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(copd OR "Pulmonary Disease, Chronic Obstructive"[Mesh])

1

Review

Respir Med

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. 2024 Sep 18:234:107809.

doi: 10.1016/j.rmed.2024.107809. Online ahead of print.

Advancements in automated classification of chronic obstructive pulmonary disease based on computed tomography imaging features through deep learning approaches

Zirui Zhu [1]

Affiliations Expand

- **PMID: 39299523**

- **DOI: 10.1016/j.rmed.2024.107809**

Abstract

Chronic Obstructive Pulmonary Disease (COPD) represents a global public health issue that significantly impairs patients' quality of life and overall health. As one of

the primary causes of chronic respiratory diseases and global mortality, effective diagnosis and classification of COPD are crucial for clinical management. Pulmonary function tests (PFTs) are standard for diagnosing COPD, yet their accuracy is influenced by patient compliance and other factors, and they struggle to detect early disease pathologies. Furthermore, the complexity of COPD pathological changes poses additional challenges for clinical diagnosis, increasing the difficulty for physicians in practice. Recently, deep learning (DL) technologies have demonstrated significant potential in medical image analysis, particularly for the diagnosis and classification of COPD. By analyzing key radiological features such as airway alterations, emphysema, and vascular characteristics in Computed Tomography (CT) scan images, DL enhances diagnostic accuracy and efficiency, providing more precise treatment plans for COPD patients. This article reviews the latest research advancements in DL methods based on principal radiological features of COPD for its classification and discusses the advantages, challenges, and future research directions of DL in this field, aiming to provide new perspectives for the personalized management and treatment of COPD.

Keywords: Automated classification; COPD; CT imaging features; Deep learning.

Conflict of interest statement

Declaration of competing interest None declared.

Supplementary info

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Multidiscip Respir Med

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. 2024 Sep 18;19(1):949.

doi: 10.5826/mrm.2024.949.

An Italian Delphi Consensus on the Triple inhalation Therapy in Chronic Obstructive Pulmonary Disease

Paolo Solidoro [1], Federico Dente [2], Claudio Micheletto [3], Giovanni Pappagallo [4], Girolamo Pelaia [5], Alberto Papi [6]

Affiliations Expand

- PMID: 39291458
- PMCID: PMC11414512
- DOI: 10.5826/mrm.2024.949

Abstract

Background: The management of chronic obstructive pulmonary disease (COPD) lacks standardization due to the diverse clinical presentation, comorbidities, and limited acceptance of recommended approaches by physicians. To address this, a multicenter study was conducted among Italian respiratory physicians to assess consensus on COPD management and pharmacological treatment.

Methods: The study employed the Delphi process using the Estimate-Talk-Estimate method, involving a scientific board and expert panel. During a 6-month period, the scientific board conducted the first Delphi round and identified 11 broad areas of COPD management to be evaluated while the second Delphi round translated all 11 items into statements. The statements were subsequently presented to the expert panel for independent rating on a nine-point scale. Consensus was considered achieved if the median score was 7 or higher. Consistently high levels of consensus were observed in the first rating, allowing the scientific board to finalize the statements without requiring further rounds.

Results: Topics generating substantial discussion included the pre-COPD phase, patient-reported outcomes, direct escalation from a single bronchodilator to triple therapy, and the role of adverse events, particularly pneumonia, in guiding triple therapy prescriptions. Notably, these topics exhibited higher standard deviations, indicating greater variation in expert opinions.

Conclusions: The study emphasized the significance that Italian pulmonologists attribute to managing mortality, tailoring treatments, and addressing cardiovascular comorbidities in COPD patients. While unanimous consensus was not achieved for all statements, the results provide valuable insights to inform clinical decision-making among physicians and contribute to a better understanding of COPD management practices in Italy.

Conflict of interest statement

Conflict of interest: PS received personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Chiesi Farmaceutici Spa, Laboratori Guidotti Spa, Neopharmed Gentili spa, Novartis, Menarini Industrie Farmaceutiche Riunite Srl, ABC farmaceutici and Biotest Italia srl, outside the submitted work. CM received

fees as a speaker in national and international congress from GSK, Novartis, Sanofi, AstraZeneca, Chiesi, Menarini, Boehringher, Berlin Chemie, Guidotti, Chesi, Zambon. AP reports grants from Chiesi, AstraZeneca, GSK, BI, TEVA, Sanofi, and consulting fees, honoraria for lectures or advisory boards from Chiesi, AstraZeneca, GSK, Novartis, Sanofi, IQVIA, Avillon, Elpen Pharmaceuticals, Zambon, and Mundipharma. The other authors have no conflicts of interest to declare.

- 122 references
- 1 figure

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Curr Opin Pulm Med

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. 2024 Sep 18.

doi: 10.1097/MCP.0000000000001122. Online ahead of print.

Hypoxic burden - definitions, pathophysiological concepts, methods of evaluation, and clinical relevance

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- PMID: 39229876

- DOI: 10.1097/MCP.0000000000001122

Abstract

Purpose of review: Obstructive sleep apnea (OSA) is a common chronic condition that affects over a billion people worldwide and is associated with adverse cardio- and cerebrovascular consequences. Currently, the go-to clinical measure that determines the presence and severity of OSA is the apnea-hypopnea index (AHI). The AHI captures the frequency of respiratory events due to changes in ventilation

that are associated with either oxygen desaturations or arousal from sleep. The AHI is poorly correlated to adverse outcomes in OSA with poor prognostic ability. To overcome the limitations of AHI and perhaps driven by the ease of acquisition, several studies have suggested characterizing nocturnal hypoxia in OSA, termed as "hypoxic burden". The purpose of this review is to focus on the hypoxic burden in OSA, its various definitions, and its utility in moving OSA diagnosis beyond the AHI.

Recent findings: Several measures and definitions of hypoxic burden have been proposed and studied that show promise in overcoming limitations of AHI and also have a greater prognostic ability than AHI. More recently, area-based measures that attempt to characterize the depth and duration of oxygen desaturations, i.e., nocturnal hypoxia in OSA, have been shown to better relate to incident cardiovascular disease than AHI. In this review, we delve into the evidence for these novel area-based metrics and also delve into the pathophysiological concepts underlying nocturnal hypoxia while cautioning the reader on interpretation of the recent findings relating hypoxic burden to adverse outcomes in OSA.

Summary: In this review on hypoxic burden, we focus on the need that has driven the sudden influx of studies assessing hypoxic burden for various outcomes of OSA, its underlying pathophysiology, the various definitions, and clinical relevance. We hope that the reader can appreciate the nuances underlying hypoxic burden in OSA and suggest the need for a cohesive framework for moving beyond the AHI with hypoxic burden.

- 57 references

Supplementary info

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Thorax

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. 2024 Sep 18;79(10):905-914.

doi: 10.1136/thorax-2023-221230.

Nasal epithelial gene expression identifies relevant asthma endotypes in the ATLANTIS study

Tatiana Karp [1 2], Alen Faiz [3], Jos van Nijnatten [4 3], Huib A M Kerstjens [4 2], Ilse Boudewijn [4 2], Monica Kraft [5], Judith M Vonk [4 6], Martijn C Nawijn [4 7], Irene H Heijink [4 2 7], Bianca Beghé [8], Klaus F Rabe [9], Alberto Papi [10], Chris Brightling [11], Dave Singh [12], Thys van der Molen [4 13], Salman Siddiqui [14], Stephanie Christenson [15], Victor Guryev [# 4 16], Maarten van den Berge [# 4 2]

Affiliations Expand

- PMID: 39009441

- DOI: 10.1136/thorax-2023-221230

Abstract

Introduction: Asthma is an inflammatory airways disease encompassing multiple phenotypes and endotypes. Several studies suggested gene expression in nasal epithelium to serve as a proxy for bronchial epithelium, being a non-invasive approach to investigate lung diseases. We hypothesised that molecular differences in upper airway epithelium reflect asthma-associated differences in the lower airways and are associated with clinical expression of asthma.

Methods: We analysed nasal epithelial gene expression data from 369 patients with asthma and 58 non-asthmatic controls from the Assessment of Small Airways Involvement in Asthma study. Unsupervised hierarchical clustering was performed on asthma-associated genes. Asthma-associated gene signatures were replicated in independent cohorts with nasal and bronchial brushes data by comparing Gene Set Variation Analysis scores between asthma patients and non-asthmatic controls.

Results: We identified 67 higher expressed and 59 lower expressed genes in nasal epithelium from asthma patients compared with controls (false discovery rate<0.05), including *CLCA1, CST1* and *POSTN*, genes well known to reflect asthma in bronchial airway epithelium. Hierarchical clustering revealed several molecular asthma endotypes with distinct clinical characteristics, including an endotype with higher blood and sputum eosinophils, high fractional exhaled nitric oxide, and more severe small airway dysfunction, as reflected by lower forced expiratory flow at 50%. In an independent cohort, we demonstrated that genes higher expressed in the nasal epithelium reflect asthma-associated changes in the lower airways.

Conclusion: Our results show that the nasal epithelial gene expression profile reflects asthma-related processes in the lower airways. We suggest that nasal epithelium may be a useful non-invasive tool to identify asthma endotypes and may advance personalised management of the disease.

Keywords: Airway Epithelium; Asthma; Asthma Genetics; Asthma Mechanisms.

Conflict of interest statement

Competing interests: The ATLANTIS study is supported by Chiesi. MK has received grants or contracts or consulting fees or payment or honoraria or support for meetings from National Institutes of Health, American Lung Association, Synairgen, Janssen, Astra-Zeneca, Sanofi, Chiesi, GSK, Kinaset, Genentech, European Respiratory Society, has patents planned, issued or pending from CoFounder and Chief Medical Officer, RaeSedo, has participated on advisory boards for ALung DSMB and has received stock or stock options from Equity ownership in RaeSedo, and other financial or non-financial interests from Section Editor, UptoDate. MCN has received grants or contracts or support for meetings from Chan Zuckerberg Initiative, European commission, Lung Foundation Netherlands, Stichting Astma Bestrijding, Belgian Respiratory Society and has a leadership role in Lung Bionetwork of the Human Cell Atlas. IHH has received grants or contracts from Boehringer Ingelheim, Roche, Rousselot. BB has received payment or honoraria from AZ, GSK, Guidotti,Chiesi, Menarini. KFR has received payment or honoraria from Astra Zeneca, Boehringer Ingelheim, Chiesi Pharmaceuticals, Novartis, Sanofi & Regeneron, GlaxoSmithKline, Berlin Chemie, Roche Pharma, has participated in advisory boards for AstraZeneca, Boehringer Ingelheim, Sanofi & Regeneron, and has a leadership role in German Center for Lung Research (DZL), German Chest Society (DGP), American Thoracic Society (ATS). AP has received grants or contracts or consulting fees from Chiesi, AstraZeneca, GSK, Sanofi, Agenzia Italiana del farmaco (AIFA), Novartis,Avillion, ELPEN Pharmaceuticals, has received payment or honoraria from Chiesi, AstraZeneca, GSK, Menarini, Novartis, Zambon, Mundipharma, Sanofi, Edmond Pharma, IQVIA, Avillion, ELPEN Pharmaceuticals, has participated on Advisory Board for Chiesi, AstraZeneca, GSK, MSD, Novartis, Sanofi, IQVIA, Avillion, ELPEN Pharmaceuticals. CB has received grants or contracts or consulting fees from GSK, AZ, Sanofi, Regeneron, Roche, Genentech, BI, Chiesi, Novartis, Mologic, Areteia. DS has received consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, EpiEndo, Genentech, GlaxoSmithKline, Glenmark, Gossamer Bio, Kinaset Therapeutics, Menarini, Novartis, Orion, Pulmatrix, Sanofi, Synairgen, Teva, Theravance Biopharma, Verona Pharma. TvdM has received payment or honoraria or support for attending meetings from GSK, Chiesi. SS has received consulting fees or payment or honoraria from Chiesi, Astra Zeneca, GSK, Areteia therapeutics, CSL Behring, AZ, Medscape. SC has received grants or contracts or consulting fees from NIH, American Lung Association, Sanofi, Regeneron, GlaxoSmithKline, AstraZeneca, Glenmark Pharmaceuticals, Amgen, Axon Advisors, and has received payment or honoraria from Sanofi/Regeneron, MJH Holdings: Physicians' Education Resource, UpToDate, Wolters Kluwer Health, GlaxoSmithKline, has received support for attending meeting from AstraZeneca, GlaxoSmithKline, Sanofi/Regeneron, has participated on advisory boards for anofi/Regeneron, AstraZeneca, GlaxoSmithKline, and has leadership or fiduciary role in American Thoracic Society. MvdB has received grants or contracts from GlaxxoSmithKline, Astra Zeneca, Novartis, Genentech, Roche.

Supplementary info

MeSH termsExpand

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"Multimorbidity"[Mesh Terms] OR Multimorbidity[Text Word]

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BMC Geriatr

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. 2024 Sep 20;24(1):777.

doi: 10.1186/s12877-024-05329-y.

The extent and burden of high multimorbidity on older adults in the US: a descriptive analysis of Medicare beneficiaries

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Affiliations Expand

- **PMID: 39304796**
- **PMCID: PMC11414248**
- **DOI: 10.1186/s12877-024-05329-y**

Abstract

Background: The impact of multimorbidity (≥ 2 chronic diseases) on the well-being of older adults is substantial but variable. The burden of multimorbidity varies by the number and kinds of conditions, and timing of onset. The impact varies by age, race, ethnicity, socioeconomic status, and health indicators. Large scale longitudinal surveys linked to medical claims provide unique opportunities to characterize this variability.

Methods: We analyzed Medicare-linked Health and Retirement Study data for respondents 65 and older with 3 or more years of fee-for-service coverage (n = 17,199; 2000-2016). We applied standardized claims algorithms for operationalizing 21 chronic diseases. We compared multimorbidity levels, demographics, and outcomes at baseline and over time and escalation to high multimorbidity levels (≥ 5 conditions).

Results: At baseline, 51.2% had no multimorbidity, 36.5% had multimorbidity, and 12.4% had high multimorbidity. Loss of function, cognitive decline, and higher healthcare utilization were up to ten times more prevalent in the high multimorbidity group. Greater rates of high multimorbidity were seen among non-Hispanic Black and Hispanic groups, those with lower wealth, younger birth cohorts, and adults with obesity. Rates of transition to high multimorbidity varied greatly and was highest among Hispanic and respondents with lower education.

Conclusions: The development and progression of multimorbidity in old age is influenced by many factors. Higher levels of multimorbidity are associated with sociodemographic characteristics, suggesting possible mitigation strategies.

Keywords: Aging; Epidemiology; Longitudinal analysis; Multimorbidity.

Conflict of interest statement

The authors declare no competing interests.

- **32 references**
- **2 figures**

Supplementary info

MeSH termsExpand

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"asthma"[MeSH Terms] OR asthma[Text Word]

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J Exp Med

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. 2024 Dec 2;221(12):e20240103.

doi: 10.1084/jem.20240103. Epub 2024 Sep 19.

Interleukin-33-activated basophils promote asthma by regulating Th2 cell entry into lung tissue

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Beyaert[4,5], David Voehringer[6], Richard M Locksley[7], Hamida Hammad[#1,2], Bart N Lambrecht[#1,2,8]

Affiliations Expand

- PMID: 39297875
- PMCID: PMC11413418 (available on 2025-03-19)
- DOI: 10.1084/jem.20240103

Abstract

Asthma is characterized by lung eosinophilia, remodeling, and mucus plugging, controlled by adaptive Th2 effector cells secreting IL-4, IL-5, and IL-13. Inhaled house dust mite (HDM) causes the release of barrier epithelial cytokines that activate various innate immune cells like DCs and basophils that can promote Th2 adaptive immunity directly or indirectly. Here, we show that basophils play a crucial role in the development of type 2 immunity and eosinophilic inflammation, mucus production, and bronchial hyperreactivity in response to HDM inhalation in C57Bl/6 mice. Interestingly, conditional depletion of basophils during sensitization did not reduce Th2 priming or asthma inception, whereas depletion during allergen challenge did. During the challenge of sensitized mice, basophil-intrinsic IL-33/ST2 signaling, and not FcεRI engagement, promoted basophil IL-4 production and subsequent Th2 cell recruitment to the lungs via vascular integrin expression. Basophil-intrinsic loss of the ubiquitin modifying molecule Tnfaip3, involved in dampening IL-33 signaling, enhanced key asthma features. Thus, IL-33-activated basophils are gatekeepers that boost allergic airway inflammation by controlling Th2 tissue entry.

Conflict of interest statement

Disclosures: The authors declare no competing interests exist.

- 87 references

Supplementary info

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Review

J Exp Med

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. 2024 Nov 4;221(11):e20240806.

doi: 10.1084/jem.20240806. Epub 2024 Sep 19.

Targeting TNF/TNFR superfamilies in immune-mediated inflammatory diseases

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Affiliations Expand

- PMID: 39297883

- PMCID: PMC11413425

- DOI: 10.1084/jem.20240806

Abstract

Dysregulated signaling from TNF and TNFR proteins is implicated in several immune-mediated inflammatory diseases (IMIDs). This review centers around seven IMIDs (rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, psoriasis, atopic dermatitis, and asthma) with substantial unmet medical needs and sheds light on the signaling mechanisms, disease relevance, and evolving drug development activities for five TNF/TNFR signaling axes that garner substantial drug development interest in these focus conditions. The review also explores the current landscape of therapeutics, emphasizing the limitations of the approved biologics, and the opportunities presented by small-molecule inhibitors and combination antagonists of TNF/TNFR signaling.

Conflict of interest statement

Disclosures: P.K. Veerasubramanian, T.A. Wynn, J. Quan, and F.J. Karlsson are employees of Pfizer and may hold stock and/or stock options with Pfizer. No other disclosures were reported.

- 230 references
- 1 figure

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Ann Intern Med

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. 2024 Sep 24.

doi: 10.7326/ANNALS-24-00363. Online ahead of print.

Artificial Intelligence-Supported Development of Health Guideline Questions

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Affiliations Expand

- **PMID: 39312778**

- **DOI: 10.7326/ANNALS-24-00363**

Abstract

Background: Guideline questions are typically proposed by experts.

Objective: To assess how large language models (LLMs) can support the development of guideline questions, providing insights on approaches and lessons learned.

Design: Two approaches for guideline question generation were assessed: 1) identification of questions conveyed by online search queries and 2) direct generation of guideline questions by LLMs. For the former, the researchers retrieved popular queries on allergic rhinitis using Google Trends (GT) and identified those conveying questions using both manual and LLM-based methods. They then manually structured as guideline questions the queries that conveyed relevant questions. For the second approach, they tasked an LLM with proposing guideline questions, assuming the role of either a patient or a clinician.

Setting: Allergic Rhinitis and its Impact on Asthma (ARIA) 2024 guidelines.

Participants: None.

Measurements: Frequency of relevant questions generated.

Results: The authors retrieved 3975 unique queries using GT. From these, they identified 37 questions, of which 22 had not been previously posed by guideline panel members and 2 were eventually prioritized by the panel. Direct interactions with LLMs resulted in the generation of 22 unique relevant questions (11 not previously suggested by panel members), and 4 were eventually prioritized by the panel. In total, 6 of 39 final questions prioritized for the 2024 ARIA guidelines were not initially thought of by the panel. The researchers provide a set of practical insights on the implementation of their approaches based on the lessons learned.

Limitation: Single case study (ARIA guidelines).

Conclusion: Approaches using LLMs can support the development of guideline questions, complementing traditional methods and potentially augmenting questions prioritized by guideline panels.

Primary funding source: Fraunhofer Cluster of Excellence for Immune-Mediated Diseases.

Conflict of interest statement

Disclosures: Disclosure forms are available with the article online.

4

Am J Respir Crit Care Med

. 2024 Sep 23.

doi: 10.1164/rccm.202406-1166SO. Online ahead of print.

Obesity-related Asthma: A Pathobiology-based Overview of Existing and Emerging Treatment Approaches

Meghan D Althoff [1], Kristina Gaietto [2], Fernando Holguin [3], Erick Forno [4]

Affiliations Expand

- PMID: 39311907

- DOI: 10.1164/rccm.202406-1166SO

Abstract

Though obesity-related asthma associated with worse asthma outcomes, optimal treatment approaches for this complex phenotype are still largely unavailable. This state-of-the-art review article synthesizes evidence for existing and emerging treatment approaches for obesity-related asthma and highlights pathways that offer potential targets for novel therapeutics. Existing treatments targeting insulin resistance and obesity, including metformin and glucagon-like-peptide 1 (GLP-1) receptor agonists, have been associated with improved asthma outcomes, though GLP-1R agonist data in asthma is limited to individuals with co-morbid obesity. Monoclonal antibodies approved for treatment of moderate to severe asthma generally appear to be effective in individuals with obesity, though this is based on retrospective or secondary analysis of clinical trials; moreover, while most of these asthma biologics are approved for use in the pediatric population, the impact of obesity on their efficacy has not been well studied in youth. Potential therapeutic targets being investigated include IL-6, arginine metabolites, nitro-fatty acids, and mitochondrial antioxidants, with clinical trials for each currently underway. Potential therapeutic targets include adipose tissue eosinophils and the GLP-1-Arginine-Advanced glycation end products axis, though data in humans is still needed. Finally, transcriptomic and epigenetic studies of "obese asthma" demonstrate enrichment of interferon-related signaling pathways, Rho-GTPase pathways, and integrins, suggesting that these too could represent future treatment targets. We advocate for further study of these potential therapeutic mechanisms and continued investigation of the distinct inflammatory pathways characteristic of obesity-related asthma, in order to facilitate effective treatment development for this unique asthma phenotype.

Keywords: Obesity-related asthma; Treatments.

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Review

J Breath Res

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. 2024 Sep 23;18(4).

doi: 10.1088/1752-7163/ad7a9a.

Exhaled breath condensate (EBC) in respiratory diseases: recent advances and future perspectives in the age of omic sciences

Mauro Maniscalco [1] [2], Claudio Candia [1], Salvatore Fuschillo [2], Pasquale Ambrosino [2], Debora Paris [3], Andrea Motta [3]

Affiliations Expand

- PMID: 39270682

- DOI: 10.1088/1752-7163/ad7a9a

Abstract

Exhaled breath condensate (EBC) is used as a promising noninvasive diagnostic tool in the field of respiratory medicine. EBC is achieved by cooling exhaled air, which contains aerosolized particles and volatile compounds present in the breath. This method provides useful information on the biochemical and inflammatory state of the airways. In respiratory diseases such as asthma, chronic obstructive pulmonary disease and cystic fibrosis, EBC analysis can reveal elevated levels of biomarkers such as hydrogen peroxide, nitric oxide and various cytokines, which correlate with oxidative stress and inflammation. Furthermore, the presence of certain volatile organic compounds in EBC has been linked to specific respiratory conditions, potentially serving as disease-specific fingerprints. The noninvasive nature of EBC sampling makes it particularly useful for repeated measures and for use in vulnerable populations, including children and the elderly. Despite its potential, the standardization of collection methods, analytical techniques and interpretation of results currently limits its use in clinical practice. Nonetheless, EBC holds significant promise for improving the diagnosis, monitoring and therapy

of respiratory diseases. In this tutorial we will present the latest advances in EBC research in airway diseases and future prospects for clinical applications of EBC analysis, including the application of the Omic sciences for its analysis.

Keywords: COPD; biomarkers; exhaled biomarkers; exhaled breath condensate; outcome.

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J Asthma

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. 2024 Sep 23:1-4.

doi: 10.1080/02770903.2024.2403011. Online ahead of print.

Asthma innovations from the second International Collaborative Asthma Network (ICAN) forum

Nizar N Jarjour [1], Tonya Winders [2], Ann M Hansen [1], Praveen Akuthota [3], Kian Fan Chung [4], Hannah Durrington [5 6], Stephen J Fowler [5 6], Benjamin Gaston [7], Eneida A Mendonca [7 8], Salman Siddiqui [4], Samantha Walker [9], Joe Zein [10], Ratko Djukanovic [11]

Affiliations Expand

- PMID: 39258900

- DOI: 10.1080/02770903.2024.2403011

Abstract

Asthma continues to cause morbidity and mortality despite advances in treatment that include biologics targeting Type 2 inflammation. The International Collaborative Asthma Network (ICAN) forum was developed with the primary goal of promoting innovative, collaborative research that focuses on mechanisms and treatment for asthma that does not respond or that responds poorly to currently available treatments. The mission of ICAN is innovation, collaboration, translation, and increasing high quality research. At the second ICAN meeting, presenters covered a broad scope and depth of asthma-related topics in the categories of complex data, novel therapeutics and diagnostics, breath analysis and microbiome, disease mechanisms, systemic effects, and circadian rhythm. Key actionable needs and research topics were identified during the group discussions. The presentations and discussions that occurred at the second ICAN had an immediate impact on asthma research in the form of new collaborations and implementation of new research ideas and techniques. The forum also served to connect early-stage investigators with investigators who are well established, thereby fostering innovation, translation, and collaboration well into the future. A third ICAN meeting is planned for 2025 to further the innovations and collaborations that will translate into novel therapies and diagnostics to improve the lives of patients with asthma.

Keywords: Asthma; Type 2 inflammation; collaboration; innovation; translation.

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Asian Pac J Allergy Immunol

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. 2024 Sep 22.

doi: 10.12932/AP-140124-1765. Online ahead of print.

Innate lymphoid cell population distributions and related gene expression characteristics in blood from allergic and nonallergic patients with eosinophilic asthma

Byung-Keun Kim [1], Hyun Seung Lee [2], Suh-Young Lee [3 4], Heung-Woo Park [3 4]

Affiliations Expand

- **PMID: 39306738**

- DOI: 10.12932/AP-140124-1765

Abstract

Background: Non-allergic eosinophilic asthma (NAEA) is a distinct subtype of asthma. However, the immune mechanisms associated with NAEA are not yet clearly understood.

Objective: To gain further insight into the pathogenesis of NAEA.

Methods: The proportion of innate lymphoid cells (ILCs) in the blood of patients with allergic eosinophilic asthma (AEA) and NAEA was evaluated. Eosinophilic asthma was defined when fractional exhaled nitric oxide measured at diagnosis (before initiating anti-asthma medications) was greater than 50 ppb. We evaluated the genome-wide gene expression profiles in peripheral blood mononuclear cells obtained at enrollment (in a stable state).

Results: A total of 57 participants were enrolled (10 healthy controls, 23 patients with NAEA, and 24 patients with AEA). We found that the type 1 ILC (ILC1) proportion significantly decreased, but the type 2 ILC (ILC2) and type 3 ILC (ILC3) proportions significantly increased in the blood of both patients with NAEA and those with AEA compared with healthy controls. However, there were no significant differences in the ILC1~3 proportions between NAEA and AEA patients. We also identified distinct biological pathways in patients with NAEA (anti-viral pathway) or AEA (IL-4 and IL-13 signaling and neutrophil degranulation pathways) based on co-expressed gene modules showing significant correlations with the ILC proportions.

Conclusion: ILC proportions in the blood did not differ between NAEA and AEA patients. However, different biological pathways were related to the ILC proportions in these patients. Our results provide further insight into eosinophilic airway inflammation in allergic and non-allergic patients.

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. 2024 Sep 20:105775.

doi: 10.1016/j.jbspin.2024.105775. Online ahead of print.

Successful treatment with Dupilumab of adult-onset asthma and periocular xanthogranuloma syndrome overlapping IgG4-related disease

Lucile Sesé [1], Michael Soussan [2], Yurdagül Uzunhan [3], Jonathan London [4], Olivia Freynet [3], Flora Finet [5], Robin Dhote [6], Sébastien Abad [6]

Affiliations Expand

- PMID: 39307296

- DOI: 10.1016/j.jbspin.2024.105775

No abstract available

Keywords: Adult onset asthma and periocular xanthogranuloma syndrome; IgG4-related disease; corticosteroid; dupilumab.

Supplementary info

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BMJ

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. 2024 Sep 20:386:e080353.

doi: 10.1136/bmj-2024-080353.

Optimising inhaled therapy for patients with asthma

Aarti Bansal [1], Lauren Franklin [2], Helen Twohig [2]

Affiliations Expand

- **PMID: 39304315**

- **DOI: 10.1136/bmj-2024-080353**

No abstract available

Conflict of interest statement

Competing interests: The BMJ has judged that the authors have no disqualifying financial ties to commercial companies that are relevant to this paper. The authors declare the following interests: AB is a director of Greener Practice, a not-for-profit community interest company which supports primary care to be more environmentally sustainable. Greener Practice has developed a high quality and low carbon asthma care quality improvement toolkit.

Supplementary info

MeSH terms, SubstancesExpand

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. 2024 Sep 20:25:e38.

doi: 10.1017/S1463423624000306.

Smoking cessation program preferences of individuals with chronic obstructive pulmonary disease: a qualitative study

Noah Tregobov [1 2], Kassandra Starnes [3], Saron Kassay [4], Maryam Mahjoob [2], Yu Seon Sarah Chae [4], Austin McMillan [5], Iraj Poureslami [2 6]

Affiliations Expand

- **PMID: 39301597**

- DOI: 10.1017/S1463423624000306

Abstract

Aim: To explore the views of tobacco-smoking chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap (ACO) patients on telehealth-based cessation programs and the role of e-cigarettes as an aid to quit smoking.

Background: Tobacco smoking accelerates the progression of COPD. Traditional smoking cessation programs often do not entirely address the unique needs of COPD patients, leading to suboptimal effectiveness for this population. This research is aimed at describing the attitudes and preferences of COPD and ACO patients toward innovative, telehealth-based smoking cessation strategies and the potential application of e-cigarettes as a quitting aid.

Methods: A qualitative exploratory approach was adopted in this study, employing both focus groups and individual interviews with English-speaking adults with diagnosed COPD or ACO. Participants included both current smokers (≥ 5 cigarettes/day) and recent ex-smokers (who quit < 12 months ago). Data were systematically coded with iterative reliability checks and subjected to thematic analysis to extract key themes.

Findings: A total of 24 individuals participated in this study. The emergent themes were the perceived structure and elements of a successful smoking cessation program, the possible integration of telehealth with digital technologies, and the strategic use of e-cigarettes for smoking reduction or cessation. The participants stressed the importance of both social and professional support in facilitating smoking cessation, expressing a high value for insights provided by ex-smokers serving as mentors. A preference was observed for group settings; however, the need for individualized plans was also highlighted, considering the diverse motivations individuals had to quit smoking. The participants perceived online program delivery as potentially beneficial as it could provide immediate access to support during cravings or withdrawals and was accessible to remote users. Opinions on e-cigarettes were mixed; some participants saw them as a less harmful alternative to conventional smoking, while others were skeptical of their efficacy and safety and called for further research.

Keywords: chronic obstructive pulmonary disease; e-cigarette; smoking cessation; telehealth; tobacco cessation.

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J Infect Dis

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. 2024 Sep 20:jiae467.

doi: 10.1093/infdis/jiae467. Online ahead of print.

Genetic susceptibility to acute viral bronchiolitis

Anu Pasanen [1], Minna K Karjalainen [2], Matti Korppi [3 4], Mikko Hallman [1], Mika Rämet [1 4]; Research Project FinnGen

Collaborators, Affiliations Expand

- PMID: 39299705

- DOI: 10.1093/infdis/jiae467

Abstract

Background: Acute viral bronchiolitis is a major cause of infant hospitalizations worldwide. Childhood bronchiolitis is considered a risk factor for asthma, suggesting shared genetic factors and biological pathways. Genetic risk loci may provide new insights into disease pathogenesis.

Methods: We conducted a genome-wide association study (GWAS) to examine the genetic contributions to bronchiolitis susceptibility in the FinnGen project data. We analyzed 1,465 infants hospitalized for bronchiolitis <2 years of age and 356,404 individuals without a history of acute lower respiratory infections (LRIs).

Results: GWAS identified associations (p<5×10-8) for variants in gasdermin B (GSDMB) and a missense variant in cadherin-related family member 3 (CDHR3). Children with bronchiolitis in infancy were more likely to develop asthma later in life compared to controls. The two associated loci were previously linked to asthma and susceptibility to wheezing illness by other causative agents than RSV. The identified loci associated with overall bronchiolitis, with larger effects in non-RSV than RSV-induced infection.

Conclusion: Our results suggest that genetic variants in CDHR3 and GSDMB modulate susceptibility to bronchiolitis, especially when caused by viruses other than RSV. Severe bronchiolitis in infancy may trigger the development of asthma in genetically susceptible individuals, or it could be a marker of genetic predisposition to asthma.

Keywords: CDHR3; GSDMB; ORMDL3; acute lower respiratory infection; asthma; bronchiolitis; genetic risk factors; non-RSV bronchiolitis; respiratory syncytial virus; rhinovirus.

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BMC Pregnancy Childbirth

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. 2024 Sep 19;24(1):610.

doi: 10.1186/s12884-024-06819-y.

Atopy and asthma in children born to mothers at risk of gestational diabetes mellitus: a follow-up study

Anu Bärenson [1 2], Aili Tagoma [3], Heili Varendi [4]; HEDIMED investigator group; Raivo Uibo [3]

Affiliations Expand

- **PMID: 39300411**
- **PMCID: PMC11414203**
- **DOI: 10.1186/s12884-024-06819-y**

Abstract

Background: Gestational diabetes mellitus (GDM) is the most prevalent metabolic disturbance during pregnancy and is associated with adverse outcomes in offspring, including an elevated risk for developing atopic diseases in early childhood. Research is limited regarding only women at risk of GDM among whom

some develop GDM while others do not. Information about adverse health outcomes in the offspring of these women is also lacking. The main aim was to assess whether maternal GDM increases the offspring's risk of atopic dermatitis (AD), asthma and allergic rhinitis at 1, 2 and 5 years of age. The second aim was to analyze the association of other maternal health characteristics on the development of these disorders in offspring.

Methods: The follow-up study group of the Gestational Diabetes Study (GDS), conducted at Tartu University Hospital, Estonia, between 2014 and 2020, comprised 223 mother-child dyads. All women had at least one risk factor for GDM, of whom only some developed GDM. Information about the diagnoses of interest was obtained from Electronic Health Records. Allergen-specific IgE from children's serum was measured using ImmunoCAP™ Phadiatop™ Infant, with results ≥ 0.35 kU/l considered positive. Statistical analysis was performed using the RStudio software (version 4.3.0).

Results: According to our results, only the cases of GDM requiring the use of antidiabetic medications were associated with the development of asthma and/or allergic rhinitis at 2 years of age (aOR 4.68, 95%CI 1.08-20.21, p = 0.039). Maternal obesity (BMI > 30) was associated with offspring´s asthma and/or allergic rhinitis diagnosis at 2 years of age (aOR 3.15, 95%CI 1.03-9.63, p = 0.045). Maternal abnormal weight gain during pregnancy was associated with asthma and/or allergic rhinitis at 5 years of age (aOR 2.76, 95%CI 1.04-7.31, p = 0.041).

Conclusion: Among pregnant women at risk for GDM, maternal weight-related factors significantly influence the development of atopic diseases in their children between 1 and 5 years of age, regardless of the GDM diagnosis. This suggests that, besides women with GDM greater attention should also be paid to women at risk but who do not develop GDM, as their children seem to be at higher risk of atopic diseases.

Keywords: Allergic rhinitis; Asthma; Atopic dermatitis; Gestational diabetes mellitus; Immune system; Maternal obesity.

Conflict of interest statement

The authors declare no competing interests.

- 36 references

Supplementary info

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. 2024 Sep 19:21:E72.

doi: 10.5888/pcd21.240051.

CDC's National Asthma Control Program: Looking Back with an Eye Toward the Future

Alisha A Etheredge [1 2], Carlene Graham [1], Maureen Wilce [3], Joy Hsu [3], Scott A Damon [3], Josephine Malilay [3], Henry Falk [4], Kanta Sircar [3], Hailay Teklehaimanot [3], Erik R Svendsen [5]

Affiliations Expand

- PMID: 39298795

- DOI: 10.5888/pcd21.240051

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Editorial

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. 2024 Sep 19:21:E73.

doi: 10.5888/pcd21.240344.

CDC's National Asthma Control Program: Public Health Actions to Reduce the Burden of Asthma

Maria C Mirabelli [1], Hailay Teklehaimanot [2], Tyra Bryant-Stephens [3]

Affiliations Expand

- PMID: 39298794

- DOI: 10.5888/pcd21.240344

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Publication types, MeSH termsExpand

Full text links

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J Asthma

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. 2024 Sep 19:1-8.

doi: 10.1080/02770903.2024.2403742. Online ahead of print.

Asthma beliefs and overuse of short-acting beta-adrenergic receptor agonists among older adults

Yoshiko Ishisaka [1], Jyoti Ankam [2], Jonathan Feldman [3], Paula Busse [4], Juan P Wisnivesky [2], Alex D Federman [2]

Affiliations Expand

- PMID: 39258932

- DOI: 10.1080/02770903.2024.2403742

Abstract

Objective: Short-acting Beta-adrenergic Receptor Agonists (SABA) carry a risk of worse asthma outcomes when overused. Beliefs about asthma controller medications are associated with medication-taking behaviors in older adults, but the association of medication beliefs with SABA use has not been previously examined. We aimed to investigate the association of asthma and controller medication beliefs with SABA use among older patients with asthma.

Methods: We performed a cross-sectional analysis of data on adults ≥ 60 years old with moderate to severe asthma in New York City, NY (*n* = 234). SABA overuse was defined as the average of ≥1 inhalation per day and controller medication adherence as ≥80% of expected inhalations, measured electronically. Illness and medication beliefs were measured using the Brief-Illness Perception Questionnaire and Beliefs about Medications Questionnaire, respectively. The associations of medication-taking behaviors with beliefs were examined in multivariable logistic regression models.

Results: The mean age was 67.6 ± 6.5 years, 84% were female, 26% were Black and 53% were Hispanic. 35% of participants overused SABA and 21% had adequate controller medication adherence. Overuse of SABA was not significantly associated with controller medication beliefs (Necessity: odds ratio [OR] 1.04, 95% confidence interval [CI] [0.97-1.12], *p* = 0.28, Concerns: OR 0.95 [95% CI 0.88, 1.03], *p* = 0.23) or asthma beliefs (OR 1.06 [95% CI 0.99, 1.15], *p* = 0.11). SABA overuse was also not significantly associated with controller medication adherence (OR 2.20 [95% CI 0.88, 5.51], *p* = 0.09).

Conclusions: SABA overuse was common among older adults with asthma and was not significantly associated with asthma controller medication or illness beliefs.

Keywords: Asthma; beliefs; medication adherence; short-acting beta-adrenergic receptor agonists.

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Thorax

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. 2024 Sep 18;79(10):905-914.

doi: 10.1136/thorax-2023-221230.

Nasal epithelial gene expression identifies relevant asthma endotypes in the ATLANTIS study

Tatiana Karp [1 2], Alen Faiz [3], Jos van Nijnatten [4 3], Huib A M Kerstjens [4 2], Ilse Boudewijn [4 2], Monica Kraft [5], Judith M Vonk [4 6], Martijn C Nawijn [4 7], Irene H Heijink [4 2 7], Bianca Beghé [8], Klaus F Rabe [9], Alberto Papi [10], Chris Brightling [11], Dave Singh [12], Thys van der Molen [4 13], Salman Siddiqui [14], Stephanie Christenson [15], Victor Guryev [# 4 16], Maarten van den Berge [# 4 2]

Affiliations Expand

- PMID: 39009441

- DOI: 10.1136/thorax-2023-221230

Abstract

Introduction: Asthma is an inflammatory airways disease encompassing multiple phenotypes and endotypes. Several studies suggested gene expression in nasal epithelium to serve as a proxy for bronchial epithelium, being a non-invasive approach to investigate lung diseases. We hypothesised that molecular differences in upper airway epithelium reflect asthma-associated differences in the lower airways and are associated with clinical expression of asthma.

Methods: We analysed nasal epithelial gene expression data from 369 patients with asthma and 58 non-asthmatic controls from the Assessment of Small Airways Involvement in Asthma study. Unsupervised hierarchical clustering was performed on asthma-associated genes. Asthma-associated gene signatures were replicated in independent cohorts with nasal and bronchial brushes data by comparing Gene Set Variation Analysis scores between asthma patients and non-asthmatic controls.

Results: We identified 67 higher expressed and 59 lower expressed genes in nasal epithelium from asthma patients compared with controls (false discovery rate<0.05), including *CLCA1, CST1* and *POSTN*, genes well known to reflect asthma in bronchial airway epithelium. Hierarchical clustering revealed several molecular asthma endotypes with distinct clinical characteristics, including an endotype with

higher blood and sputum eosinophils, high fractional exhaled nitric oxide, and more severe small airway dysfunction, as reflected by lower forced expiratory flow at 50%. In an independent cohort, we demonstrated that genes higher expressed in the nasal epithelium reflect asthma-associated changes in the lower airways.

Conclusion: Our results show that the nasal epithelial gene expression profile reflects asthma-related processes in the lower airways. We suggest that nasal epithelium may be a useful non-invasive tool to identify asthma endotypes and may advance personalised management of the disease.

Keywords: Airway Epithelium; Asthma; Asthma Genetics; Asthma Mechanisms.

Conflict of interest statement

Competing interests: The ATLANTIS study is supported by Chiesi. MK has received grants or contracts or consulting fees or payment or honoraria or support for meetings from National Institutes of Health, American Lung Association, Synairgen, Janssen, Astra-Zeneca, Sanofi, Chiesi, GSK, Kinaset, Genentech, European Respiratory Society, has patents planned, issued or pending from CoFounder and Chief Medical Officer, RaeSedo, has participated on advisory boards for ALung DSMB and has received stock or stock options from Equity ownership in RaeSedo, and other financial or non-financial interests from Section Editor, UptoDate. MCN has received grants or contracts or support for meetings from Chan Zuckerberg Initiative, European commission, Lung Foundation Netherlands, Stichting Astma Bestrijding, Belgian Respiratory Society and has a leadership role in Lung Bionetwork of the Human Cell Atlas. IHH has received grants or contracts from Boehringer Ingelheim, Roche, Rousselot. BB has received payment or honoraria from AZ, GSK, Guidotti,Chiesi, Menarini. KFR has received payment or honoraria from Astra Zeneca, Boehringer Ingelheim, Chiesi Pharmaceuticals, Novartis, Sanofi & Regeneron, GlaxoSmithKline, Berlin Chemie, Roche Pharma, has participated in advisory boards for AstraZeneca, Boehringer Ingelheim, Sanofi & Regeneron, and has a leadership role in German Center for Lung Research (DZL), German Chest Society (DGP), American Thoracic Society (ATS). AP has received grants or contracts or consulting fees from Chiesi, AstraZeneca, GSK, Sanofi, Agenzia Italiana del farmaco (AIFA), Novartis,Avillion, ELPEN Pharmaceuticals, has received payment or honoraria from Chiesi, AstraZeneca, GSK, Menarini, Novartis, Zambon, Mundipharma, Sanofi, Edmond Pharma, IQVIA, Avillion, ELPEN Pharmaceuticals, has participated on Advisory Board for Chiesi, AstraZeneca, GSK, MSD, Novartis, Sanofi, IQVIA, Avillion, ELPEN Pharmaceuticals. CB has received grants or contracts or consulting fees from GSK, AZ, Sanofi, Regeneron, Roche, Genentech, BI, Chiesi, Novartis, Mologic, Areteia. DS has received consulting fees from Aerogen, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, CSL Behring, EpiEndo, Genentech, GlaxoSmithKline, Glenmark, Gossamer Bio, Kinaset Therapeutics, Menarini, Novartis, Orion, Pulmatrix, Sanofi, Synairgen, Teva, Theravance Biopharma, Verona Pharma. TvdM has received payment or honoraria or support for attending meetings from GSK, Chiesi. SS has received consulting fees or payment or honoraria from Chiesi, Astra Zeneca, GSK, Areteia therapeutics, CSL Behring, AZ, Medscape. SC has received grants or contracts or consulting fees from NIH, American Lung Association, Sanofi, Regeneron, GlaxoSmithKline, AstraZeneca, Glenmark Pharmaceuticals, Amgen, Axon Advisors, and has received payment or

honoraria from Sanofi/Regeneron, MJH Holdings: Physicians' Education Resource, UpToDate, Wolters Kluwer Health, GlaxoSmithKline, has received support for attending meeting from AstraZeneca, GlaxoSmithKline, Sanofi/Regeneron, has participated on advisory boards for anofi/Regeneron, AstraZeneca, GlaxoSmithKline, and has leadership or fiduciary role in American Thoracic Society. MvdB has received grants or contracts from GlaxxoSmithKline, Astra Zeneca, Novartis, Genentech, Roche.

Supplementary info

MeSH termsExpand

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"rhinitis"[MeSH Terms] OR rhinitis[Text Word]

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Review

Nursing

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. 2024 Oct 1;54(10):44-47.

doi: 10.1097/NSG.0000000000000059. Epub 2024 Sep 20.

Pearls and pitfalls of over-the-counter nasal sprays for seasonal allergy

Eunhee Hong [1], Paige Lewis, Dan Sheridan

Affiliations Expand

- PMID: 39302751

- DOI: 10.1097/NSG.0000000000000059

Abstract

Allergic rhinitis (AR), commonly called hay fever, is primarily caused by the release of histamine after exposure to an allergen. This article reviews over-the-counter nasal spray options for the prevention and treatment of AR, including mechanisms of action, risks and benefits, and patient education.

- 20 references

Supplementary info

Publication types, MeSH terms, SubstancesExpand

Full text links

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J Investigi Allergol Clin Immunol

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. 2024 Sep 25:0.

doi: 10.18176/jiaci.1010. Online ahead of print.

Impact of Allergic Rhinitis on Academic Performance in Adolescents and Adults: a Bayesian Analysis of MASK-air® Real-world Direct Patient Data

R J Vieira [1 2], A M Pereira [1 3 4], N G Papadopoulos [5], T Zuberbier [6 7], N Pham-Thi [8 9 10], M Giovannini [11 12], E Melén [13 14], L F Azevedo [1 2], J A Fonseca [1 2], J Bousquet [6 7 15], B Sousa-Pinto [1 2]

Affiliations Expand

- PMID: 39319541

- DOI: 10.18176/jiaci.1010

No abstract available

Keywords: Academic performance; Allergic rhinitis; Asthma; Real-world data.

Full text links

Ear Nose Throat J

. 2024 Sep 24:1455613241285134.

doi: 10.1177/01455613241285134. Online ahead of print.

Clinical Outcomes After Innovative Multipoint Impedance-Controlled Radiofrequency Ablation of the Posterior Nasal Nerve for Treatment of Chronic Rhinitis

Greg E Davis [1], Randall A Ow [2], David M Yen [3], Ellen M O'Malley [4], Anthony G Del Signore [5]

Affiliations Expand

- PMID: 39315465

- DOI: 10.1177/01455613241285134

Abstract

Objective: Chronic rhinitis substantially impacts a person's quality of life. We evaluated a novel, multipoint, impedance-controlled, radiofrequency ablation device for the treatment of chronic rhinitis. Methods: This was a prospective, multicenter, single-arm clinical study of posterior nasal nerve ablation in adults with chronic rhinitis. The primary efficacy endpoint was the change in reflective Total Nasal Symptom Score (rTNSS) at 6-month follow-up. Additional assessments included the Eustachian Tube Dysfunction Questionnaire (ETDQ-7), Nasal Obstruction Symptom Evaluation (NOSE), and mini-Rhinoconjunctivitis Quality of Life Questionnaire (mini-RQLQ). The primary safety endpoint was the incidence of related serious adverse events. Results: Seventy-nine of 80 enrolled participants completed 6-month follow-up. Statistically significant improvements were observed for mean change in rTNSS (-4.2), ETDQ-7 (-1.2), NOSE (-33.5), and mini-RQLQ (-1.8; *P* < .0001 for all). Allergic and nonallergic rhinitis subgroups demonstrated significant improvement in all assessments (*P* < .0001) with no significant differences between subgroups. Higher baseline rTNSS was associated with greater improvements at follow-up. One serious adverse event of epistaxis was reported. Conclusions: The results of this study demonstrate the efficacy and safety of a multipoint, impedance-controlled,

radiofrequency ablation device for the treatment of chronic rhinitis. Significant improvements were observed in rTNSS, ETDQ-7, NOSE, and mini-RQLQ assessments.Study registration: www.clinicaltrials.gov. Unique identifier NCT05591989.

Keywords: ETDQ-7; Eustachian tube dysfunction; NOSE; chronic rhinitis; impedance-controlled radiofrequency ablation; mini-RQLQ; posterior nasal nerve ablation; postnasal drip/drainage; quality of life; rTNSS.

Conflict of interest statement

Declaration of Conflicting InterestsThe author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: G.E.D., D.M.Y., and A.G.D.S. are medical advisor consultants. E.M.O. is a medical writing consultant to Neurent Medical Ltd. The other authors have no conflicts to declare.

Supplementary info

Associated dataExpand

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Ann Intern Med

. 2024 Sep 24.

doi: 10.7326/ANNALS-24-00363. Online ahead of print.

Artificial Intelligence-Supported Development of Health Guideline Questions

Bernardo Sousa-Pinto [1], Rafael José Vieira [1], Manuel Marques-Cruz [1], Antonio Bognanni [2], Sara Gil-Mata [1], Slava Jankin [3], Joana Amaro [4], Liliane Pinheiro [1], Marta Mota [1], Mattia Giovannini [5], Leticia de Las Vecillas [6], Ana Margarida Pereira [1], Justyna Lityńska [7], Boleslaw Samolinski [8], Jonathan Bernstein [9], Mark Dykewicz [10], Martin Hofmann-Apitius [11], Marc Jacobs [11], Nikolaos Papadopoulos [12], Sian Williams [13], Torsten Zuberbier [14], João A Fonseca [15], Ricardo Cruz-Correia [16], Jean Bousquet [17], Holger J Schünemann [18]

Affiliations Expand

- **PMID: 39312778**

- **DOI: 10.7326/ANNALS-24-00363**

Abstract

Background: Guideline questions are typically proposed by experts.

Objective: To assess how large language models (LLMs) can support the development of guideline questions, providing insights on approaches and lessons learned.

Design: Two approaches for guideline question generation were assessed: 1) identification of questions conveyed by online search queries and 2) direct generation of guideline questions by LLMs. For the former, the researchers retrieved popular queries on allergic rhinitis using Google Trends (GT) and identified those conveying questions using both manual and LLM-based methods. They then manually structured as guideline questions the queries that conveyed relevant questions. For the second approach, they tasked an LLM with proposing guideline questions, assuming the role of either a patient or a clinician.

Setting: Allergic Rhinitis and its Impact on Asthma (ARIA) 2024 guidelines.

Participants: None.

Measurements: Frequency of relevant questions generated.

Results: The authors retrieved 3975 unique queries using GT. From these, they identified 37 questions, of which 22 had not been previously posed by guideline panel members and 2 were eventually prioritized by the panel. Direct interactions with LLMs resulted in the generation of 22 unique relevant questions (11 not previously suggested by panel members), and 4 were eventually prioritized by the panel. In total, 6 of 39 final questions prioritized for the 2024 ARIA guidelines were not initially thought of by the panel. The researchers provide a set of practical insights on the implementation of their approaches based on the lessons learned.

Limitation: Single case study (ARIA guidelines).

Conclusion: Approaches using LLMs can support the development of guideline questions, complementing traditional methods and potentially augmenting questions prioritized by guideline panels.

Primary funding source: Fraunhofer Cluster of Excellence for Immune-Mediated Diseases.

Conflict of interest statement

Disclosures: Disclosure forms are available with the article online.

Full text links

Occup Med (Lond)

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. 2024 Sep 23;74(6):430-437.

doi: 10.1093/occmed/kqae057.

Trends in occupational respiratory conditions with short latency in the UK

A Barradas [1 2], I Iskandar [3], M Carder [1], M Gittins [4], D Fishwick [1], M Seed [1], M van Tongeren [1]

Affiliations Expand

- PMID: 39163888
- PMCID: PMC11419704
- DOI: 10.1093/occmed/kqae057

Abstract

Background: Occupational short-latency respiratory disease (SLRD; predominantly asthma, rhinitis, hypersensitivity pneumonitis, and occupational infections) prevalence is difficult to determine but certain occupations may be associated with increased susceptibility.

Aims: This study aimed to examine which occupations and industries are currently at high risk for SLRD and determine their respective suspected causal agents.

Methods: SLRD cases reported to the SWORD scheme between 1999 and 2019 were analysed to determine directly standardized rate ratios (SRR) by occupation against the average rate for all other occupations combined.

Results: 'Bakers and flour confectioners' and 'vehicle spray painters' showed significantly raised SRR for SLRD in general, mostly due to occupational rhinitis (234.4; 95% CI 200.5-274.0) and asthma (63.5; 95% CI 51.5-78.3), respectively. Laboratory technicians also showed significantly raised SRR for occupational rhinitis (18.7; 95% CI 15.1-23.1), primarily caused by laboratory animals and insects.

Metal machining setters and setter-operators showed increased SRR for occupational hypersensitivity pneumonitis (42.0; 95% CI 29.3-60.3), largely due to cutting/soluble oils. The occupation mostly affected by infectious disease was welding trades (12.9; 95% CI 5.7-29.3), mainly attributable to microbial pathogenicity.

Conclusions: This study identified the occupational groups at increased risk of developing an SLRD based on data recorded over a recent two-decade period in the UK. Occupational asthma and rhinitis were identified as the prevailing conditions and hypersensitivity pneumonitis as a potentially rising respiratory problem in the metalworking industry.

Conflict of interest statement

None declared.

- **51 references**
- **3 figures**

Supplementary info

MeSH terms, Grants and fundingExpand

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Asian Pac J Allergy Immunol

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. 2024 Sep 22.

doi: 10.12932/AP-140224-1785. Online ahead of print.

Allergic rhinitis in remission with house dust mite subcutaneous immunotherapy

Supamas Harintajinda [1], Natchanun Klangkalya [1], Watcharoot Kanchongkittiphon [1], Ticha Rerkpattanapipat [2], Saowanee Kerddonfak [3], Wiparat Manuyakorn [1]

Affiliations Expand

- PMID: 39306739

- DOI: 10.12932/AP-140224-1785

Abstract

Background: House dust mite subcutaneous immunotherapy (HDM SCIT) is a therapeutic option for allergic rhinitis (AR) patients who are unable to properly manage symptoms with standard medications.

Objective: This study aimed to determine long-term efficacy and identify predictive factors in the clinical remission of AR patients who completed and discontinued HDM SCIT.

Methods: This study included 240 AR patients, who completed a three-year course of HDM SCIT at two tertiary hospitals and were currently being discontinued. We followed-up the patients to ask about their current symptoms and allergy medication. Clinical remission was defined by patients who no longer required daily intranasal steroid or oral antihistamine. We compared patients in clinical remission to those still taking medication.

Results: The enrolled patients had a median age of 21.0 (11.0-36.0) years at the time they began HDM SCIT. The clinical remission of AR was achieved in 174 (72.5%) patients. Starting HDM SCIT before the age of 15 and not having asthma were identified as significant and independent predictors of remission (aOR 4.44; 95%CI, 1.72-11.50; p-value 0.002, and 2.67, 95%CI 1.00-7.12; p-value 0.049), respectively, as determined by multivariate logistic regression analysis. There were no significant differences in HDM SCIT duration or sensitization patterns between patients in remission and those on medication after discontinuing HDM SCIT for at least one year.

Conclusion: HDM SCIT exhibited persistent long-term efficacy after treatment discontinuation. Starting HDM SCIT before the age of 15 and without asthma comorbidity might be predictors of AR remission with HDM SCIT.

7

Randomized Controlled Trial

Sci Rep

. 2024 Sep 20;14(1):21968.

doi: 10.1038/s41598-024-64669-2.

Safety and effectiveness of a drug-loaded haemostatic sponge in chronic rhinosinusitis: a randomized, controlled, double-blind study

Xujin Jia [#1], Jia Meng [#2], Jiayan Wang [1], Wei Wang [1], Di Wu [1], Ming Xu [3]

Affiliations Expand

- PMID: 39304658
- PMCID: PMC11415490
- DOI: 10.1038/s41598-024-64669-2

Abstract

Some cases of chronic rhinosinusitis (CRS) require surgical treatment and postoperative nasal packing, but bleeding and adhesion are common complications after nasal surgery. Biodegradable drug-loaded implants hold great therapeutic options for the treatment of CRS, but little data are available regarding the safety and efficacy of a novel drug-loaded haemostatic sponge (DLHS) in the sinus. The aim of this study was to investigate the safety and efficacy of DLHS in the sinus. We conducted a prospective, randomized, controlled, double-blind clinical trial. In this clinical trial, 49 patients were enrolled and randomly divided into 2 groups: group A (n = 25) had the DLHS containing 1 mg budesonide and 0.67 mg sodium hyaluronate placed into the sinus, and group B (n = 24) had the Nasopore placed after ESS. Endoscopic follow-up was performed for 12 weeks, and the findings were classified using the discharge, inflammation, polyps/oedema (DIP) endoscopic appearance scores. All patients completed questionnaires to evaluate their sinonasal symptoms by using the sinonasal outcome test-22 (SNOT-22) Chinese version and visual analogue scale (VAS). Serum cortisol concentration in group A was measured prior to surgery and at days 1, 3, 7, and 14 after nasal surgery. Comparing group A and group B, at 2 weeks, no significant differences were observed in either objective or subjective parameters. The mean value of VAS for rhinorrhoea and DIP for oedema and the mean value of nasal adhesion were significantly lower in Group A than in

Group B at 6 and 12 weeks, but a significant difference did not occur in SNOT-22 and VAS for dysosmia between the two groups at 6 and 12 weeks. The mean serum cortisol concentrations in group A at the follow-up were within normal limits without remarkable fluctuations. This study demonstrates the safety and efficacy of a novel biodegradable DLHS with the possibility of being used in CRS patients, and this sponge may reduce inflammation and minimize adhesions via controlled local drug delivery without measurable systemic exposure.

Keywords: Chronic rhinosinusitis; Sinus surgery; Sustained-release implants; Therapy outcome.

Conflict of interest statement

The authors declare no competing interests.

- **23 references**
- **4 figures**

Supplementary info

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Review

Nat Sci Sleep

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Mutual Influence Between Allergic Rhinitis and Sleep: Factors, Mechanisms, and interventions-A Narrative Review

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Affiliations Expand

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- PMCID: PMC11420902
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Abstract

Patients with allergic rhinitis (AR) have a high incidence of sleep disorders, such as insomnia, which can easily exacerbate nasal symptoms. The aggravation of nasal symptoms further promotes the deterioration of sleep disorders, forming a vicious cycle. Severe cases may even trigger psychological and neurological issues, such as anxiety, depression, and cognitive impairment, causing significant distress to patients, making clinical diagnosis and treatment difficult, and increasing costs. Furthermore, satisfactory therapeutics remain lacking. As the pathogenesis of AR-associated sleep disorders is not clear and research is still insufficient, paying attention to and understanding AR-related sleep disorders is crucial in clinical practice. Multiple studies have shown that the most crucial issues in current research on AR and sleep are analyzing the relationship between AR and sleep disorders, searching for the influencing factors, and investigating potential targets for diagnosis and treatment. This review aimed to identify and summarize the results of relevant studies using "AR" and "sleep disorders" as search terms. In addition, we evaluated the correlation between AR and sleep disorders and examined their interaction and potential mechanisms, offering a foundation for additional screening of potential diagnostic biomarkers and therapeutic targets.

Keywords: allergic rhinitis; biological rhythm; immune inflammatory; neurological regulation; sleep disorders.

Conflict of interest statement

The authors report no conflicts of interest in this work.

Supplementary info

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chronic cough

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ERJ Open Res

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Prevalence of refractory and unexplained chronic cough in adults treated in cough centre

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- PMID: 39319047

- PMCID: PMC11417602

- DOI: 10.1183/23120541.00254-2024

Abstract

Background: Refractory chronic cough and unexplained chronic cough pose significant clinical challenges, impairing patients' quality of life. However, a precise definition of refractory chronic cough remains elusive. This study aimed to assess the prevalence of refractory and unexplained chronic cough among patients referred to our cough centre and to analyse the prevalence of refractory chronic cough relative to its definition.

Methods: This prospective cohort study included all patients who were diagnosed at a cough clinic between 2018 and 2022. The response to therapy was measured based on reduction in cough severity (*via* a visual analogue scale) and improvement in cough-related quality of life (*via* the Leicester Cough Questionnaire). Refractory chronic cough was defined as persistent cough severity, with no or minimal improvement (change in visual analogue scale <30 mm) after two or more treatment attempts and cough severity ≥40 out of 100 mm on the visual analogue scale.

Results: Of 201 patients treated for chronic cough, only three (1.5%) were diagnosed with unexplained chronic cough. Among 166 patients monitored for therapy response, 71 (42.8%) experienced a cough severity reduction of ≥30 mm on the visual analogue scale, while 100 (60.2%) showed an improvement of ≥1.5 points on the Leicester Cough Questionnaire. Based on the basic refractory chronic cough definition, 51 of 166 patients (30.7%) were diagnosed with refractory chronic cough. If applying stricter criteria (persistent severe cough (≥40 mm on the visual analogue scale), insufficient therapy response (<30 mm reduction on the visual analogue scale) and <1.5-point improvement on the Leicester Cough Questionnaire), 45 of 166 patients (27.1%) would be diagnosed with refractory chronic cough.

Conclusions: Refractory chronic cough is common in patients referred to cough clinics. The prevalence of refractory chronic cough differs slightly depending on the diagnostic criteria. Therefore, the definition of refractory chronic cough used in routine practice needs to be clarified.

Conflict of interest statement

Conflict of interest: All authors declare no conflict of interest related to the manuscript.

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Case Reports

Tohoku J Exp Med

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Primary Ciliary Dyskinesia with Identical Genotype but Distinct Phenotypes in Two Siblings

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Affiliations Expand

- PMID: 38811211

- DOI: 10.1620/tjem.2024.J035

Free article

Abstract

In this study, we report two cases of siblings diagnosed with primary ciliary dyskinesia (PCD) sharing an identical genotype yet exhibiting distinct phenotypes. A 13-year-old girl with acute pneumonia was admitted to our hospital. Chest and sinus radiography revealed situs inversus and bilateral maxillary sinusitis. Chest computed tomography revealed bronchiectasis. Her 6-year-old brother with acute bronchitis was admitted and was diagnosed with bronchial asthma due to recurrent wheezing. Unlike his sister, he did not have situs inversus. Both patients had a chronic wet cough and were diagnosed with bronchial asthma by their family doctor. The mean PCD rule (PICADAR) scores were 9 and 7, respectively. Genetic analysis confirmed the presence of the same homozygous mutation (c.546C > A,pTyr182Ter) in DNAI2. To date, there have been four reports of the same pathogenic variants but different PCD phenotypes. Pathological variants of DNAI2 cause the loss of the outer dynein arm, the absence of which results in a lack of primary ciliary movement involved in the left-right axis formation during the embryonic period. A lack of functional cilia results in randomized visceral asymmetry; hence, the same pathogenic variant may exhibit different phenotypes. PCD is often overlooked and is sometimes managed as bronchial asthma, as in these siblings. In our case, the PICADAR score was useful in predicting the clinical diagnosis of PCD.

Keywords: bronchial asthma; dynein axonemal intermediate chain 2 (DNAI2); primary ciliary dyskinesia; siblings; the mean PCD rule (PICADAR) score.

"bronchiectasis"[MeSH Terms] OR bronchiectasis[Text Word]

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J Clin Immunol

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. 2024 Sep 21;45(1):13.

doi: 10.1007/s10875-024-01805-7.

Levels of Natural Antibodies Before and After Immunoglobulin Replacement Treatment Affect the Clinical Phenotype in Common Variable Immunodeficiency

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- **PMCID: PMC11416378**
- **DOI: 10.1007/s10875-024-01805-7**

Abstract

Natural antibodies (NAbs) occurring in individuals without prior exposure to specific antigens, provide direct first barrier protection against pathogens, and exert immunoregulation thus actively contributing to the maintenance of immune homeostasis, controlling inflammatory processes and preventing autoimmunity. Common variable immunodeficiency (CVID) is a heterogeneous group of disorders characterized by a compromised immune function that brings into focus the role of NAbs. Our aim was to explore whether NAb levels could serve as potential key indicators in CVID for monitoring disease progression and predicting outcomes. In this study, we analyzed a Hellenic cohort of 56 patients with CVID (31 newly diagnosed and 25 under immunoglobulin replacement therapy-IgRT) and 33 healthy controls, for total Ig levels and serum IgM and IgG NAb levels against five informative target-antigens of NAbs, namely, actin, DNA, carbonic anhydrase, $F(ab')_2$ fragments of human IgG and TriNitroPhenyl. In addition, follow-up pre- and post- IgRT samples were analyzed in ten (10) patients of our cohort. Results showed that Ig-treated patients exhibited significantly lower IgM NAb levels than untreated patients and healthy controls against all panel antigens. In the follow-up samples,

pre-treatment IgM NAb levels negatively correlated with total serum IgM. This imbalance was only partially restored after IgRT, with a significant decrease in IgM NAb levels observed in nine out of ten patients. Moreover, post-treatment patients with recurrent infections presented significantly lower IgM NAb levels, a reduction also observed in patients with bronchiectasis independently of treatment status. On the contrary, post-treatment patients with enteropathy had significantly higher IgM NAb levels against all panel antigens, an increase also noted in patients with autoimmune diseases. Regarding IgG NAbs, replacement therapy restored levels to those of healthy controls. In conclusion, impaired NAb levels are found in CVID patients, particularly related to certain phenotypes. Moreover, the significant decrease in IgM NAb levels after IgRT suggests a potential association with disease course and complications. The results suggest that administration of human IgM NAbs may be an effective combinatorial treatment in selected patients. Further research is needed to understand the functional roles of NAbs in CVID and its complex clinical phenotypes.

Keywords: CVID; Clinical phenotype; IgG; IgM; Immunoglobulin Replacement Treatment (IgRT); Natural Antibodies (NAbs).

Conflict of interest statement

The authors declare no competing interests.

- 43 references
- 4 figures

Supplementary info

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Respir Investig

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doi: 10.1016/j.resinv.2024.08.017. Online ahead of print.

Exercise intolerance and oxygen dynamics in nontuberculous mycobacteria with bronchiectasis

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- PMID: 39305533

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Abstract

Background: Nontuberculous mycobacterial pulmonary disease (NTM-PD) patients often have exercise intolerance. Pulmonary rehabilitation (PR) to improve such patients' conditions is often not based on its exercise pathophysiology. We have reported that the oxygen consumption (ΔF_{O2}) by expiratory gas analysis, i.e., the inspired-expired-expiratory mean oxygen concentration difference, is related to the minute ventilation-carbon dioxide output (V'_E-V'_{CO2})-slope and oxygen uptake (V'_{O2}) independent of the V'_E. The aim of this study was to investigate how ΔF_{O2} is related to dynamic ventilatory variables, chest computed tomography (CT), and echocardiography findings in NTM-PD patients to understand their pathophysiological conditions.

Methods: Clinical data of NTM-PD patients with exertional dyspnea (n = 29) who underwent incremental exercise testing, chest CT, and echocardiography at the same time were compared with those of control participants (n = 12).

Results: In the NTM-PD group, 1) peak V'_{O2} decreased (NTM-PD: 17.6 vs. controls: 28.7 $mL \cdot min^{-1} \cdot kg^{-1}$), and 2) ΔF_{O2} at peak exercise was negatively correlated with respiratory frequency at peak exercise (correlation coefficient: r = -0.80, p < 0.0001), V'_E-V'_{CO2}-slope (r = -0.75, p < 0.0001), bronchiectasis CT score (r = -0.52, p = 0.0042), and the trans-tricuspid pressure gradient (r = -0.39, p = 0.0417), and positively correlated with peak V'_{O2} (r = 0.71, p < 0.0001) and the body mass index (r = 0.42, p = 0.0217), but it was not correlated with V'_E at peak exercise and the cavity CT score.

Conclusions: Exertional oxygen consumption, independent of ventilatory ability, is associated with exercise tolerance and ventilatory efficiency, while being related to tachypnea and bronchiectasis rather than cavitation in NTM-PD patients. These findings may be useful in considering exercise physiology-based PR for NTM-PD patients with exertional dyspnea.

Keywords: And ventilation; Cardiopulmonary exercise testing; Dyspnea; Pulmonary rehabilitation; Tachypnea.

Conflict of interest statement

Declaration of competing interest The authors have no conflicts of interest.

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Ann Pharmacother

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Inhaled Medications for Maintenance Therapy in Pediatric Noncystic Fibrosis Bronchiectasis

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- **PMID: 39297217**

- **DOI: 10.1177/10600280241279602**

Abstract

Objective: This review focuses on evaluating literature for the use of inhaled mucolytics (hypertonic saline, mannitol, and dornase alfa), inhaled antibiotics (tobramycin, aztreonam, colistin, and amikacin), and inhaled corticosteroids in pediatric noncystic fibrosis bronchiectasis.

Data sources: A literature search via PubMed was conducted using the search terms "non-cystic fibrosis bronchiectasis," "primary ciliary dyskinesia," and "bronchiectasis" in combination with each inhaled agent of interest.

Study selection and data extraction: Studies were included if they were specific to patients with a clinical diagnosis of noncystic fibrosis bronchiectasis published from 1998 to July 2024.

Data synthesis: Several inhaled medications can be considered as maintenance therapies for pediatric patients with noncystic fibrosis bronchiectasis. Hypertonic saline could be considered for its potential airway clearance benefits and low risk of causing harm. Inhaled antipseudomonal antibiotics should be considered in patients who are colonized with *Pseudomonas aeruginosa*. Inhaled corticosteroid therapy should be reserved for patients with concomitant asthma. Dornase alfa has shown worse outcomes in adults with noncystic fibrosis bronchiectasis and should be used with caution. Risks and benefits should be carefully considered when evaluating these therapies for use in noncystic fibrosis bronchiectasis, and patient-specific treatment regimens should be developed.

Relevance to patient care and clinical practice: Chronic management of pediatric noncystic fibrosis bronchiectasis remains challenging due to paucity of applicable literature. Risks and benefits of different agents are discussed in this article with recommendations for application to clinical practice based on studies performed in both adult and pediatric patients with noncystic fibrosis bronchiectasis.

Conclusion: Several inhaled medications could be considered as maintenance therapies for pediatric patients with noncystic fibrosis bronchiectasis, with more robust evidence to support use of inhaled antipseudomonal antibiotics and hypertonic saline compared with other available agents. Further investigation is needed to identify a clear place in therapy for inhaled therapies in pediatric noncystic fibrosis bronchiectasis.

Keywords: antibiotics; bronchiectasis; cystic fibrosis; inhaled corticosteroids; inhaled mucolytics; inhalers; noncystic fibrosis bronchiectasis; pediatrics; primary ciliary dyskinesia; pulmonary.

Conflict of interest statement

Declaration of Conflicting InterestsThe authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Eur Respir Rev

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Neutrophil serine proteases in cystic fibrosis: role in disease pathogenesis and rationale as a therapeutic target

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Affiliations Expand

- **PMID: 39293854**
- **PMCID: PMC11409056**
- **DOI: 10.1183/16000617.0001-2024**

Abstract

Chronic airway inflammation is a central feature in the pathogenesis of bronchiectasis (BE), which can be caused by cystic fibrosis (CFBE; hereafter referred to as CF lung disease) and non-CF-related conditions (NCFBE). Inflammation in both CF lung disease and NCFBE is predominantly driven by neutrophils, which release proinflammatory cytokines and granule proteins, including neutrophil serine proteases (NSPs). NSPs include neutrophil elastase, proteinase 3 and cathepsin G. An imbalance between NSPs and their antiproteases has been observed in people with CF lung disease and people with NCFBE. While the role of the protease/antiprotease imbalance is well established in both CF lung disease and NCFBE, effective therapies targeting NSPs are lacking. In recent years, the introduction of CF transmembrane conductance regulator (CFTR) modulator therapy has immensely improved outcomes in many people with CF (pwCF). Despite this, evidence suggests that airway inflammation persists, even in pwCF treated with CFTR modulator therapy. In this review, we summarise current data on neutrophilic inflammation in CF lung disease to assess whether neutrophilic inflammation and high, uncontrolled NSP levels play similar roles in CF lung disease and in NCFBE. We discuss similarities between the neutrophilic inflammatory profiles of people with CF lung disease and NCFBE, potentially supporting a similar therapeutic approach. Additionally, we present evidence suggesting that neutrophilic inflammation persists in pwCF treated with CFTR

modulator therapy, at levels similar to those in people with NCFBE. Collectively, these findings highlight the ongoing need for new treatment strategies targeting neutrophilic inflammation in CF lung disease.

Conflict of interest statement

Conflict of interest: M.A. Mall has received research grants paid to their institution from the German Research Foundation (DFG), German Ministry for Education and Research (BMBF), German Innovation Fund and Vertex Pharmaceuticals; consultancy fees from Abbvie, Antabio, Arrowhead, Boehringer Ingelheim, Enterprise Therapeutics, Kither Biotec, Prieris, Recode, Santhera, Splisense and Vertex Pharmaceuticals; speaker fees from Vertex Pharmaceuticals; and travel grants for participation in advisory boards for Boehringer Ingelheim and Vertex Pharmaceuticals. M.A. Mall is listed as inventor on an issued patent filed by the University of North Carolina at Chapel Hill, describing the Scnn1b-transgenic mouse. M.A. Mall also reports advisory board participation for Abbvie, Antabio, Arrowhead, Boehringer Ingelheim, Enterprise Therapeutics, Kither Biotec, Pari and Vertex Pharmaceuticals, and is a fellow of ERS. J.C. Davies has received research grants from the UK Cystic Fibrosis Trust, Cystic Fibrosis Foundation, Cystic Fibrosis Ireland, EPSRC and NIHR, has received fees for clinical trial leadership and/or advisory board participation and speaking roles from Abbvie, Algipharma, Arcturus, Boehringer Ingelheim, Eloxx, Enterprise Therapeutics, Genentech, LifeArc, Recode, Tavanta and Vertex Pharmaceuticals, and is the Deputy Editor for the Journal of Cystic Fibrosis. J.C. Davies acknowledges funding from the National Institute of Health and Care Research through the Imperial Biomedical Research Centre and a Senior Investigator Award and grant funding from the Cystic Fibrosis Trust. S.H. Donaldson reports grants from the Cystic Fibrosis Foundation and the NIH; clinical trial contracts from AstraZeneca, Calithera and Vertex Pharmaceuticals; consulting fees from Chiesi USA, Inc., Polarean and 501 Ventures; and travel grants from Enterprise Therapeutics and Gilead Sciences. S.H. Donaldson also reported advisory board participation for Boehringer Ingelheim and data and safety monitoring board participation for Abbvie. R. Jain reports research grants from the CF Foundation, consulting fees from Boehringer Ingelheim, Insmed and Recode, and payment of honoraria for participation in the Vertex Innovation Awards review committee from Vertex Pharmaceuticals. R. Jain also reports advisory/data and safety monitoring board participation for Armata. J.D. Chalmers has received research grants from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Gilead Sciences, Grifols, Novartis, Insmed and Zambon, and has received consultancy fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Insmed, Pfizer and Zambon. M. Shteinberg reports having received research grants paid to their institution from GlaxoSmithKline, Novartis and Trudell; travel grants from Actelion, Boehringer Ingelheim, GlaxoSmithKline, Novartis, and Rafa; speaker fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Kamada, Novartis, Sanofi and Teva; and consultancy fees from Boehringer Ingelheim, GlaxoSmithKline, Kamada and Zambon. M. Shteinberg also reports data and safety monitoring board participation for Bonus Therapeutics, Israel and has unpaid roles in EMBARC, the Israel Pulmonology Society board and the Israel Society for TB and Mycobacterial Diseases.

- **120 references**

- 1 figure

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