

**CME / CNE Accreditation in application**
**Online Application from website: http://www.fmshk.org**

香港兒童呼吸及過敏學會
Hong Kong Society of
PAEDIATRIC RESPIROLOGY AND ALLERGY

# 2nd Greater Bay Area Paediatric Respirology, Allergy and Critical Care Forum cum 27th HKSPRA Annual Scientific Meeting

13 October 2024 (Sunday) • CORDIS, Hong Kong

## Topics

- Allergy
- Respirology
- Critical Care
- Sleep Disordered Breathing
- Infection
- Free Papers Oral Presentation

## Speakers

Professor Anne Chang, *Brisbane-Australia*
Dr. David Hill, *Ohio-USA*
Professor Ellis Kam-lun Hon, *The Chinese University of Hong Kong*
Professor Rosemary Horne, *Melbourne-Australia*
Professor Sushil Kabra, *New Delhi-India*
Professor Peter Le Souef, *Perth-Australia*
Professor Mohammad Ashkan Moslehi, *Kuwait*
Professor Leyla Namazova, *Moscow-Russia*
Professor Qiang Qin, *Beijing-China*
Dr. Alfred Yat-cheung Tam, *Private Practice*
Dr. Bone Siu-fai Tang, *Hong Kong Sanatorium and Hospital*
Dr. Rina Triasih, *Yogyakarta-Indonesia*
Professor Hugo Van Bever, *Singapore*
Professor Yong-hong Yang, *Beijing-China*
Professor Hua-yan Zhang, *Philadelphia-USA*

## Chairpersons

Dr. Yan-min Bao, *Shenzhen*
Dr. Eric Yat-tung Chan, *Kwong Wah Hospital*
Dr. Wa-keung Chiu, *United Christian Hospital*
Professor Be-tau Hwang, *Taichung City*
Dr. May Kin-mui leong, *Macau SAR*
Dr. Daniel Wai-tai Ko, *Pamela Youde Nethersole Eastern Hospital*
Dr. Ping Lam, *Caritas Medical Centre*
Dr. Gen Lu, *Guangzhou*
Dr. Ting-yat Miu, *Private Practice*
Dr. Shu-chi Mu, *Taipei City*
Professor Leyla Namazova, *Moscow*
Dr. Daniel Kwok-keung Ng, *Hong Kong Sanatorium and Hospital*
Dr. Alfred Yat-cheung Tam, *Private Practice*
Dr. Rina Triasih, *Yogyakarta*
Dr. Michelle Yuk-ping Tsang, *United Christian Hospital*
Dr. Gui-lan Wang, *Zhongshan*

## Meeting and Membership Enquiry

27th HKSPRA Annual Scientific Meeting
c/o International Conference Consultants Ltd
Tel: (852) 2559 9973
Meeting: hkspraasm@icc.com.hk
Membership: hkspra@gmail.com

**www.hkspra.org**

## Registration

**Registration Fees**

| | Doctors | Allied-health Professionals |
|---|---|---|
| Members of HKSPRA and Supporting Organizations | HK$300 | HK$150 |
| Non-members | HK$800 | HK$400 |

**Registration Deadline**
5 October 2024 (Space is limited, registration will be confirmed only when payment is made and cleared.)

**Online Registration**

https://bit.ly/3W7LyrU

## Academic Accreditations

CME (HKCPaed, HKCFP, HKCPhysicians, MCHK), CNE (HKPNA) and CPD (HKPA, MPS) points will be applied for the meeting.

Supporting Organizations: