LIBRA JOURNAL CLUB
26 FEBRUARY – 5 MARCH 2023

COPD

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Review

Targeted Literature Review of the Burden of Respiratory Syncytial Infection among High–Risk and Elderly Patients in Asia Pacific Region

Daisuke Kurai [1], JoonYoung Song [2], Yhu-Chering Huang [3], Zhijun Jie [4], Petar Atanasov [5], Xiaobin Jiang [6], Luis Hernandez-Pastor [7], Tom Hsun-Wei Huang [8], SeongBeom Park [9], KyungHwa Lim [10], Peter C Richmond [11]

Affiliations expand

- PMID: 36869266

Abstract

Introduction: The burden of respiratory syncytial virus (RSV), which causes acute respiratory illness, is well recognized among the pediatric population but also imposes a significant risk to the elderly (age ≥ 60) and those with underlying comorbidities. The study aimed to review the most recent data on epidemiology and burden (clinical and economic) of RSV in the elderly/high-risk populations in China, Japan, South Korea, Taiwan, and Australia.

Methods: A targeted review was conducted of English, Japanese, Korean, and Chinese language articles published from 1 January 2010 to 7 October 2020 relevant for the purpose.

Results: A total of 881 studies were identified, and 41 were included. The median proportion of elderly patients with RSV in all adult patients with acute respiratory infection (ARI) or community acquired pneumonia was 79.78% (71.43-88.12%) in Japan, 48.00% (3.64-80.00%) in China, 41.67% (33.33-50.00%) in Taiwan, 38.61% in Australia, and 28.57% (22.76-33.33%) in South Korea. RSV was associated with a high clinical burden on those patients with comorbidities such as asthma and chronic obstructive pulmonary disease. In China, inpatients with ARI showed a significantly higher rate of RSV-related hospitalization than outpatients (13.22% versus 4.08%, $p < 0.01$). The median length of hospital stay among elderly patients with RSV was longest in Japan (30 days) and shortest in China (7 days). Mortality data varied by region with some studies reporting rates as high as 12.00% (9/75) in hospitalized elderly patients. Finally, data on the economic burden was only available for South Korea, with the median cost of a medical admission for an elderly patient with RSV being US dollar (USD) 2933.

Conclusion: RSV infection is a major source of disease burden among elderly patients, especially in regions with aging populations. It also complicates the management of those with underlying diseases. Appropriate prevention strategies are required to reduce the burden among the adult, especially the elderly, population. Data gaps regarding economic burden of RSV infection in the Asia Pacific region indicates the need for further research to increase our understanding on the burden of this disease in this region.

Keywords: Acute respiratory infection; Asia Pacific; Disease burden; Economic burden; Respiratory syncytial virus.

- 70 references

Early diagnostic BioMARKers in exacerbations of chronic obstructive pulmonary disease: protocol of the exploratory, prospective, longitudinal, single-centre, observational MARKED study

Kiki Waeijen-Smit [1][2], Antonio DiGiandomenico [3], Jessica Bonnell [3], Kristoffer Ostridge [4][5], Ulf Gehrmann [4], Bret R Sellman [3], Tara Kenny [3], Sander van Kuijk [6], Daphne Peerlings [7], Martijn A Spruit [7][2], Sami O Simons [2], Sarah Houben-Wilke [7], Frits M E Franssen [7][2]

Affiliations expand

- PMID: 36868599

- DOI: 10.1136/bmjopen-2022-068787

Abstract

Introduction: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) play a pivotal role in the burden and progressive course of chronic obstructive pulmonary disease (COPD). As such, disease management is predominantly based on the prevention of these episodes of acute worsening of respiratory symptoms. However, to date, personalised prediction and early and accurate diagnosis of AECOPD remain unsuccessful. Therefore, the current study was designed to explore which frequently measured biomarkers can predict an AECOPD and/or respiratory infection in patients with COPD. Moreover, the study aims to increase our understanding of the heterogeneity of AECOPD as well as the role of microbial composition and hostmicrobiome interactions to elucidate new disease biology in COPD.

Methods and analysis: The 'Early diagnostic BioMARKers in Exacerbations of COPD' study is an exploratory, prospective, longitudinal, single-centre, observational study with 8-week follow-up enrolling up to 150 patients with COPD admitted to inpatient pulmonary rehabilitation at Ciro (Horn, the Netherlands). Respiratory symptoms, vitals, spirometry and nasopharyngeal, venous blood, spontaneous sputum and stool samples will be frequently collected for exploratory biomarker analysis, longitudinal characterisation of AECOPD (ie, clinical, functional and microbial) and to identify host-microbiome interactions. Genomic sequencing will be performed to identify mutations associated with increased risk of AECOPD and microbial infections. Predictors of time-to-first AECOPD will be modelled using Cox proportional hazards' regression. Multiomic analyses will provide a novel integration tool to generate predictive models and testable hypotheses about disease causation and predictors of disease progression.

Ethics and dissemination: This protocol was approved by the Medical Research Ethics Committees United (MEC-U), Nieuwegein, the Netherlands (NL71364.100.19).

Trial registration number: [NCT05315674](NCT05315674).

Keywords: BACTERIOLOGY; Chronic airways disease; Microbiology; Molecular diagnostics; Rehabilitation medicine; Thoracic medicine.

Conflict of interest statement

Review

[The impact of chronic obstructive pulmonary disease on the prognosis outcomes of patients with percutaneous coronary intervention or coronary artery bypass grafting: A meta-analysis](#)

[Yanqi Li](#)[1], [Huiqiu Zheng](#)[1], [Wenyan Yan](#)[1], [Ning Cao](#)[1], [Tao Yan](#)[1], [Hao Zhu](#)[1], [Han Bao](#)[2]

Affiliations expand

Abstract

Background: Coronary artery disease (CAD) is one of the main types of cardiovascular disease and is characterized by myocardial ischemia as a result of narrowing of the coronary arteries.

Objective: To evaluate the impact of chronic obstructive pulmonary disease (COPD) on outcomes in patients with CAD treated by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).

Methods: We searched PubMed, Embase, Web of Science, and Cochrane Library for observational studies and post-hoc analyses of randomized controlled trials published before Jan 20, 2022, in English. Adjusted odds ratios (ORs), risk ratios (RRs), and hazard ratios (HRs) for short-term outcomes (in-hospital and 30-day all-cause mortality) and long-term outcomes (all-cause mortality, cardiac death, major adverse cardiac events) were extracted or transformed.

Results: Nineteen studies were included. The risk of short-term all-cause mortality was significantly higher in patients with COPD than in those without COPD (RR 1.42, 95% CI 1.05-1.93), as were the risks of long-term all-cause mortality (RR 1.68, 95% CI 1.50-1.88) and long-term cardiac mortality (HR 1.84, 95% CI 1.41-2.41). There was no significant between-group difference in the long-term revascularization rate (HR 1.01, 95% CI 0.99-1.04) or in short-term and long-term stroke rates (OR 0.89, 95% CI 0.58-1.37 and HR 1.38, 95% CI 0.97-1.95). Operation significantly affected heterogeneity and combined results for long-term mortality (CABG, HR 1.32, 95% CI 1.04-1.66; PCI, HR 1.84, 95% CI 1.58-2.13).

Conclusions: COPD was independently associated with poor outcomes after PCI or CABG after adjustment for confounders.

Keywords: Chronic obstructive pulmonary disease; Coronary artery bypass grafting; Coronary artery disease; Percutaneous coronary intervention.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

SUPPLEMENTARY INFO

Publication typesexpand

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Cite

The Effect of a Healthcare Services Hotline on Quality of Life and Hospital Readmissions for Patients with Chronic Obstructive Pulmonary Disease

Shahrokh Maghsoudi, Seyed Reza Mazloom, Hossein Rafiei, Farshid Mohammadmousaei, Mohammad Sajjad Ghaderi, Mohamad Hossein Mafi

Abstract

Chronic obstructive pulmonary disease (COPD) is a common debilitating disease marked by frequent exacerbations and hospitalizations, economic burden, and reduced quality of life. This study aimed to determine the effect of a healthcare hotline on quality of life and hospital readmissions within 30 days of discharge for patients with COPD. Sixty patients with COPD who needed home healthcare services were recruited for this quasi-experimental study. A direct hotline was provided to patients and their caregivers in the intervention group to answer their questions about the disease. Data were collected using a demographics checklist, and St. George Respiratory Questionnaire. The number of hospitalizations and mean length of hospital stay in the intervention group within 30 days was significantly lower than the control group ($p < 0.05$). As for quality of life, only the mean score of symptoms was significantly different between the intervention and control groups ($p < 0.05$). The results showed the positive effect of a healthcare hotline on reducing readmission rates within 30 days of discharge and its low effect on quality of life of COPD patients.

- <u>30 references</u>

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Trends and Rural-Urban Differences in the Initial Prescription of Low-Value Inhaled Corticosteroids among US Veterans with COPD

<u>Kevin I Duan</u> [1], <u>Lucas M Donovan</u> [2][3], <u>Laura J Spece</u> [4], <u>Laura C Feemster</u> [5][6], <u>Alexander D Bryant</u> [7], <u>Robert Plumley</u> [8], <u>Margaret P Collins</u> [9], <u>David H Au</u> [10]

Affiliations expand

- PMID: 36867427

- DOI: <u>10.1513/AnnalsATS.202205-458OC</u>

Abstract

Rationale: Guidelines recommend inhaled corticosteroids (ICS) for patients with chronic obstructive pulmonary disease (COPD) and select indications, including asthma history, high exacerbation risk, or high serum eosinophils. ICS are commonly prescribed outside of these indications despite evidence of harm. We defined "low-value" ICS prescription as

receipt of an ICS without evidence of a guideline-recommended indication. ICS prescription patterns are not well characterized and could inform health system interventions to reduce low-value practices.

Objective: To evaluate the national trends in initial low-value ICS prescriptions in the Department of Veterans Affairs and determine whether rural-urban differences in low-value ICS prescribing exist.

Methods: We performed a cross-sectional study between January 4, 2010 and December 31, 2018, identifying Veterans with COPD and who were new users of inhaler therapy. We defined low-value ICS as prescription in patients with (1) no asthma, (2) low risk of future exacerbation (GOLD groups A or B), and (3) serum eosinophils <300 cells/microliter. We performed multivariable logistic regression to evaluate trends in low-value ICS prescription over time, adjusting for potential confounders. We performed fixed effects logistic regression to assess rural-urban prescribing patterns.

Results: We identified a total of 131,009 Veterans with COPD starting inhaler therapy, of which 57,472 (44%) were prescribed low-value ICS as initial therapy. From 2010 to 2018, the probability of receiving low-value ICS as initial therapy increased by 0.42 percentage points per year (95% CI 0.31 - 0.53). Compared to urban residence, rural residence was associated with a 2.5 percentage point (95% CI 1.9 - 3.1) higher probability of receiving low-value ICS as initial therapy.

Conclusions: The prescription of low-value ICS as initial therapy is common and increasing slightly over time for both rural and urban Veterans. Given the widespread and persistent nature of low-value ICS prescribing, health system leaders should consider system-wide approaches to address this low-value prescribing practice.

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Chronic obstructive pulmonary disease: 10 years of precision-guided success

Sanjay Ramakrishnan[1]

Affiliations expand

- PMID: 36863785

- DOI: 10.1016/S2213-2600(23)00013-9

No abstract available

Conflict of interest statement

I have received salary support from the National Institute for Health and Care Research through a grant to my institution, and speaker honoraria from AstraZeneca, all outside of the submitted work. I am working on a clinical trial partly funded by AstraZeneca, through an unrestricted grant to my institution.
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Palliative Care Interventions in Advanced Chronic Obstructive

Pulmonary Disease: An Integrative Review

Jessica Madiraca [1], Kathleen Lindell [1], Patrick Coyne [2], Sarah Miller [1]

Affiliations expand

- PMID: 36862125

- DOI: 10.1089/jpm.2022.0356

Abstract

Background: Chronic obstructive pulmonary disease (COPD), the sixth leading cause of death in the United States, is associated with higher mortality rates in women. Women also experience tremendous symptom burden, including dyspnea, anxiety, and depression, in comparison to men with COPD. Palliative care (PC) provides symptom management and addresses advanced care planning for serious illness, but little is known about the use of PC in women with COPD. **Objective:** The purpose of this integrative review was to identify known PC interventions in advanced COPD and to understand the problem of gender and sex disparities. **Methods:** Whittemore and Knafl's methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses were used to guide this integrative review, and the quality of the articles was appraised using the Mixed Methods Appraisal Tool2018 version. A database search was conducted in PubMed, SCOPUS, ProQuest, and CINAHL complete between 2009 and 2021. **Results:** Application of search terms yielded 1005 articles. After screening 877 articles, 124 met inclusion criteria, resulting in a final sample of 15 articles. Study characteristics were evaluated for common concepts and synthesized using the Theory of Unpleasant Symptoms influencing factors (physiological, situational, and performance). All 15 studies discussed PC interventions with the focus on dyspnea management or improvement in quality of life. None of the studies identified in this review focused specifically on women with advanced COPD receiving PC, despite the significant impact that this illness has on women. **Conclusion:** It remains unknown if any intervention is more beneficial than another for women with advanced COPD. Future research is needed to provide an understanding of the unmet PC needs of women with advanced COPD.

Keywords: chronic obstructive pulmonary disease (COPD); integrative review; interventions; palliative care.

SUPPLEMENTARY INFO

Publication typesexpand

Psychometric properties of the Hospital Anxiety and Depression Scale (HADS) in individuals with stable chronic obstructive pulmonary disease (COPD): a systematic review

Aleksandra Nikolovski [1], Lara Gamgoum [1], Arshpreet Deol [1], Shea Quilichini [1], Ethan Kazemir [1], Jonathan Rhodenizer [1], Ana Oliveira [1 2 3], Dina Brooks [1 2 4], Sanaa Alsubheen [1]

Affiliations expand

- PMID: 36861817

- DOI: 10.1080/09638288.2023.2182918

Abstract

Purpose: The Hospital Anxiety and Depression Scale (HADS) is used to assess anxiety and depression in individuals with chronic obstructive pulmonary disease (COPD); however, its measurement properties lack critical appraisal. We aimed to summarize and critically appraise the validity, reliability, and responsiveness of the HADS in COPD.

Materials and methods: Five electronic databases were searched. The Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines were used to assess the methodological and evidence quality in the selected studies.

Results: Twelve studies assessed the psychometric properties of the HADS-Total and its subscales HADS-Anxiety and HADS-Depression in COPD. High-quality evidence supported the structural and criterion validity of the HADS-A, the internal consistency of the HADS-T, HADS-A, and HADS-D with Cronbach's alpha values of 0.73-0.87, and before-after treatment responsiveness of HADS-T and its subscales (minimal clinically important difference = 1.4-2; effect size = 0.45-1.40). Moderate-quality evidence supported the test-retest reliability of the HADS-A and HADS-D with excellent coefficient values of 0.86-0.90.

Conclusions: The HADS-A is recommended for use in individuals with stable COPD. The lack of high-quality evidence on the validity of the HADS-D and HADS-T prevented drawing robust conclusions about their clinical utility in COPD.Implications for rehabilitationAnxiety and depression are common in individuals with chronic obstructive pulmonary disease (COPD).Anxiety and depression can negatively impact the physical and mental health of individuals with COPD.The HADS can be used to assess anxiety and depression in COPD in rehabilitation settings.

Keywords: COPD; HADS; reliability; responsiveness; validity.

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Comorbid conditions as predictors of mortality in severe COPD – an eight-year follow-up cohort study

[Gabriella Eliasson](#) [1], [Christer Janson](#) [2], [Gunnar Johansson](#) [3], [Kjell Larsson](#) [4], [Anders Lindén](#) [4 5], [Claes-Göran Löfdahl](#) [6], [Thomas Sandström](#) [7], [Josefin Sundh](#) [1]

Affiliations expand

Abstract

Purpose: Co-morbidities are common in chronic obstructive pulmonary disease (COPD) and are associated with increased morbidity and mortality. The aim of the present study was to explore the prevalence of several comorbid conditions in severe COPD, and to investigate and compare their associations with long-term mortality.

Methods: In May 2011 to March 2012, 241 patients with COPD stage 3 or 4 were included in the study. Information was collected on sex, age, smoking history, weight and height, current pharmacological treatment, number of exacerbations the recent year and comorbid conditions. At December 31st, 2019, mortality data (all-cause and cause specific) were collected from the National Cause of Death Register. Data were analyzed using Cox-regression analysis with gender, age, previously established predictors of mortality and comorbid conditions as independent variables, and all-cause mortality and cardiac and respiratory mortality, respectively, as dependent variables.

Results: Out of 241 patients, 155 (64%) were deceased at the end of the study period; 103 patients (66%) died of respiratory disease and 25 (16%) of cardiovascular disease. Impaired kidney function was the only comorbid condition independently associated with increased all-cause mortality (HR (95% CI) 3.41 (1.47-7.93) p=0.004) and respiratory mortality (HR (95%CI) 4.63 (1.61 to 13.4), p = 0.005). In addition, age ≥70, BMI <22 and lower FEV1 expressed as %predicted were significantly associated with increased all-cause and respiratory mortality.

Conclusion: In addition to the risk factors high age, low BMI and poor lung function; impaired kidney function appears to be an important risk factor for mortality in the long term, which should be taken into account in the medical care of patients with severe COPD.

Conflict of interest statement

No potential conflict of interest was reported by the authors.

- 42 references
- 2 figures

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Clinical validation of a contactless respiration rate monitor

Bartosz Bujan [1], Tobit Fischer [2], Sarah Dietz-Terjung [2], Aribert Bauerfeind [3], Piotr Jedrysiak [4], Martina Große Sundrup [2], Janne Hamann [3], Christoph Schöbel [2]

Affiliations expand

- PMID: 36859403

- PMCID: PMC9975830

Abstract

Respiratory rate (RR) is an often underestimated and underreported vital sign with tremendous clinical value. As a predictor of cardiopulmonary arrest, chronic obstructive pulmonary disease (COPD) exacerbation or indicator of health state for example in COVID-19 patients, respiratory rate could be especially valuable in remote long-term patient monitoring, which is challenging to implement. Contactless devices for home use aim to overcome these challenges. In this study, the contactless Sleepiz One+ respiration monitor for home use during sleep was validated against the thoracic effort belt. The agreement of instantaneous breathing rate and breathing rate statistics between the Sleepiz One+ device and the thoracic effort belt was initially evaluated during a 20-min sleep window under controlled conditions (no body movement) on a cohort of 19 participants and secondly in a more natural setting (uncontrolled for body movement) during a whole night on a cohort of 139 participants. Excellent agreement was shown for instantaneous breathing rate to be within 3 breaths per minute (Brpm) compared to thoracic effort band with an accuracy of 100% and mean absolute error (MAE) of 0.39 Brpm for the setting controlled for movement, and an accuracy of 99.5% with a MAE of 0.48 Brpm for the whole night measurement, respectively. Excellent agreement was also achieved for the respiratory rate statistics over the whole night with absolute errors of 0.43, 0.39 and 0.67 Brpm for the 10th, 50th and 90th percentiles, respectively. Based on these results we conclude that the Sleepiz One+ can estimate instantaneous respiratory rate and its summary statistics at high accuracy in a clinical setting. Further studies are required to evaluate the performance in the home environment, however, it is expected that the performance is at similar level, as the measurement conditions for the Sleepiz One+ device are better at home than in a clinical setting.

Conflict of interest statement

- 47 references
- 6 figures

SUPPLEMENTARY INFO

MeSH termsexpand

Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary

Alvar Agustí [1][2], Bartolome R Celli [3][2], Gerard J Criner [4], David Halpin [5], Antonio Anzueto [6], Peter Barnes [7], Jean Bourbeau [8], MeiLan K Han [9], Fernando J Martinez [10], Maria Montes de Oca [11], Kevin Mortimer [12][13][14], Alberto Papi [15], Ian Pavord [16], Nicolas Roche [17], Sundeep Salvi [18], Don D Sin [19], Dave Singh [20], Robert Stockley [21], M Victorina López Varela [22], Jadwiga A Wedzicha [7], Claus F Vogelmeier [23]

Affiliations expand

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Air pollution and long-term risk of hospital admission due to chronic obstructive pulmonary disease exacerbations in Poland: a time-stratified, case-crossover study

Piotr Dąbrowiecki, Andrzej Chciałowski, Agata Dąbrowiecka, Anna Piórkowska, Artur Badyda

Free article

Abstract

Introduction: Airborne pollutants may worsen the course of chronic obstructive pulmonary disease (COPD). Previous studies have shown that both particulate and gaseous pollutants increase airway inflammation, which may lead to an exacerbation of COPD.
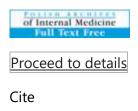
Objectives: To study the association between exposure to airborne pollutants and the risk of COPD exacerbations in the three largest urban agglomerations in Poland: Warsaw, Cracow, and the Tricity.

Patients and methods: We used a case-crossover approach to analyze data from 2011 to 2018. This time-series study used distributed lag nonlinear models to analyze the risk of hospital admission due to COPD exacerbations during 21 days following exposure to particulate matter (PM), NO2, and SO2.

Results: Overall, there were 26,948 admissions due to COPD exacerbations. During 21 days after exposure, the rate ratio (95% confidence interval) for admissions per 10 µg/m3 was 1.028 (1.008-1.049) for PM10; 1.030 (1.006-1.055) for PM2.5; 1.032 (0.988-1.078 for NO2; and 1.145 (1.038-1.262) for SO2. The risk for admission peaked at 10 days after exposure to PM10 and PM2.5, whereas for NO2 and SO2 the risk was greatest on the day of exposure. The proportions (95% confidence interval) of hospitalizations attributable to air pollution were 9.08% (3.10%-15.08%) for PM10; 7.61% (1.27%-13.49%) for PM2.5; 9.77% (3.63%-21.48%) for NO2; and 7.70% (2.30%- 12.84%) for SO2.

Conclusions: PM2.5, PM10, NO2, and SO2 pollution was associated with an increased risk of COPD exacerbations that needed treatment in hospital. There were different risk patterns for particulate and gaseous pollutants. Improving air quality in Polish cities could reduce the burden of COPD.

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Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary

Alvar Agustí [1], Bartolome R Celli [2], Gerard J Criner [3], David Halpin [4], Antonio Anzueto [5], Peter Barnes [6], Jean Bourbeau [7], MeiLan K Han [8], Fernando J Martinez [9], Maria Montes de Oca [10], Kevin Mortimer [11], Alberto Papi [12], Ian Pavord [13], Nicolas Roche [14], Sundeep Salvi [15], Don D Sin [16], Dave Singh [17], Robert Stockley [18], M Victorina López Varela [19], Jadwiga A Wedzicha [6], Claus F Vogelmeier [20]

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- PMID: 36856440

No abstract available

- 198 references

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Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary

Alvar Agustí [1], Bartolome R Celli [2], Gerard J Criner [3], David Halpin [4], Antonio Anzueto [5], Peter Barnes [6], Jean Bourbeau [7], MeiLan K Han [8], Fernando J Martinez [9], Maria Montes de Oca [10], Kevin Mortimer [11][12][13], Alberto Papi [14], Ian Pavord [15], Nicolas Roche [16], Sundeep Salvi [17], Don D Sin [18], Dave Singh [19], Robert Stockley [20], M Victorina López Varela [21], Jadwiga A Wedzicha [6], Claus F Vogelmeier [22]

Affiliations expand

- PMID: 36856433

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[Chronic Hypoxemia Triggers a Neuropathic Process in Chronic Obstructive Pulmonary Disease: Insight From In Vivo Neurophysiological Assessments](#)

[Seon Min Yoon](#)[1], [Young Bum Park](#)[2], [Yousang Ko](#)[3], [Jong Seok Bae](#)[4]

Affiliations expand

Abstract

Background and purpose: Peripheral neuropathies (PNs) are a common but poorly understood complication of chronic obstructive pulmonary disease (COPD). To clarify the initial trigger of a PN in COPD, we investigated the excitability of peripheral nerves in patients with COPD.

Methods: The automated nerve excitability test (NET) using the threshold-tracking paradigm was applied to 20 COPD patients. The recording protocol calculated the strength-duration time constant, threshold electrotonus (TE), current-threshold relationship, and recovery cycle (RC). Each NET parameter was compared with two control groups: normal controls group (NC group) and smokers without COPD group (smoker group).

Results: In the motor NETs, the change in the threshold in the mid-depolarizing phase of TE (40-60 ms) was smaller in the COPD group (50.7%±1.2%, mean±SEM; n=20) than in the NC group (54.5%±0.7%, n=25; $p<0.01$), as was the prominence of superexcitability in the RC (-22.6%±1.5% and -26.4%±1.1%, respectively; p=0.04). There were no significant differences in the sensory NETs. Comparisons between the COPD and smoker groups (n=25) also showed no differences in either the motor or sensory NETs.

Conclusions: The pattern of excitability in COPD revealed a membrane depolarization attributable to Na^+-K^+-ATPase failure in the axolemma of distal motor nerves. This finding suggests that chronic hypoxemia and adaptative process can alter axonal excitability and trigger a resultant neuropathic process that is antecedent to PN in COPD.

Keywords: hypoxemia; nerve excitability; peripheral nervous system diseases; pulmonary disease, chronic obstructive; threshold tracking.

Conflict of interest statement

The authors have no potential conflicts of interest to disclose.

- 34 references
- 3 figures

SUPPLEMENTARY INFO

Grant supportexpand

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General practice management of COPD patients following acute exacerbations: a qualitative study

Bianca Perera [1], Chris Barton [2], Christian Osadnik [3]

Affiliations expand

- PMID: 36823067

- PMCID: PMC9975965

- DOI: 10.3399/BJGP.2022.0342

Abstract

Background: Exacerbations are the strongest risk factor for future exacerbations for patients living with chronic obstructive pulmonary disease (COPD). The period immediately following exacerbation is a high-risk period for recurrence and hospital admission, and is a critical time to intervene. GPs are ideally positioned to deliver this care.

Aim: To explore perceptions of GPs regarding the care of patients following exacerbations of COPD and to identify factors affecting the provision of evidence-based care.

Design and setting: A descriptive qualitative study was undertaken involving semi-structured, in-depth interviews with Australian GPs who volunteered to participate following a national survey of general practice care for COPD patients following exacerbations.

Method: Interviews were conducted via the Zoom video conference platform, which were audio-recorded and transcribed verbatim. QSR NVivo was used to support data management, coding, and inductive thematic analysis.

Results: Eighteen GPs completed interviews. Six key themes were identified: 1) GPs' perceptions and knowledge in the management of COPD patients following exacerbation and admission to hospital; 2) pharmacological management; 3) consultation time; 4) communication between healthcare professionals; 5) access to other health services; and 6) patient compliance.

Conclusion: Delivery of post-exacerbation care to COPD patients is affected by GPs, patients, and health service-related factors. The care of COPD patients may be further improved by supporting GPs to overcome identified barriers.

Keywords: COPD; exacerbations; general practice; general practitioners; qualitative research.

- [39 references](#)

SUPPLEMENTARY INFO

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High inhaler resistance does not limit successful inspiratory maneuver among patients with asthma or COPD

[Ville A Vartiainen](#) [1 2], [Federico Lavorini](#) [3], [Anna C Murphy](#) [4], [Klaus F Rabe](#) [5]

Affiliations expand

- PMID: 36820500

- DOI: [10.1080/17425247.2023.2179984](#)

Abstract

Introduction: There has been an active discussion on the sustainability of inhaler therapy in respiratory diseases, and it has cast a shadow on pMDIs which rely on propellant with high global warming potential (GWP). DPIs offer a lower GWP and effective alternative, but there has been concern whether all patients can generate sufficient inspiratory effort to disperse the drug. This review focuses on airflow resistance of DPIs and its clinical relevance.

Areas covered: For this narrative review, we searched the literature for studies comparing flow patterns with different devices. We also included a section on clinical trials comparing reliever administration with DPI, pMDI with spacer, and nebulizer during exacerbation.

Expert opinion: The evidence supports the efficacy of DPIs irrespective of respiratory condition or age of the patient even during acute exacerbations. Air flow resistance does not limit the use of DPIs and the patients were able to generate sufficient inspiratory flow rate with almost any device studied. None of 16 identified clinical trials comparing reliever administration via DPIs to other types of devices during exacerbation or bronchial challenge showed statistically significant difference between the device types in FEV1 recovery. DPIs performed as well as other types of inhaler devices even during asthma or COPD exacerbation.

Keywords: Inhaler; dry powder inhaler; metered dose inhaler; peak inspiratory flow rate.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Are beta-blockers safe and effective after myocardial infarction in patients with COPD?

Lindsay E Davis [1], Elizabeth K Pogge, Rajeev Garg

Affiliations expand

- PMID: 36815843

- DOI: 10.1097/01.JAA.0000918804.17000.75

Abstract

Clinicians may be hesitant to prescribe beta-blockers in patients with chronic obstructive pulmonary disease (COPD) who have a comorbid compelling cardiovascular indication for beta-blocker therapy. This article summarizes the available data on the safety and efficacy of beta-blockers in patients with COPD and recent myocardial infarction.

- 21 references

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Nocturnal Dyspnea During Severe Exacerbations Is Associated With Mortality Risk in COPD

Rafael Golpe [1], Juan M Figueira-Gonçalves [2], David Dacal-Rivas [3], Nagore Blanco-Cid [3], Indhira Guzmán-Peralta [3], Olalla Castro-Añón [3], Luis A Pérez-de-Llano [3]

Affiliations expand

No abstract available

Conflict of interest statement

The authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Final Version Respir Care

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The Effect of Adding Noninvasive Ventilation to High-Intensity Exercise on Peripheral and Respiratory Muscle Oxygenation

Cássia da Luz Goulart [1], Flávia Rossi Caruso [1], Adriana S Garcia de Araújo [1], Sílvia Cristina Garcia de Moura [2], Aparecida Maria Catai [2], Polliana Batista Dos Santos [1], Érika Z Kabbach [1], Ross Arena [3], Renata Gonçalves Mendes [1], Audrey Borghi-Silva [4]

Abstract

Background: We sought to assess whether noninvasive ventilation (NIV) as an adjunct with high-intensity exercise (HIEx) is more effective than exercise alone or exercise + sham on respiratory and peripheral oxygenation and vascular function in subjects with coexisting COPD and heart failure (HF).

Methods: On separate days, subjects performed incremental cardiopulmonary exercise testing and 3 constant load tests: HIEx, HIEx+NIV, and HIEx+sham (bi-level mode, Astral 150). Subjects were randomized with a 1:1 block allocation for the HIEx+NIV group and HIEx+sham group until the limit of tolerance (Tlim). Peripheral and respiratory oxygenation were assessed by oxyhemoglobin (O_2Hb) and deoxyhemoglobin (Hb) using near-infrared spectroscopy in the respiratory and peripheral musculature. Vascular function was assessed by endothelial function using the flow-mediated vasodilation (FMD) method.

Results: There was a significant increase in FMD (mm), FMD (%), and shear stress in the HIEx+NIV group when compared to HIEx or HIEx+sham ($P < .05$). Less extraction of O_2 (Hb) in the peripheral and respiratory muscles was observed in the HIEx+NIV group ($P < .05$). We also found correlations between peripheral muscle oxygenation (O_2Hb) at the moment 80% of Tlim ($r = 0.71$, $P = .009$) and peak of Tlim (100%) ($r = 0.76$, $P = .004$) with absolute FMD (mm) immediately after HIEx+NIV.

Conclusions: NIV as an adjunct to HIEx can acutely unload the respiratory musculature with better redistribution of available blood flow and beneficially modulate endothelial function. These results may influence the approach to cardiopulmonary rehabilitation in patients with coexisting COPD-HF.

Keywords: COPD; blood flow muscle; heart failure; oxygenation.

Conflict of interest statement

The authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

Revealing EXPH5 as a potential diagnostic gene biomarker of the late stage of COPD based on machine learning analysis

Yuwei Yang [1], Yan Cao [2], Xiaobo Han [3], Xihui Ma [4], Rui Li [5], Rentao Wang [6], Li Xiao [7], Lixin Xie [8]

Affiliations expand

- PMID: 36746116

- DOI: 10.1016/j.compbiomed.2023.106621

Free article

Abstract

Chronic obstructive pulmonary disease is a kind of chronic lung disease characterized by persistent air flow obstruction, which was the third leading cause of death in China. The incidence of COPD is steadily and increasing and has been a globally sever disease.

Accordingly, it is urgently needed to explore how to diagnose and treat COPD timely. This study aims to find key genes to diagnose COPD as soon as possible to avoid COPD processing and analyze immune cell infiltration between COPD early stage and late stage. Two GEO datasets were merged as the merge data for analyses. 157 DEGs were used for GSEA analysis to find the pathway between COPD early stage and late stage. Above all, gene EXPH5 stood out from the screen as the most likely candidate diagnosis biomarker of COPD indicating the late-stage by least LASSO and SVM-RFE. ROC curves of EXPH5 were applied to represent the discriminatory ability through the area under the curve which is the gold standard to evaluate the accuracy of diagnosis and survival rate. The CIBERSORT algorithm was used to assess the distribution of tissue-infiltrating immune cells between two COPD stages. The diagnosis biomarker, gene EXPH5 had a positive correlation with NK cells resting; mast cell resting, eosinophils, and negative correlation with T cell gamma delta, macrophages M1, which underscore the role of gene and immune cell infiltration. To make results more reliable, we further analyzed the gene EXPH5 expression in single-cell transcriptome data and showed again that EXPH5 genes significantly downregulated in the late stage of COPD especially in the main lung cell types AT1 and AT2. In a word, our study identified genes EXPH5 as a marker gene, which adds to the knowledge for clinical diagnosis and pharmaceutical design of COPD.

Keywords: Bioinformatics analysis; COPD; Differential expressed genes; EXPH5; Machine learning.

Conflict of interest statement

Declaration of competing interest The authors declare no conflict of interest.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Eur J Radiol

CT-based emphysema characterization per lobe: A proof of concept

Hendrik Joost Wisselink [1], Xiaofei Yang [2], Mieneke Rook [3], Marjolein A Heuvelmans [4], Wenzhen Jiang [5], Jianing Zhang [5], Yihui Du [2], Marleen Vonder [2], Monique D Dorrius [2], Zhaoxiang Ye [5], Geertruida H de Bock [2], Rozemarijn Vliegenthart [6]

Affiliations expand

- PMID: 36731401

- DOI: 10.1016/j.ejrad.2023.110709

Abstract

Purpose: The Fleischner society criteria are global criteria to visually evaluate and classify pulmonary emphysema on CT. It may group heterogeneous disease severity within the same category, potentially obscuring clinically relevant differences in emphysema severity. This proof-of-concept study proposes to split emphysema into more categories and to assess each lobe separately, and applies this to two general population-based cohort samples to assess what information such an extension adds.

Method: From a consecutive sample in two general population-based cohorts with low-dose chest CT, 117 participants with more than a trace of emphysema were included. Two independent readers performed an extended per-lobe classification and assessed overall severity semi-quantitatively. An emphysema sum score was determined by adding the severity score of all lobes. Inter-reader agreement was quantified with Krippendorff Alpha.

Results: Based on Fleischner society criteria, 69 cases had mild to severe centrilobular emphysema, and 90 cases had mild or moderate paraseptal emphysema (42 had both types of emphysema). The emphysema sum score was significantly different between mild (10.7 ± 4.3, range 2-22), moderate (20.1 ± 3.1, range: 15-24), and severe emphysema (23.6 ± 3.4, range: 17-28, p < 0.001), but ranges showed significant overlap. Inter-reader agreement for the extended classification and sum score was substantial (alpha 0.79 and

0.85, respectively). Distribution was homogenous across lobes in never-smokers, yet heterogenous in current smokers, with upper-lobe predominance.

Conclusions: The proposed emphysema evaluation method adds information to the original Fleischner society classification. Individuals in the same Fleischner category have diverse emphysema sum scores, and lobar emphysema distribution differs between smoking groups.

Keywords: CT; Emphysema; Per-lobe assessment; Proof of concept; Visual assessment.

Conflict of interest statement

SUPPLEMENTARY INFO

MeSH termsexpand

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Review

Curr Opin HIV AIDS

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. 2023 Mar 1;18(2):93-101.

HIV and chronic lung disease

Janice M Leung [1][2]

Affiliations expand

- PMID: 36722198

- DOI: 10.1097/COH.0000000000000777

Abstract

Purpose of review: As people living with human immunodeficiency virus (HIV, PLWH) age, aging-related comorbidities have come into focus as major challenges to their overall health. In this review, an in-depth overview of the two most commonly encountered chronic lung diseases in PLWH, chronic obstructive pulmonary disease (COPD) and lung cancer, is provided.

Recent findings: The risk for both COPD and lung cancer remains significantly higher in PLWH compared to the HIV-uninfected population, although fortunately rates of lung cancer appear to be declining over the last two decades. Outcomes for PLWH with these conditions, though, continue to be poor with worse survival rates in comparison to the general population. PLWH still face major barriers in accessing care for these conditions, including a higher likelihood of being underdiagnosed with COPD and a lower likelihood of being referred for lung cancer screening or treatment. A lack of evidence for optimal treatment strategies for both COPD and lung cancer still hampers the care of PLWH with these conditions.

Summary: COPD and lung cancer represent substantial burdens of disease in PLWH. Improved access to standard-of-care screening and treatment and greater investigation into therapeutic responses specifically in this population are recommended.

- 169 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Byssinosis and lung health among cotton textile workers: baseline findings of the MultiTex trial in Karachi, Pakistan

Asaad Ahmed Nafees [1][2], Muhammad Zia Muneer [3], Muhammad Irfan [4], Muhammad Masood Kadir [3], Sean Semple [5], Sara De Matteis [2][6], Peter Burney [2], Paul Cullinan [2]

Affiliations expand

- PMID: 36717255

- DOI: 10.1136/oemed-2022-108533

Abstract

Objectives: To assess the association of exposure in cotton mills in Karachi with different definitions of byssinosis and lung health.

Methods: This cross-sectional survey took place between June 2019 and October 2020 among 2031 workers across 38 spinning and weaving mills in Karachi. Data collection

involved questionnaire-based interviews, spirometry and measurements of personal exposure to inhalable dust. Byssinosis was defined using both WHO symptoms-based (work-related chest tightness), and Schilling's criteria (symptoms with decreased forced expiratory volume in 1 s (FEV_1). Values of FEV_1/forced vital capacity ratio below the lower limit of normality on postbronchodilator test were considered as 'chronic airflow obstruction' (CAO).

Results: 56% of participants had at least one respiratory symptom, while 43% had shortness of breath (grade 1). Prevalence of byssinosis according to WHO criteria was 3%, it was 4% according to Schilling's criteria, and likewise for CAO. We found low inhalable dust exposures (geometric mean: 610 $\mu g/m^3$). Cigarette smoking (≥ 3.5 pack-years), increasing duration of employment in the textile industry and work in the spinning section were important factors found to be associated with several respiratory outcomes.

Conclusion: We found a high prevalence of respiratory symptoms but a low prevalence of byssinosis. Most respiratory outcomes were associated with duration of employment in textile industry. We have discussed the challenges faced in using current, standard guidelines for identifying byssinosis.

Keywords: Dust; Epidemiology; Occupational Health; Particulate Matter; Respiratory Function Tests.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Respir Med

Prevalence of abnormal spirometry in individuals with a smoking history and no known obstructive lung disease

Thuonghien V Tran [1], Gregory L Kinney [2], Alejandro Comellas [3], Karin F Hoth [4], Arianne K Baldomero [5], A James Mamary [6], Jeffrey L Curtis [7], Nicola Hanania [8], Richard Casaburi [9], Kendra A Young [2], Victor Kim [6], Barry Make [10], Emily S Wan [11], Alejandro A Diaz [12], John Hokanson [2], James D Crapo [10], Edwin K Silverman [13], Surya P Bhatt [14], Elizabeth Regan [15], Spyridon Fortis [16]; COPDGene® Investigators – Core Units; COPDGene® Investigators – Clinical Centers

Collaborators, Affiliations expand

Abstract

Introduction: Recent evidence suggests a high prevalence of undiagnosed chronic obstructive pulmonary disease (COPD). These individuals are at risk of exacerbations and delayed treatment. We analyzed an at-risk population for the prevalence of abnormal spirometry to provide clarity into who should undergo early spirometry.

Methods: We analyzed data from the COPDGene study. Participants with ≥10 pack-years of smoking were included. Individuals with self-reported or physician-diagnosed COPD, asthma, chronic bronchitis, emphysema and/or were on inhalers were excluded. Parsimonious multivariable logistic regression models identified factors associated with abnormal spirometry, defined as either airflow obstruction (AFO) or preserved ratio impaired spirometry. Variables were selected for the final model using a stepwise backward variable elimination process which minimized Akaike information criterion (AIC). Similarly, during the 5-year follow-up period, we assessed factors associated with incident diagnosis of COPD.

Results: Of 5055 individuals, 1064 (21%) had undiagnosed AFO. Age, pack-years, current smoking and a history of acute bronchitis were associated with AFO while body mass

index, female sex, and Black race were inversely associated. Among 2800 participants with 5-year follow-up, 532 (19%) had an incident diagnosis of COPD. Associated risk factors included mMRC ≥2, chronic productive cough, respiratory exacerbations during the follow-up period, and abnormal spirometry. Age was inversely associated.

Conclusions: The prevalence of undiagnosed COPD is high in at-risk populations. We found multiple factors associated with undiagnosed COPD and incident diagnosis of COPD at follow up. These results can be used to identify those at risk for undiagnosed COPD to facilitate earlier diagnosis and treatment.

Keywords: Chronic obstructive pulmonary disease; Diagnosis.

Conflict of interest statement

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Physical frailty related to cognitive impairment and COPD exacerbation: A cross-sectional study

Chen-Liang Tsai [1], Wen Pei Chang [2], Yen-Kuang Lin [3], Shu-Chuan Ho [4], Yu-Huei Lin [5]

Affiliations expand

No abstract available

Conflict of interest statement

Declaration of competing interest None.

SUPPLEMENTARY INFO

MeSH termsexpand

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Estimating the contribution of respiratory pathogens to acute exacerbations of COPD using routine data

Shanya Sivakumaran [1], Mohammad A Alsallakh [2], Ronan A Lyons [2], Jennifer K Quint [3], Gwyneth A Davies [2]

Affiliations expand

- PMID: 36706962

- DOI: 10.1016/j.jinf.2023.01.012

Abstract

Objectives: To characterise microbiology testing and results associated with emergency admissions for acute exacerbation of COPD (AECOPD), and determine the accuracy of ICD-10 codes in retrospectively identifying laboratory-confirmed respiratory pathogens in this setting.

Methods: Using person-level data from the Secure Anonymised Information Linkage Databank in Wales, we extracted emergency admissions for COPD from 1/12/2016 to 30/11/2018 and undertook linkage of admissions data to microbiology data to identify laboratory-confirmed infection. We further used these data to assess the accuracy of pathogen-specific ICD-10 codes.

Results: We analysed data from 15,950 people who had 25,715 emergency admissions for COPD over the two-year period. 99.5% of admissions could be linked to a laboratory test

within 7 days of admission date. Sputum was collected in 5,013 (19.5%) of admissions, and respiratory virus testing in 1,219 (4.7%). Where respiratory virus testing was undertaken, 46.7% returned any positive result. Influenza was the virus most frequently detected, in 21.5% of admissions where testing was conducted. ICD-10 codes exhibited low sensitivity in detecting laboratory-confirmed respiratory pathogens.

Conclusions: In people admitted to hospital with AECOPD, increased testing for respiratory viruses could enable more effective antibiotic stewardship and isolation of cases. Linkage with microbiology data achieves more accurate and reliable case definitions.

Keywords: Chronic obstructive; Electronic health records; Pulmonary disease; Respiratory tract infections.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Assessment of incidence of cerebral vascular diseases and prediction of

stroke risk in chronic obstructive pulmonary disease patients using multimodal biomarkers

Marwa Y Badr [1], Amira A Elkholy [2], Sara M Shoeib [3], Marwa G Bahey [4], Esraa A Mohamed [4], Alaa M Reda [5]

Affiliations expand

Abstract

Background: Early assessment of cerebrovascular disease in chronic obstructive pulmonary disease (COPD) patients is an important issue for a favorable influence on the quality of life.

Methodology: This cross-sectional case-control study was conducted on 38 eligible COPD patients (mean age 55.5 ± 11.5, 25 males, and 13 females) and 26 age-/sex-matched healthy controls. All participants were subjected to stroke risk screening instruments that included the Stroke Riskometer™, the Framingham 10-Year Risk Score, the stroke risk screening tool (the Department of Disease Control of Thailand), the My Risk Stroke Calculator, and Q Stroke. Radiologically, diffusion tensor imaging (DTI) and echo-gradient MRI (T2 star) T2 star imaging were done. Color-coded duplex sonography was done. Laboratory investigations included C-reactive protein (CRP), serum amyloid A, plasma fibrinogen level, serum IL6, 8-Isoprostane, vWF and urinary albumin creatinine ratio.

Results: Stroke risk screening instruments revealed a significant increase in COPD patients. DTI showed a significant bilateral reduction in fractional isotropy and a significant bilateral increase in mean diffusivity of white matter through many areas in COPD patients. Patients also had a significant increase of intima-media thickness, presence of atherosclerotic focal thicknesses or plaques on duplex sonography. There was a significant elevation of CRP, serum amyloid A, plasma fibrinogen level, serum IL6, 8-isoprostane, von Willebrand factor (vWF), and urinary albumin creatinine ratio in COPD patients.

Conclusion: COPD patients had an increased risk for stroke that could be assessed on stroke risk screening instruments, DTI, T2 star, duplex sonography, and laboratory investigation and could be correlated with the severity of the disease.

Conflict of interest statement

The researchers declared that they have no known competing financial interests or personal relations that could affect the work reported in this study.

- 57 references
- 3 figures

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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J Physiol

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. 2023 Mar;601(5):883-885.

doi: 10.1113/JP284297. Epub 2023 Feb 7.

Sarcopenia in chronic obstructive pulmonary disease: skeletal muscle gasping for air?

Valdemar Brimnes Ingemann Johansen [1] [2]

Affiliations expand

No abstract available

- 5 references

SUPPLEMENTARY INFO

MeSH termsexpand

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The Journal of Physiology

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Clinical Trial

Respir Med

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-

Improvements in health status with revefenacin, a once-daily, nebulized, long-acting muscarinic antagonist for chronic obstructive pulmonary disease

James F Donohue [1], Gary T Ferguson [2], Jill A Ohar [3], David A Lombardi [4], Roslyn F Schneider [5], Karmon Johnson [6]

Affiliations expand

Free article

Abstract

Background: Replicate, 12-week, phase 3 trials (0126 and 0127) of once-daily nebulized revefenacin 175 µg vs placebo demonstrated significant bronchodilation and improvements in health status in patients with moderate to very severe chronic obstructive pulmonary disease (COPD). This post hoc analysis evaluated improvement in patient-reported outcomes (PROs), including the St. George's Respiratory Questionnaire (SGRQ), COPD Assessment Test (CAT), and Clinical COPD Questionnaire (CCQ) in both women and men.

Methods: Participants were pooled from the two 12-week studies (411 [51%] women and 401 [49%] men). Changes in PROs were assessed overall and separately in men and women.

Results: Revefenacin improved SGRQ and CAT total scores from baseline in both studies; improvement in CCQ total score reached significance only in 0126. In pooled data, a greater proportion of patients achieved clinically meaningful response in SGRQ score (≥4-unit decrease from baseline) with revefenacin vs placebo (odds ratio, 1.5; 95% confidence interval, 1.1-2.1; P = 0.012). Clinically meaningful responses were also seen in CAT (≥2-unit decrease from baseline) and CCQ (≥0.4-unit decrease from baseline) scores with

revefenacin vs placebo. When stratified by sex, improvements from baseline in SGRQ, CAT, and CCQ scores following revefenacin vs placebo reached statistical significance only in women.

Conclusions: Maintenance treatment with revefenacin improved health status in patients with moderate to very severe COPD; however, the effect was more pronounced for women than men.

Clinicaltrials: GOV: [NCT02459080](#); [NCT02512510](#).

Keywords: COPD; COPD Assessment Test; Clinical COPD Questionnaire; Patient-reported outcomes; Revefenacin; St. George's Respiratory Questionnaire.

Conflict of interest statement

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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Interrelationships between tuberculosis and chronic obstructive pulmonary disease

Michael J Zavala[1], Greta L Becker, Robert J Blount

Affiliations expand

- PMID: 36647566

- PMCID: PMC9877200 (available on 2024-03-01)

- DOI: 10.1097/MCP.0000000000000938

Abstract

Purpose of review: Our objective was to review the current literature regarding socioeconomic, environmental, clinical, and immunologic factors common to chronic obstructive pulmonary disease (COPD) and tuberculosis (TB).

Recent findings: Recent studies suggest that TB patients might be at increased risk for developing COPD. Conversely, additional prospective cohort studies have determined that COPD patients are at increased risk for active TB: a risk that appears to be partially mediated through inhaled corticosteroid use. Tobacco smoking, poverty, air pollution, and malnutrition are associated with COPD and TB. Vitamin D has been shown to prevent COPD exacerbations, but its use for preventing TB infection remains unclear. Surfactant deficiency, elevated matrix metalloproteinases, and toll-like receptor 4 polymorphisms play key roles in the pathogenesis of both diseases.

Summary: Recent studies have elucidated interrelationships between COPD and TB. Future research is needed to optimize clinical and public health approaches that could mitigate risk factors contributing to both diseases.

Conflict of interest statement

Conflicts of interest:
We have no conflicts of interest on this project.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Review

Ageing and chronic obstructive pulmonary disease: interrelationships

Krishna Kakkera [1][2], William T Atchley [1][2], Maneetha Kodali [2], Thaddeus Bartter [1][2]

Affiliations expand

Abstract

Purpose of review: As life expectancy increases, the ageing population accrues an increasing burden of chronic conditions and functional compromise. Some conditions that lead to compromise are deemed part of 'natural ageing,' whereas others are considered to represent disease processes. Ageing ('a natural process') and chronic obstructive pulmonary disease ('a disease') share many common features, both pulmonary and systemic. At times, the pathways of injury are the same, and at times they are concurrent. In some cases, age and disease are separated not by the presence but by the severity of a finding or condition. This brief review aims to compare some of the similarities between ageing and COPD and to compare/contrast mechanisms for each.

Recent findings: At the cellular level, the natural process of ageing includes multiple systemic and molecular mechanisms. COPD, though defined by progressive pulmonary compromise, can also be a systemic disease/process. It has become evident that specific senescence pathways like p-16 and the sirtuin family of proteins are implicated both in ageing and in COPD. Also common to both ageing and COPD are increased inflammatory markers, leucocyte response abnormalities, and DNA-level abnormalities.

Summary: The prevalence of COPD increases with increasing age. COPD contributes to the accrued burden of chronic disease and is a significant contributor to morbidity and mortality in this population. This review attempts to summarize some of similarities between ageing and COPD and their underlying mechanisms.

- 45 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Wolters Kluwer

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Cite

Noninvasive positive pressure in acute exacerbations of chronic obstructive pulmonary disease

[Avantika Nathani](#)[1], [Umur Hatipoğlu](#), [Eduardo Mireles-Cabodevila](#)

Affiliations expand

Abstract

Purpose of review: Noninvasive positive pressure ventilation (NIV) is standard of care for patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). We review the most current evidence and highlight areas of uncertainty and ongoing research. We highlight key concepts for the clinician caring for patients with AECOPD which require NIV.

Recent findings: Implementation of NIV in AECOPD is not uniform in spite of the evidence and guidelines. Initiation of NIV should be done early and following protocols. Low-intensity NIV remains the standard of care, although research and guidelines are evaluating higher intensity NIV. Scores to predict NIV failure continue to be refined to allow early identification and interventions. Several areas of uncertainty remain, among them are

interventions to improve tolerance, length of support and titration and nutritional support during NIV.

Summary: The use of NIV in AECOPD is the standard of care as it has demonstrated benefits in several patient-centered outcomes. Current developments and research is related to the implementation and adjustment of NIV.

- 78 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Association Between Chronic Obstructive Pulmonary Disease and All-Cause Mortality After Aortic Valve Replacement for Aortic Stenosis

Rinchyenkhand Myagmardorj [1], Takeru Nabeta [1], Kensuke Hirasawa [1], Gurpreet K Singh [1], Frank van der Kley [1], Arend de Weger [2], Nina Ajmone Marsan [1], Jeroen J Bax [3], Victoria Delgado [4]

Abstract

Chronic obstructive pulmonary disease (COPD) and aortic stenosis (AS) are the most common diseases in which age plays a major role in the increase of their prevalence and when they co-exist, the outcomes prognosis worsens significantly. The aim of the present study was to evaluate the association between pulmonary functional parameters and all-cause mortality after aortic valve replacement (transcatheter or surgical). A total of 400 patients with severe AS and preoperative pulmonary functional test were retrospectively analyzed. Echocardiography and pulmonary functional parameters before aortic valve replacement were collected. COPD severity was defined according to criteria from the Society of Thoracic Surgeons. COPD was present in 128 patients (32%) with severe AS. Patients without COPD had smaller left ventricular (LV) mass and LV end-systolic volume and better LV function than the group with COPD. During a median follow-up of 32 months, 92 patients (23%) died. The survival rates were significantly lower in patients with moderate and severe COPD (log-rank p = 0.003). In the multivariable Cox regression analysis, any grade of COPD was associated with an approximately 2-fold increased risk of all-cause mortality (hazard ratio 1.933; 95% confidence interval 1.166 to 3.204; p = 0.011 for mild COPD and hazard ratio 2.028; 95% confidence interval 1.154 to 3.564; p = 0.014 for moderate or severe COPD). In addition to other clinical factors, any grade of COPD was associated with 2-fold increased risk of all-cause mortality.

Conflict of interest statement

Review

Scoping Review of Pulmonary Telemedicine Consults: Current Knowledge and Research Gaps

Brandon Li [1], Kari R Gillmeyer [2], Brianne Molloy-Paolillo [3], Varsha G Vimalananda [4][3], A Rani Elwy [3][5], Renda Soylemez Wiener [2][6], Seppo T Rinne [2][3]

Affiliations expand

- PMID: 36490386

- DOI: 10.1513/AnnalsATS.202205-404OC

Abstract

Rationale: Telemedicine consults, including video consults, telephone consults, electronic consults, and virtual conferences, may be particularly valuable in the management of chronic pulmonary diseases, but there is limited guidance on best practices for pulmonary telemedicine consults. **Objectives:** This scoping review aims to identify, characterize, and analyze gaps in the published literature on telemedicine consults health providers use to manage patients with chronic pulmonary diseases. **Methods:** We searched PubMed, Embase, Web of Science, and Cochrane Library from database origin through July 10, 2021. We included manuscripts describing applications of telemedicine consults for patients with chronic pulmonary diseases (asthma, chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, and interstitial lung disease). We restricted our review to full-length articles published in English about provider-led (as opposed to nurse-led) telemedicine consults. **Results:** Our search yielded 3,118 unique articles; 27 articles met the inclusion criteria. All telemedicine consult modalities and chronic pulmonary conditions were well represented in the review except for pulmonary hypertension and interstitial lung disease, which were represented by one and no articles, respectively. Most articles described a small, single-center, observational study that focused on the acceptability, feasibility, use, and/or clinical effectiveness of the telemedicine consult. Few studies had objectively measured clinical outcomes or included a comparator group, and none compared telemedicine consult modalities against one another. **Conclusions:** Our scoping review identified limited literature describing pulmonary telemedicine consults and highlighted several gaps in the literature that warrant increased attention. Providers treating chronic pulmonary diseases are left with limited guidance on best practices for telemedicine consults.

Keywords: chronic pulmonary diseases; telemedicine.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Heart Lung

- •

Exertional dyspnea responses to the Dyspnea Challenge in heart failure: Comparison to chronic obstructive pulmonary disease

Craig R Aitken [1], Glenn M Stewart [2], James R Walsh [3], Tanya Palmer [4], Lewis Adams [4], Surendran Sabapathy [5], Norman R Morris [2]

Affiliations expand

- PMID: 36455422

- DOI: 10.1016/j.hrtlng.2022.11.010

Abstract

Background: In heart failure (HF), exertional dyspnea is a common symptom, but validated field-based tests for its measurement are limited. The Dyspnea Challenge is a two-minute uphill treadmill walk designed to measure exertional dyspnea in cardiopulmonary disease.

Objectives: The purpose of this study was to establish the test-retest reliability of the Dyspnea Challenge in HF and to compare the exercise responses to a group with chronic obstructive pulmonary disease (COPD).

Methods: The study was an experimental, single-blind, randomized, multi-site project that recruited individuals with HF (New York Heart Association I-III) and COPD (Global Initiative for Chronic Obstructive Lung Disease II-IV). Participants completed two visits. On the first visit, participants performed two six-minute walk tests (6MWT), followed by two to three Dyspnea Challenges to calculate treadmill speed and gradient. At Visit Two, participants performed two separate Dyspnea Challenges, with one including measures of pulmonary gas exchange and central hemodynamics.

Results: Twenty-one individuals with HF (10 female; 66±11years; ejection fraction:45.3 ± 6.1%; six-minute distance(6MWD) 520 ± 97 m), and 25 COPD (11 female; 68 ± 10 yr; forced expiratory volume in 1 s:47.6 ± 11.5%; 6MWD: 430 ± 101 m). Intraclass correlation

coefficients demonstrated excellent test-retest reliability for HF (0.94, P<.01) and COPD (0.95, P<.01). While achieving similar end-exercise exertional dyspnea intensities (P=.60), the HF group walked at a higher average speed (4.2 ± 0.8 vs. 3.5 ± 0.8km·h⁻¹) and gradient (10.3 ± 2.8 vs. 9.6 ± 2.8%) and a greater oxygen uptake (P<.01) and ventilation (P<.01) than those with COPD. While achieving similar cardiac outputs (P=.98), stroke volumes (P=.97), and heart rates (P=.83), those with HF displayed a larger arteriovenous oxygen difference (P<.01), while those with COPD exhibited greater decreases in inspiratory capacity (P=.03), arterial oxygen saturation (P=.02), and breathing reserve (P<.01).

Conclusions: The Dyspnea Challenge is a reliable test-retest measure of exertional dyspnea in HF. Typical to their pathologies, HF seemed limited by an inadequate modulation of cardiac output, while ventilatory constraints hampered those with COPD.

Keywords: Activity; COPD; Dyspnea; Exercise; Exertional; HF; Physiology.

Conflict of interest statement

Conflicts of interest No author has any conflict of interest to report

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

ELSEVIER
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☐ 37

Observational Study

Heart Lung

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-
-

. 2023 Mar-Apr;58:91-97.

Respiratory and peripheral muscle strength influence recovery of exercise capacity after severe exacerbation of COPD? An observational prospective cohort study

Alessandro D Heubel [1], Erika Z Kabbach [1], Naiara T Leonardi [1], Nathany S Schafauser [1], Débora M O Kawakami [1], Anna Claudia Sentanin [1], Valéria A Pires Di Lorenzo [1], Audrey Borghi Silva [1], John R Hurst [2], Renata G Mendes [3]

Affiliations expand

- PMID: 36434827

- DOI: 10.1016/j.hrtlng.2022.11.009

Abstract

Background: Patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) have decreased exercise tolerance, which may persist for months. In this context, little is known about the associations between muscle strength and recovery of exercise capacity.

Objective: To assess whether respiratory and peripheral muscle strength influence recovery of exercise capacity in patients hospitalized due to AECOPD.

Methods: Twenty-seven AECOPD patients (aged 69 ± 7 years, 56% male) were included. The following assessments were performed within 24 to 72 h of hospital admission: (i) respiratory muscle strength, measured by maximal inspiratory and expiratory pressures (MIP and MEP); (ii) peripheral muscle strength, assessed by handgrip and quadriceps muscle strength; and (iii) exercise capacity, measured by 6-min walking distance (6MWD). The 6MWD was reassessed 30 days later to determine the recovery of exercise capacity.

Results: After 30 days, while 63% of the patients showed clinically important improvement in the 6MWD (recovery ≥ 30 m), 37% showed no change (recovery < 30 m). During hospital stay, the non-recovered group had lower quadriceps muscle strength compared to the recovered group (15 ± 5 vs. 22 ± 6 kgf; P = 0.006), with no significant difference for

MIP, MEP and handgrip strength. Only quadriceps muscle strength was associated with recovery of exercise capacity (r = 0.56; P = 0.003).

Conclusion: AECOPD patients with quadriceps muscle weakness during hospitalization have poor recovery of exercise capacity after 30 days. This finding suggests the importance of early rehabilitation to improve quadriceps strength and accelerate functional recovery after AECOPD.

Keywords: COPD; Exercise capacity; Hospitalization; Muscle strength.

Conflict of interest statement

Declarations of Competing Interest None.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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How Important is Spirometry for Identifying Patients with COPD Appropriate for Palliative Care?

[Allison V Lange](#) [1], [Anuj B Mehta](#) [2], [David B Bekelman](#) [3]

Affiliations expand

- PMID: 36423798

Abstract

Background: Providing palliative care to patients with chronic obstructive pulmonary disease (COPD) is a priority. Spirometry demonstrating airflow limitation is a diagnostic test for COPD and a common inclusion criterion for palliative care research. However, requiring spirometry with airflow limitation may exclude appropriate patients unable to complete spirometry, or patients with preserved-ratio impaired spirometry and symptoms or imaging consistent with COPD.

Measures: To determine differences in quality of life (QOL) and symptoms between patients with COPD identified based on International Classification of Diseases (ICD) codes and spirometry with airflow limitation compared to ICD codes only.

Intervention: Patients with COPD enrolled in a palliative care trial were included. Patients were at high risk of hospitalization and death and reported poor QOL. Baseline measures of QOL (Functional Assessment of Cancer Therapy-General (FACT-G), the Clinical COPD Questionnaire, and Quality of Life at the End of Life), and symptoms (Patient Health Questionnaire-8, Generalized Anxiety Disorder-7, fatigue, Insomnia Severity Index) were compared.

Outcomes: Two hundred eight patients with COPD were predominantly male, White, and average age was 68.4. Between patients with ICD codes and spirometry with airflow limitation compared to patients with ICD codes only, there were no significant differences in FACT-G (59.0 vs. 55.0, P = 0.33), other measures of QOL, or symptoms between groups.

Conclusion: These results imply that spirometry may not need to be a requirement for inclusion into palliative care research or clinical care for patients with poor quality of life and at high risk for adverse outcomes.

Keywords: COPD; clinical trial; palliative care; quality of life.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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The Impact of Wearing a Mask on Oxygenation and Hemodynamics in Patients with Mild to Moderate Chronic Obstructive Pulmonary Disease

Sang-Heon Kim[1], Ran Heo[1], Sun-Kyung Lee[1], Sang Won Lee[2], Hyekyung Seo[3], Hyukjae Kwon[1], Sung Jun Chung[1], Hyun Lee[1], Dong Won Park[1], Young-Hyo Lim[1], Jinho Shin[1], Jang Won Sohn[1], Ho Joo Yoon[1]

Affiliations expand

- PMID: 36416877

- DOI: 10.1513/AnnalsATS.202206-551RL

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Association between inpatient palliative care encounter and 30-day all-cause readmissions after index hospitalization for chronic obstructive pulmonary disease

Ali Yazdanyar [1], Ashley Vojtek [2], Sachin Gupta [3], Aditya Iyer [4], Alaynna C Kears [2], Kaitlyn Musco [2], Shuisen Li [5], Shadi Jarjous [6]

Affiliations expand

- PMID: 36410155

- DOI: 10.1016/j.hrtlng.2022.11.003

Abstract

Background: Studies exist on the association between inpatient Palliative Care Encounter (iPCE) and 30-day rehospitalization among cancer and several non-cancer conditions but limited in persons with Chronic Obstructive Pulmonary Disease (COPD).

Objective: To assess the association between an iPCE with the risk of 30-day rehospitalization after an index hospitalization for COPD.

Methods: We conducted a cross-sectional analysis of the Nationwide Readmissions Database (2010-2014). Index hospitalizations were defined as persons ≥ 18 years of age, discharge destinations of either Home/Routine, Home with Home Care, or a Facility, and an index hospitalization with Diagnosis Related Group of COPD. The International Classification of Diseases, 9th revision codes were used to extract comorbidities and a Palliative Care Encounter (V66.7).

Results: There were 3,163,889 index hospitalizations and iPCE occurred in 21,330 (0.67%). There were 558,059 (17.63%) with a 30-day rehospitalization. An iPCE was associated with a significantly lower adjusted odds of 30-day readmission (Odds Ratio [OR], 0.50; 95% Confidence Interval [CI], 0.46 to 0.54). By discharge destination, the odds of 30-day rehospitalization were for a discharged to a facility (OR, 0.37; 95% CI, 0.32 to 0.42), to home with home health (OR, 0.42; 95% CI, 0.37 to 0.47), and to home (OR, 0.98; 95% CI, 0.85 to 1.12) for those with relative to without iPCE.

Conclusion: Inpatient PCE was associated with a 50% lower relative odds of 30-day rehospitalization after an index hospitalization for COPD. This association varied by discharge destination being statistically significant among those with a discharge destination of a facility (63%) and home with home care (58%).

Conflict of interest statement

Declaration of Competing Interest Authors have no conflict of interest.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

ELSEVIER
FULL-TEXT ARTICLE

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Cite

Selective androgen receptor modulation for muscle weakness in chronic obstructive pulmonary disease: a randomised control trial

Divya Mohan [1], Harry Rossiter [2], Henrik Watz [3], Charles Fogarty [4], Rachael A Evans [5], William Man [6], Maggie Tabberer [7], Misba Beerahee [8], Subramanya Kumar [7], Helen Millns [8], Sebin Thomas [9], Ruth Tal-Singer [10], Alan J Russell [1], Marie Claire Holland [1], Chika Akinseye [8], David Neil [1], Michael I Polkey [11] [12]

Affiliations expand

- PMID: 36283827

- DOI: 10.1136/thorax-2021-218360

Abstract

Background: Selective androgen receptor modulators (SARMs) increase muscle mass via the androgen receptor. This phase 2A trial investigated the effects of a SARM, GSK2881078, in conjunction with exercise, on leg strength in patients with chronic obstructive pulmonary disease (COPD) and impaired physical function.

Methods: 47 postmenopausal women and 50 men with COPD (forced expiratory volume in 1 s 30%-65% predicted; short physical performance battery score: 3-11) were enrolled into a randomised double-blind, placebo control trial. Patients were randomised 1:1 to once daily placebo or oral GSK2881078 (females: 1.0 mg; males: 2.0 mg) for 13 weeks with a concurrent home-exercise programme, involving strength training and physical activity. Primary endpoints were change from baseline in leg strength at 90 days (one-repetition maximum; absolute (kg) and relative (% change)) and multiple safety outcomes. Secondary endpoints included lean body mass, physical function and patient-reported outcomes.

Results: GSK2881078 increased leg strength in men. The difference in adjusted mean change from baseline and adjusted mean percentage change from baseline between treatment and placebo were: for women, 8.0 kg (90% CI -2.5 to 18.4) and 5.2% (90% CI -4.7 to 15.0), respectively; for men, 11.8 kg (90% CI -0.5 to 24.0) and 7.0% (90% CI 0.5 to 13.6), respectively. Lean body mass increased, but no changes in patient-reported outcomes were observed. Reversible reductions in high-density lipoprotein-cholesterol and transient elevations in hepatic transaminases were the main treatment-related safety findings.

Conclusions: GSK2881078 was well tolerated and short-term treatment increased leg strength, when expressed as per cent predicted, in men with COPD more than physical training alone.

Trial registration number: [NCT03359473](NCT03359473).

Keywords: COPD pathology; COPD pharmacology; exercise; pulmonary rehabilitation.

Conflict of interest statement

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Associated dataexpand

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Editorial

Welcome to the Neighborhood: Tissue-Resident Lung Natural Killer Cells in Chronic Obstructive Pulmonary Disease and Viral Infections

Dawit T Mengistu [1], Christine M Freeman [1][2]

Affiliations expand

- PMID: 36255201

- DOI: [10.1164/rccm.202210-1867ED](#)

No abstract available

Comment on

- [Antiviral Responses of Tissue-resident CD49a+ Lung Natural Killer Cells Are Dysregulated in Chronic Obstructive Pulmonary Disease.](#)
  Cooper GE, Mayall J, Donovan C, Haw TJ, Budden KF, Hansbro NG, Blomme EE, Maes T, Kong CW, Horvat JC, Khakoo SI, Wilkinson TMA, Hansbro PM, Staples KJ.Am J Respir Crit Care Med. 2023 Mar 1;207(5):553-565. doi: 10.1164/rccm.202205-0848OC.PMID: 36170617

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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J Palliat Med

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. 2023 Mar;26(3):353-359.

doi: 10.1089/jpm.2022.0028. Epub 2022 Oct 12.

Patient–Centered Discussions About Disease Progression, Symptom, and Treatment Burden in Chronic Obstructive Pulmonary Disease Could

Facilitate the Integration of End-of-Life Discussions in the Disease Trajectory: Patient, Clinician, and Literature Perspectives: A Multimethod Approach

Nuno Tavares [1], Nikki Jarrett [1], Tom M A Wilkinson [2][3], Katherine J Hunt [4]

Affiliations expand

- PMID: 36251863

- DOI: 10.1089/jpm.2022.0028

Abstract

Background: Patients with chronic obstructive pulmonary disease (COPD) seldom discuss preferences for future care/treatments with clinicians. The lack of discussions prevents the delivery of care grounded on patient preferences. Instead, treatments become increasingly burdensome as disease progresses and patients approach the end of life. **Objective:** Identify current and best practice in initiating and conducting conversations about future and palliative care, by integrating data from multiple sources. **Design:** Multiphasic study where the findings of a systematic literature review and qualitative interviews were combined and synthesized using a triangulation protocol. **Setting/Participants:** Thirty-three patients with COPD and 14 clinicians from multiple backgrounds were recruited in the United Kingdom. **Results:** Clinicians' and patients' poor understanding about palliative care and COPD, difficulties in timing and initiating discussions, and service rationing were the main factors for late discussions. Divergent perspectives between patients and clinicians about palliative care discussions often prevented their start. Instead, early and gradual patient-centered discussions on treatment choices, symptom, and treatment burden were recommended by patients, clinicians, and the literature. Earlier patient-centered discussions may reduce their emotional impact and enable patients to participate fully, while enabling clinicians to provide timely and accurate information on illness progression and appropriate self-management techniques. **Conclusion:** Current approaches toward palliative care discussions in COPD do not guarantee that patients' preferences are met. Early and gradual patient-centered discussions may enable patients to fully express their care preferences as they evolve over time, while minimizing the impact of symptom and treatment burden.

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Lifetime spirometry patterns of obstruction and restriction, and their risk factors and outcomes: a prospective cohort study

Shyamali C Dharmage [1], Dinh S Bui [2], Eugene H Walters [3], Adrian J Lowe [2], Bruce Thompson [4], Gayan Bowatte [2], Paul Thomas [5], Judith Garcia-Aymerich [6], Debbie Jarvis [7], Garun S Hamilton [8], David P Johns [2], Peter Frith [9], Chamara V Senaratna [2], Nur S Idrose [2], Richard R Wood-Baker [10], John Hopper [2], Lyle Gurrin [2], Bircan Erbas [11], George R Washko [12], Rosa Faner [13], Alvar Agusti [14], Michael J Abramson [15], Caroline J Lodge [2], Jennifer L Perret [2]

Affiliations expand

Abstract

Background: Interest in lifetime lung function trajectories has increased in the context of emerging evidence that chronic obstructive pulmonary disease (COPD) can arise from multiple disadvantaged lung function pathways, including those that stem from poor lung function in childhood. To our knowledge, no previous study has investigated both obstructive and restrictive lifetime patterns concurrently, while accounting for potential overlaps between them. We aimed to investigate lifetime trajectories of the FEV_1/forced vital capacity (FVC) ratio, FVC, and their combinations, relate these combined trajectory groups to static lung volume and gas transfer measurements, and investigate both risk factors for and consequences of these combined trajectory groups.

Methods: Using z scores from spirometry measured at ages 7, 13, 18, 45, 50, and 53 years in the Tasmanian Longitudinal Health Study (n=2422), we identified six FEV_1/FVC ratio trajectories and five FVC trajectories via group-based trajectory modelling. Based on whether trajectories of the FEV_1/FVC ratio and FVC were low (ie, low from childhood or adulthood) or normal, four patterns of lifetime spirometry obstruction or restriction were identified and compared against static lung volumes and gas transfer. Childhood and adulthood characteristics and morbidities of these patterns were investigated.

Findings: The prevalence of the four lifetime spirometry patterns was as follows: low FEV_1/FVC ratio only, labelled as obstructive-only, 25·8%; low FVC only, labelled as restrictive-only, 10·5%; both low FEV_1/FVC ratio and low FVC, labelled as mixed, 3·5%; and neither low FEV_1/FVC ratio nor low FVC, labelled as reference, 60·2%. The prevalence of COPD at age 53 years was highest in the mixed pattern (31 [37%] of 84 individuals) followed by the obstructive-only pattern (135 [22%] of 626 individuals). Individuals with the mixed pattern also had the highest prevalence of parental asthma, childhood respiratory illnesses, adult asthma, and depression. Individuals with the restrictive-only pattern had lower total lung capacity and residual volume, and had the highest prevalence of childhood underweight, adult obesity, diabetes, cardiovascular conditions, hypertension, and obstructive sleep apnoea.

Interpretation: To our knowledge, this is the first study to characterise lifetime phenotypes of obstruction and restriction simultaneously using objective data-driven techniques and unique life course spirometry measures of FEV_1/FVC ratio and FVC from childhood to middle age. Mixed and obstructive-only patterns indicate those who might benefit from early COPD interventions. Those with the restrictive-only pattern had evidence of true lung restriction and were at increased risk of multimorbidity by middle age.

Funding: National Health and Medical Research Council of Australia, The University of Melbourne, Clifford Craig Medical Research Trust of Tasmania, The Victorian, Queensland & Tasmanian Asthma Foundations, The Royal Hobart Hospital, Helen MacPherson Smith Trust, and GlaxoSmithKline.

Conflict of interest statement

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The Six-minute Step Test as an Exercise Outcome in Chronic Obstructive Pulmonary Disease

Suhani Patel [1][2], Sarah E Jones [1], Jessica A Walsh [1], Ruth E Barker [1][3], Oliver Polgar [1], Matthew Maddocks [4], Nicholas S Hopkinson [2], Claire M Nolan [1][5], William D-C Man [1][2][4]

Affiliations expand

- PMID: 36240127

No abstract available

Randomized Controlled Trial

Chronic Obstructive Pulmonary Disease Patients With High Peripheral Blood Eosinophil Counts Have Better Predicted Improvement in 6MWD After Rehabilitation: A PRELIMINARY STUDY

Li-Li Shui [1], Ji-Jun Cai, Xiao-Qing Zhong, You-Lun Li, Mao-Rui He, Ya-Juan Chen

Affiliations expand

- PMID: 36223406

- DOI: 10.1097/HCR.0000000000000726

Abstract

Purpose: The objective of this investigation was to determine whether chronic obstructive pulmonary disease (COPD) patients with high blood eosinophil (EOS) counts had better improvement in 6-min walk test (6MWT) after pulmonary rehabilitation (PR).

Methods: Fifty COPD patients were randomly assigned to either the rehabilitation group (RG) or the control group (CG). Patients in the RG (8 wk PR + routine medication) and the CG (routine medication) were followed for 32 wk. According to the blood EOS level, the RG was divided into an EOS ≥ 200 cells/μL group and EOS < 200 cells/μL group. The 6MWT distance, Borg Scale, and COPD Assessment Test (CAT) were evaluated before intervention and 8 wk and 32 wk later.

Results: After the 8-wk intervention, 37 patients (19 RG/18 CG) completed the study. At 8-wk and 32-wk follow-up from baseline, a statistically significant difference was found between these two groups in the 6MWT, Borg Scale, and CAT. Compared with baseline, the 6MWT in the RG increased 49.1 ± 40.2 m (95% CI, 29.7-68.5, P < .001) at 8 wk and 60.8 ± 42.1 m (95% CI, 40.5-81.6, P < .001) at 32 wk. In addition, the improvement of 6MWT in the EOS ≥ 200 cells/μL RG group was higher than that in the EOS < 200 cells/μL group (40.1 ± 17.6 m, 95% CI, 36.8-43.4; P = .036) at 32-wk follow-up from baseline.

Conclusion: An 8-wk PR can improve the exercise capacity of COPD patients, and the benefits persistent for 24 wk. The improvement in the 6MWT was more significant in COPD patients with a high blood EOS count.

Conflict of interest statement

The authors declare no conflicts of interest.

- 41 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Wolters Kluwer

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Gender and Age as Determinants of Success of Pulmonary Rehabilitation in Individuals With Chronic Obstructive Pulmonary Disease

[Article in English, Spanish]

Roberto Maestri [1], Michele Vitacca [2], Mara Paneroni [3], Elisabetta Zampogna [4], Nicolino Ambrosino [5]

Affiliations expand

- PMID: 36192251

- DOI: 10.1016/j.arbres.2022.09.008

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

FULL TEXT AT
Archivos de Bronconeumología

Proceed to details

Antiviral Responses of Tissue-resident CD49a+ Lung Natural Killer Cells Are Dysregulated in Chronic Obstructive Pulmonary Disease

Grace E Cooper [1], Jemma Mayall [2], Chantal Donovan [2][3], Tatt J Haw [2], Kurtis F Budden [2], Nicole G Hansbro [3], Evy E Blomme [4], Tania Maes [4], Chia Wei Kong [1], Jay C Horvat [2], Salim I Khakoo [1], Tom M A Wilkinson [1][5][6], Philip M Hansbro [2][3], Karl J Staples [1][5][6]

Affiliations expand

- PMID: 36170617

- DOI: 10.1164/rccm.202205-0848OC

Abstract

Rationale: Tissue-resident natural killer (trNK) cells have been identified in numerous organs, but little is known about their functional contribution to respiratory immunity, in particular during chronic lung diseases such as chronic obstructive pulmonary disease (COPD). **Objectives:** To investigate the phenotype and antiviral responses of trNK cells in murine cigarette smoke-induced experimental COPD and in human lung parenchyma from COPD donors. **Methods:** Mice were exposed to cigarette smoke for 12 weeks to induce COPD-like lung disease. Lung trNK cell phenotypes and function were analyzed by flow cytometry in both murine and human disease with and without challenge with influenza A virus. **Measurements and Main Results:** In the mouse lung, CD49a+CD49b+EOMES+ and

CD49a$^+$CD49b$^-$EOMES^{lo} NK cell populations had a distinct phenotype compared with CD49a$^-$ circulating NK cells. CD49a$^+$ NK cells were more extensively altered earlier in disease onset than circulating NK cells, and increased proportions of CD49a$^+$ NK cells correlated with worsening disease in both murine and human COPD. Furthermore, the presence of lung disease delayed both circulating and trNK cell functional responses to influenza infection. CD49a$^+$ NK cells markedly increased their NKG2D, CD103, and CD69 expression in experimental COPD after influenza infection, and human CD49a$^+$ NK cells were hyperactive to *ex vivo* influenza infection in COPD donors. **Conclusions:** Collectively, these results demonstrate that trNK cell function is altered in cigarette smoke-induced disease and suggests that smoke exposure may aberrantly prime trNK cell responsiveness to viral infection. This may contribute to excess inflammation during viral exacerbations of COPD.

Keywords: COPD; human influenza; innate immunity; mucosal immunity.

Comment in

- Welcome to the Neighborhood: Tissue-Resident Lung Natural Killer Cells in Chronic Obstructive Pulmonary Disease and Viral Infections.
  Mengistu DT, Freeman CM.Am J Respir Crit Care Med. 2023 Mar 1;207(5):500-502. doi: 10.1164/rccm.202210-1867ED.PMID: 36255201 No abstract available.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

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A Hands-Free, Oral Positive Expiratory Pressure Device for Exertional Dyspnea and Desaturation in COPD

Muhammad Ahsan Zafar [1], Ashley Cattran [2], Rachel Baker [2], Roman Jandarov [3], Ralph J Panos [4]

Affiliations expand

No abstract available

Conflict of interest statement

Drs Zafar and Panos are the co-inventors of the o-PEP device and are the owners of PEP Buddy LLC. The University of Cincinnati Institutional Review Board has approved their involvement in this study. The remaining authors have disclosed no conflicts of interest.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Final Version
Respir Care

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Eur Heart J Qual Care Clin Outcomes

-

Atrial fibrillation and chronic obstructive pulmonary disease: diagnostic sequence and mortality risk

Peder E Warming [1], Rodrigue Garcia [1][2][3], Carl J Hansen [1], Sami O Simons [4], Christian Torp-Pedersen [5][6], Dominik Linz [7][8][9], Jacob Tfelt-Hansen [1][10]

Affiliations expand

- PMID: 36069895

- DOI: 10.1093/ehjqcco/qcac059

Abstract

Background and aims: Chronic obstructive pulmonary disease (COPD) is present in 13% of atrial fibrillation (AF) patients. In patients diagnosed with both AF and COPD, we aimed to assess overall mortality risk and its association with temporal sequence in AF and COPD diagnosis.

Methods: This nationwide study assessed all patients aged 18-85 years diagnosed with both COPD and AF between 1999 and 2018 in Denmark. Three groups were defined according to the temporal sequence of diagnosis: COPD diagnosed at least 6 months before AF (COPD-First), AF diagnosed at least 6 months before COPD (AF-First) and COPD, and AF diagnosed within a 6-months' time frame (AF~COPD).

Results: We included 62 806 patients (75.0 years; 56.5% males). After 5 years of follow-up, 31 494 (50.1%) died. Mortality was highest in the COPD-First group (COPD-First: 52.8%; AF-First: 46.0%; AF~COPD 50.6%). In a multivariable Cox-regression model adjusted for age, sex, type 2 diabetes, history of acute myocardial infarction, hypertension, heart failure, dyslipidemia, cancer, chronic kidney disease, and stroke, the AF~COPD group (HR 1.19, 95% CI 1.16-1.23; P < 0.001) and COPD-First group (HR 1.30, 95% CI 1.27-1.33; P < 0.001) had a higher risk of death compared with the AF-First group. A restricted cubic spline analysis showed that the earlier the COPD was diagnosed, the worse is the prognosis.

Conclusion: Patients with concomitant AF and COPD had a very poor prognosis and the temporal sequence in diagnosis was differentially associated with prognosis, where a COPD diagnosis preceding an AF diagnosis was accompanied with a higher mortality risk compared with a COPD diagnosis following an AF diagnosis.

Keywords: atrial fibrillation; chronic obstructive pulmonary disease; epidemiology.

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Review

The prevalence of comorbidity in the lung cancer screening population: A systematic review and meta-analysis

Anas Almatrafi [1][2], Owen Thomas [1], Matthew Callister [3], Rhian Gabe [4], Rebecca J Beeken [1][5], Richard Neal [1][6]

Abstract

Objective: Comorbidity is associated with adverse outcomes for all lung cancer patients, but its burden is less understood in the context of screening. This review synthesises the prevalence of comorbidities among lung cancer screening (LCS) candidates and summarises the clinical recommendations for screening comorbid individuals.

Methods: We searched MEDLINE, EMBASE, EBM Reviews, and CINAHL databases from January 1990 to February 2021. We included LCS studies that reported a prevalence of comorbidity, as a prevalence of a particular condition, or as a summary score. We also summarised LCS clinical guidelines that addressed comorbidity or frailty for LCS as a secondary objective for this review. Meta-analysis was used with inverse-variance weights obtained from a random-effects model to estimate the prevalence of selected comorbidities.

Results: We included 69 studies in the review; seven reported comorbidity summary scores, two reported performance status, 48 reported individual comorbidities, and 12 were clinical guideline papers. The meta-analysis of individual comorbidities resulted in an estimated prevalence of 35.2% for hypertension, 23.5% for history of chronic obstructive pulmonary disease (COPD) (10.7% for severe COPD), 16.6% for ischaemic heart disease (IHD), 13.1% for peripheral vascular disease (PVD), 12.9% for asthma, 12.5% for diabetes, 4.5% for bronchiectasis, 2.2% for stroke, and 0.5% for pulmonary fibrosis.

Conclusions: Comorbidities were highly prevalent in LCS populations and likely to be more prevalent than in other cancer screening programmes. Further research on the burden of comorbid disease and its impact on screening uptake and outcomes is needed. Identifying individuals with frailty and comorbidities who might not benefit from screening should become a priority in LCS research.

Keywords: Lung cancer; comorbidity; frailty; low-dose computed tomography; screening.

Conflict of interest statement

Declaration of conflicting interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

- 121 references
- 1 figure

Airflow obstruction and small airway dysfunction following pulmonary tuberculosis: a cross-sectional survey

Zhenzhen Xing [# 1 2], Tieying Sun [# 1], Jean-Paul Janssens [3], Di Chai [1], Weiming Liu [4], Yaqi Tong [1], Yuxia Wang [1], Yali Ma [1], Mingming Pan [1], Jia Cui [1], Chen Wang [5 6 7 8], YanFei Guo [9]

Affiliations expand

Abstract

Objectives: Pulmonary function impairment and chronic respiratory symptoms after tuberculosis are relatively common in low-income and middle-income countries. We aimed to estimate the impact of post-tuberculosis (post-TB) on pulmonary function.

Methods: This large cross-sectional, population-based study included subjects aged 15 years or older with technically acceptable postbronchodilator spirometry measurements. Post-TB was diagnosed on the basis of radiological evidence and/or medical history. Airflow obstruction was defined as a postbronchodilator forced expiratory volume in 1 s/forced vital capacity ratio below the lower limit of normal of Global Lung Function Initiative (GLI) lung function equations. Small airway dysfunction was diagnosed if at least two of the following indicators were less than 65% of predicted: maximal mid-expiratory flow, forced expiratory flow (FEF) 50% or FEF 75%.

Results: In this population sample (N=8680, mean age: 40.1 years), 610 (7.0% (95% CI 6.5 to 7.6) participants were post-TB. Post-TB subjects had more frequent respiratory symptoms (46.8% vs 28.3%). Among post-TB subjects, 130 (21.3% (95% CI 18.1 to 24.8)) had airflow obstruction; OR of airflow obstruction was significantly associated with post-TB after adjustment for other confounding factors (OR 1.31, 95% CI 1.05 to 1.62). Post-TB was also associated with small airway dysfunction (OR 1.28, 95% CI1.07 to 1.53), which was present in 297 (48.9% (95% CI 33.9 to 53.0)) post-TB subjects.

Conclusions: Our findings support existing knowledge that post-TB is positively associated with pulmonary function impairment and make for frequent respiratory symptoms. Post-TB should be considered as a potentially important cause of airflow obstruction and respiratory symptoms in patients originating from countries with a high burden of tuberculosis.

Keywords: COPD epidemiology; respiratory infection; tuberculosis.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Randomized Controlled Trial

Does inspiratory muscle training provide additional benefits during pulmonary rehabilitation in people with interstitial lung disease? A randomized control trial

Saima Zaki [1], Jamal Ali Moiz [1], Aqsa Mujaddadi [1], Mir Shad Ali [2], Deepak Talwar [3]

Affiliations expand

- PMID: 35001815

- DOI: 10.1080/09593985.2021.2024311

Abstract

Background: Interstitial lung disease (ILD) encompasses a diverse group of chronic lung conditions which is often characterized by inspiratory muscle weakness (IMW). Despite the

potential importance of inspiratory muscle dysfunction in ILD, the effect of inspiratory muscle training (IMT) added to pulmonary rehabilitation (PR) in ILD largely remains unknown.

Objective: The primary objective of the present study was to evaluate the benefits of IMT added to PR on inspiratory muscle strength and secondary objectives were to assess its effects on functional capacity, health-related quality of life (HRQoL), pulmonary function test (PFT) and dyspnea in ILD along with IMW.

Methods: Fifty-one participants were randomly allocated into two groups; PR + IMT (n = 26) or PR alone (n = 25). The primary outcome [maximal inspiratory pressure (PI_{max})] and secondary outcomes [6-min walk distance (6MWD), St. George's Respiratory Questionnaire (SGRQ), PFT and modified Medical Research Council dyspnea scale (mMRC)] were evaluated before and after the 8-weeks intervention. Independent t-test or Mann Whitney-U test was applied for between-group comparisons while for within-group comparison Wilcoxon's Sign Rank test or paired t test was performed.

Results: At the end of 8 weeks exercise intervention inspiratory muscle strength (PI_{max} + 11.10 cm H_2O, $p<$ .001), functional capacity (6MWD, + 47.90 m, $p=$ .001), HRQoL (SGRQ-total - 4 points, $p=$ .038) and dyspnea (mMRC dyspnea scale, -1.27, $p<$ .001) improved significantly in PR+IMT group alone.

Conclusion: Inclusion of IMT to PR may have superior benefits as compared to PR alone in ILD accompanied with IMW.

Keywords: Interstitial lung disease; inspiratory muscle training; inspiratory muscle weakness; pulmonary rehabilitation.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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ASTHMA

LMAN1 is a receptor for house dust mite allergens

[Madelyn H Miller](#) [1], [Lindsay G Swaby](#) [2], [Vanessa S Vailoces](#) [2], [Maggie LaFratta](#) [2], [Yuan Zhang](#) [3], [Xiang Zhu](#) [2], [Dorilyn J Hitchcock](#) [2], [Travis J Jewett](#) [2], [Bin Zhang](#) [3], [Justine T Tigno-Aranjuez](#) [4]

Affiliations expand

Abstract

Development of therapies with the potential to change the allergic asthmatic disease course will require the discovery of targets that play a central role during the initiation of an allergic response, such as those involved in the process of allergen recognition. We use a receptor glycocapture technique to screen for house dust mite (HDM) receptors and identify LMAN1 as a candidate. We verify the ability of LMAN1 to directly bind HDM allergens and demonstrate that LMAN1 is expressed on the surface of dendritic cells (DCs) and airway epithelial cells (AECs) in vivo. Overexpression of LMAN1 downregulates NF-κB signaling in response to inflammatory cytokines or HDM. HDM promotes binding of LMAN1 to the FcRγ and recruitment of SHP1. Last, peripheral DCs of asthmatic individuals show a significant reduction in the expression of LMAN1 compared with healthy controls. These findings have potential implications for the development of therapeutic interventions for atopic disease.

Keywords: CP: Immunology; ERGIC-53; LMAN1; allergen receptors; allergens; asthma; house dust mite.

Conflict of interest statement

Declaration of interests The authors declare no competing interests.
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☐   2

Examining pharmacists' anti-doping knowledge and skills in assisting athletes to avoid unintentional use of prohibited substances

Deborah H Greenbaum[1], Andrew J McLachlan[1], Rebecca H Roubin[1], Rebekah Moles[1], Betty B Chaar[1]

Affiliations expand

- PMID: 36869840

- DOI: 10.1093/ijpp/riad015

Abstract

Objectives: To explore the knowledge and skills of pharmacists practicing in Sydney, Australia, in preventing the use of prohibited medications by athletes.

Methods: Using a simulated-patient study design, the researcher (an athlete and pharmacy student herself) contacted 100 Sydney pharmacies by telephone requesting advice about taking a salbutamol inhaler (a WADA-prohibited substance with conditional

requirements), for exercise-induced asthma, following a set interview protocol. Data were assessed for both clinical and anti-doping advice appropriateness.

Key findings: Appropriate clinical advice was provided by 66% of pharmacists in the study, appropriate anti-doping advice was provided by 68%, and 52% provided appropriate advice across both aspects. Of the respondents, only 11% provided both clinical and anti-doping advice at a comprehensive level. Identification of accurate resources was made by 47% of pharmacists.

Conclusions: Whilst most participating pharmacists had the skills to deliver assistance regarding the use of prohibited substances in sports, many lacked core knowledge and resources to enable them to deliver comprehensive care to prevent harm and protect athlete-patients from anti-doping violations. A gap was identified regarding advising/counselling athletes, indicating the need for additional education in sport-related pharmacy. This education would need to be coupled with the incorporation of sport-related pharmacy into current practice guidelines to enable pharmacists to uphold their duty of care and for athletes to benefit from their medicines-related advice.

Keywords: anti-doping; athlete; pharmacist; prohibited substances; supplements.

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Food protein induced enterocolitis syndrome among children in northern

Sweden – a retrospective review 2004–2018

Magnus Öhlund [1], Sara Liljeholm [2], Åsa Strinnholm [1], Anna Winberg [1]

Affiliations expand

Abstract

Aim: To describe clinical presentation and development of tolerance among children with Food protein induced enterocolitis syndrome (FPIES) in a population in northern Sweden.

Methods: A retrospective review of medical records of children presenting with FPIES symptoms from January 1, 2004, to May 31, 2018.

Results: Sixty children (65% boys) with FPIES were included. The estimated incidence gradually increased to 0.45% in 2016-2017. The most common food triggers were cow's milk (40%), fish (37%), and oat (23%). Symptoms presented in 31 (60%) children before six months and in 57 (95%) before one year of age. The median age for FPIES diagnosis was 7 (range 3-134) months and for fish FPIES 13 (range 7-134) months. By three years of age, 67% of children with FPIES to milk and oat but none of the children with fish FPIES had developed tolerance. Allergic conditions like eczema and asthma were reported in 52% of the children.

Conclusion: The cumulative FPIES incidence was 0.45% in 2016-2017. Most children presented with symptoms before one year of age, but the diagnosis was often delayed, especially for FPIES to fish. Tolerance development occurred at an earlier age when FPIES was triggered by milk and oat compared to fish.

Keywords: Children; FPIES; Food protein induced enterocolitis syndrome; food allergy; tolerance development.

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Asthma and atopic dermatitis as risk factors for rheumatoid arthritis: a bidirectional mendelian randomization study

Chuiji Chen [1], Le Su [2], Wenhao Duan [3], Yansen Zheng [4], Dianzhong Zhang [1], Yucai Wang [5]

Affiliations expand

- PMID: 36869337

- DOI: 10.1186/s12920-023-01461-7

Abstract

Background: Previous observational studies have shown an association between asthma, atopic dermatitis (AD) and rheumatoid arthritis (RA). However, the bidirectional cause-effect chain between asthma and AD and RA has not been proven yet.

Methods: We performed bidirectional two-sample Mendelian randomization (TSMR) and selected single nucleotide polymorphisms (SNPs) associated with asthma, AD, and RA as instrumental variables. All of the SNPs were obtained from the latest genome-wide association study in Europeans. Inverse variance weighted (IVW) was the main method used in MR analysis. MR-Egger, weighted model, simple model, and weighted median were used for quality control. The robustness of the results was tested by sensitivity analysis.

Results: Asthma was found to be the largest effect size for RA susceptibility using the IVW method (OR, 1.35;95%CI, 1.13-1.60; P, 0.001), followed by AD (OR, 1.10;95%CI, 1.02-1.19; P, 0.019). In contrast, there was no causal relationship between RA and asthma (IVW: P =

0.673) or AD (IVW: P = 0.342). No pleiotropy or heterogeneity was found in the sensitivity analysis.

Conclusion: Findings from this study showed a causal relationship between genetic susceptibility to asthma or AD and increased risk of RA, but do not support a causal relationship between genetic susceptibility to RA and asthma or AD.

Keywords: Asthma; Atopic dermatitis; Genetics; Mendelian randomization; Rheumatoid arthritis.

- 54 references

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Editorial

Peripheral Blood Counts in Asthma Control: Is it Relevant?

Sheetal Agarwal [1], Kana Ram Jat [2]

Affiliations expand

- PMID: 36869276

No abstract available

- 5 references

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☐ 6

Review

Targeted Literature Review of the Burden of Respiratory Syncytial Infection among High–Risk and Elderly Patients in Asia Pacific Region

Daisuke Kurai [1], JoonYoung Song [2], Yhu-Chering Huang [3], Zhijun Jie [4], Petar Atanasov [5], Xiaobin Jiang [6], Luis Hernandez-Pastor [7], Tom Hsun-Wei Huang [8], SeongBeom Park [9], KyungHwa Lim [10], Peter C Richmond [11]

Affiliations expand

Abstract

Introduction: The burden of respiratory syncytial virus (RSV), which causes acute respiratory illness, is well recognized among the pediatric population but also imposes a significant risk to the elderly (age ≥ 60) and those with underlying comorbidities. The study aimed to review the most recent data on epidemiology and burden (clinical and economic) of RSV in the elderly/high-risk populations in China, Japan, South Korea, Taiwan, and Australia.

Methods: A targeted review was conducted of English, Japanese, Korean, and Chinese language articles published from 1 January 2010 to 7 October 2020 relevant for the purpose.

Results: A total of 881 studies were identified, and 41 were included. The median proportion of elderly patients with RSV in all adult patients with acute respiratory infection (ARI) or community acquired pneumonia was 79.78% (71.43-88.12%) in Japan, 48.00% (3.64-80.00%) in China, 41.67% (33.33-50.00%) in Taiwan, 38.61% in Australia, and 28.57% (22.76-33.33%) in South Korea. RSV was associated with a high clinical burden on those patients with comorbidities such as asthma and chronic obstructive pulmonary disease. In China, inpatients with ARI showed a significantly higher rate of RSV-related hospitalization than outpatients (13.22% versus 4.08%, $p < 0.01$). The median length of hospital stay among elderly patients with RSV was longest in Japan (30 days) and shortest in China (7 days). Mortality data varied by region with some studies reporting rates as high as 12.00% (9/75) in hospitalized elderly patients. Finally, data on the economic burden was only available for South Korea, with the median cost of a medical admission for an elderly patient with RSV being US dollar (USD) 2933.

Conclusion: RSV infection is a major source of disease burden among elderly patients, especially in regions with aging populations. It also complicates the management of those with underlying diseases. Appropriate prevention strategies are required to reduce the burden among the adult, especially the elderly, population. Data gaps regarding economic burden of RSV infection in the Asia Pacific region indicates the need for further research to increase our understanding on the burden of this disease in this region.

Keywords: Acute respiratory infection; Asia Pacific; Disease burden; Economic burden; Respiratory syncytial virus.

- 70 references

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Questionnaire for diagnosing asthma-COPD overlap in COPD: Development of ACO screening questionnaire (ACO-Q)

Yuki Suzuki[1], Hiroyuki Nagase[2], Hikaru Toyota[1], Sho Ohyatsu[3], Konomi Kobayashi[1], Yuri Takeshita[1], Yuuki Uehara[1], Saya Hattori[1], Mana Ishizuka[1], Hirokazu Sakasegawa[1], Michio Kuramochi[1], Tadashi Kohyama[3], Naoya Sugimoto[1]

Affiliations expand

- PMID: 36868950

- DOI: 10.1016/j.alit.2023.01.004

Abstract

Background: The considerable prevalence and worse outcomes of asthma-COPD overlap (ACO) in COPD have been reported, and optimal introduction of ICS is essential for ACO. However, diagnostic criteria for ACO consist of multiple laboratory tests, which is challenging during this COVID-19 era. The purpose of this study was to create a simple questionnaire to diagnose ACO in patients with COPD.

Methods: Among 100 COPD patients, 53 were diagnosed with ACO based on the Japanese Respiratory Society Guidelines for ACO. Firstly, 10 candidate questionnaire items were generated and further selected by a logistic regression model. An integer-based scoring system was generated based on the scaled estimates of items.

Results: Five items, namely a history of asthma, wheezing, dyspnea at rest, nocturnal awakening, and weather- or season-dependent symptoms, contributed significantly to the diagnosis of ACO in COPD. History of asthma was related to FeNO >35 ppb. Two points were assigned to history of asthma and 1 point to other items in the ACO screening questionnaire (ACO-Q), and the area under the receiver operating characteristic curve was 0.883 (95% CI: 0.806-0.933). The best cutoff point was 1 point, and the positive predictive value was 100% at a cutoff of 3 points or higher. The result was reproducible in the validation cohort of 53 patients with COPD.

Conclusions: A simple questionnaire, ACO-Q, was developed. Patients with scores ≥3 could be reasonably recommended to be treated as ACO, and additional laboratory testing would be recommended for patients with 1 and 2 points.

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Development of a patient-centred electronic review template to support self-management in primary care

[Kirstie McClatchey](#) [1], [Aimee Sheldon](#) [2], [Liz Steed](#) [3], [Jessica Sheringham](#) [4], [Francis Appiagyei](#) [5], [David Price](#) [4], [Victoria Hammersley](#) [2], [Stephanie Taylor](#) [3], [Hilary Pinnock](#) [2]

Affiliations expand

Abstract

Background: Electronic templates are frequently used in long-term condition reviews (e.g. asthma) to act as reminders and improve documentation, however, they can restrict patient-centred care and opportunities for patients to discuss concerns and self-management.

Aim: The IMPlementing IMProved Asthma self-management as RouTine (IMP^{2}ART) programme aimed to develop a patient-centred asthma review template that encourages supported self-management.

Design & setting: This was a mixed-methods study, which integrated qualitative and systematic review data, primary care Professional Advisory Group feedback, and qualitative data from clinician interviews.

Method: Aligned with the Medical Research Council complex intervention framework, a template was developed in three phases: 1) Development phase: qualitative exploration with clinicians and patients, a systematic review, and prototype template development; 2) Feasibility pilot phase: feedback from clinicians (n=7); 3) Pre-piloting phase: delivering the template within the IMP^{2}ART implementation strategy (incorporating the template with patient and professional resources) and eliciting clinician feedback (n=6).

Results: Template development was guided by the preliminary qualitative work and the systematic review. A prototype template was developed with an opening question to establish patient agendas, and a closing prompt to confirm agendas have been addressed and an asthma action plan provided. The feasibility pilot identified refinements needed, including focusing the opening question to asthma. Pre-piloting ensured integration with the IMP^{2}ART strategy.

Conclusion: Following the multi-stage development process, the implementation strategy including the asthma review template is now being tested in a cluster randomised controlled trial.

Keywords: Asthma.

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9

LEAPing into the void: Implementing population-level food allergy prevention by means of early introduction of allergenic solids

Christopher Warren [1], Sai R Nimmagadda [2]

Affiliations expand

- PMID: 36868722

- DOI: 10.1016/j.anai.2022.12.015

No abstract available

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Galectin-10 and our expanding knowledge of olfactory cleft cytokines in olfactory dysfunction

Julian S De La Chapa [1], Jose L Mattos [2]

Affiliations expand

- PMID: 36868721

- DOI: 10.1016/j.anai.2022.12.028

No abstract available

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Skin prick testing technique: Under pressure to improve?

Kevin M White[1]

Affiliations expand

- PMID: 36868720

- DOI: 10.1016/j.anai.2022.12.029

No abstract available

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Adult and pediatric food allergy: Identifying key differences

Stephanie Leeds [1], Mehr Mathew [1], Anna Nowak-Wegrzyn [2]

Affiliations expand

- PMID: 36868719

- DOI: 10.1016/j.anai.2023.01.002

No abstract available

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☐ 13

Early diagnostic BioMARKers in exacerbations of chronic obstructive

pulmonary disease: protocol of the exploratory, prospective, longitudinal, single-centre, observational MARKED study

Kiki Waeijen-Smit [1] [2], Antonio DiGiandomenico [3], Jessica Bonnell [3], Kristoffer Ostridge [4] [5], Ulf Gehrmann [4], Bret R Sellman [3], Tara Kenny [3], Sander van Kuijk [6], Daphne Peerlings [7], Martijn A Spruit [7] [2], Sami O Simons [2], Sarah Houben-Wilke [7], Frits M E Franssen [7] [2]

Affiliations expand

Abstract

Introduction: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) play a pivotal role in the burden and progressive course of chronic obstructive pulmonary disease (COPD). As such, disease management is predominantly based on the prevention of these episodes of acute worsening of respiratory symptoms. However, to date, personalised prediction and early and accurate diagnosis of AECOPD remain unsuccessful. Therefore, the current study was designed to explore which frequently measured biomarkers can predict an AECOPD and/or respiratory infection in patients with COPD. Moreover, the study aims to increase our understanding of the heterogeneity of AECOPD as well as the role of microbial composition and hostmicrobiome interactions to elucidate new disease biology in COPD.

Methods and analysis: The 'Early diagnostic BioMARKers in Exacerbations of COPD' study is an exploratory, prospective, longitudinal, single-centre, observational study with 8-week follow-up enrolling up to 150 patients with COPD admitted to inpatient pulmonary rehabilitation at Ciro (Horn, the Netherlands). Respiratory symptoms, vitals, spirometry and nasopharyngeal, venous blood, spontaneous sputum and stool samples will be frequently collected for exploratory biomarker analysis, longitudinal characterisation of AECOPD (ie, clinical, functional and microbial) and to identify host-microbiome interactions. Genomic sequencing will be performed to identify mutations associated with increased risk of AECOPD and microbial infections. Predictors of time-to-first AECOPD will be modelled using Cox proportional hazards' regression. Multiomic analyses will provide a novel integration tool to generate predictive models and testable hypotheses about disease causation and predictors of disease progression.

Ethics and dissemination: This protocol was approved by the Medical Research Ethics Committees United (MEC-U), Nieuwegein, the Netherlands (NL71364.100.19).

Trial registration number: [NCT05315674](#).

Keywords: BACTERIOLOGY; Chronic airways disease; Microbiology; Molecular diagnostics; Rehabilitation medicine; Thoracic medicine.

Conflict of interest statement

SUPPLEMENTARY INFO

Associated dataexpand

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J Allergy Clin Immunol Pract

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. 2023 Mar 1;S2213-2198(23)00227-1.

doi: 10.1016/j.jaip.2023.02.023. Online ahead of print.

[Poorer caregiver mental and social health is associated with worse](#)

respiratory outcomes in preschool children with recurrent wheezing

Anne M Fitzpatrick [1], Badiallo Diani [2], Dio Kavalieratos [3], Alison Corace [4], Carrie Mason [4], Morgan Van Dresser [4], Jocelyn R Grunwell [5]

Affiliations expand

Abstract

Background: Mental and social health in preschool caregivers has been inadequately studied but may influence respiratory symptom recognition and management.

Objective: This study identified preschool caregivers at highest risk for poor mental and social health outcomes based on patient-reported outcome measures. We hypothesized that caregivers with the poorest mental and social health would have worse quality of life and preschool children with more wheezing episodes.

Methods: Female caregivers (N=129) with a preschool child 12-59 months of age with recurrent wheezing and at least one exacerbation in the previous year completed eight validated patient-reported outcome measures of mental and social health. K-means cluster analysis was performed utilizing each instrument T-score. Caregiver/child dyads were followed for 6 months. Primary outcomes included caregiver quality of life and wheezing episodes in their preschool children.

Results: Three clusters of caregivers were identified ("low risk", n=38; "moderate risk", n=56; "high risk", n=35). The high risk cluster had the lowest life satisfaction, meaning and purpose and emotional support and the highest social isolation, depression, anger, perceived stress, and anxiety that persisted over six months. This cluster had the poorest quality of life and marked disparities in social determinants of health. Preschool children from high risk caregivers had more frequent respiratory symptoms and a higher occurrence of any wheezing episode, but lesser outpatient physician utilization for wheezing management.

Conclusion: Caregiver mental and social health is associated with respiratory outcomes in preschool children. Routine assessment of mental and social health in caregivers is warranted to promote health equity and improve wheezing outcomes in preschool children.

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Clinical Implications of Longitudinal Blood Eosinophil Counts in Patients With Severe Asthma

Eugene R Bleecker [1], Deborah A Meyers [2], Dean Billheimer [3], Huashi Li [2], Paul Newbold [4], Justin Kwiatek [5], Ian Hirsch [6], Rohit Katial [5], Xingnan Li [2]

Affiliations expand

- PMID: 36868471

- DOI: 10.1016/j.jaip.2023.02.020

Abstract

Background: The stability and variability of blood eosinophil counts (BECs) to phenotype patients with severe asthma is not fully understood.

Objective: This post hoc, longitudinal, pooled analysis of placebo-arm patients from 2 phase 3 studies evaluated the clinical implications of BEC stability and variability in moderate-to-severe asthma.

Methods: This analysis included patients from SIROCCO and CALIMA who received maintenance medium- to high-dosage inhaled corticosteroids plus long-acting β_2-agonists; 2:1 patients with BECs ≥300 and <300 cells/μL were enrolled. BECs were measured 6 times over 1 year in a centralized laboratory. Exacerbations, lung function, and Asthma Control Questionnaire 6 scores were documented across patients grouped by BEC (<300 or ≥300 cells/μL) and variability (<80% or ≥80% BECs below or above 300 cells/μL).

Results: Among 718 patients, 42.2% (n = 303) had predominantly high, 30.9% (n = 222) had predominantly low, and 26.9% (n = 193) had variable BECs. Prospective exacerbation rates (mean ± SD) were significantly greater in patients with predominantly high (1.39 ± 2.20) and variable (1.41 ± 2.09) BECs versus predominantly low (1.05 ± 1.66) BECs. Similar results were observed for the number of exacerbations while on placebo.

Conclusion: Although patients with variable BECs had intermittently high and low BECs, they experienced similar exacerbation rates to the predominantly high group, which were greater than those in the predominantly low group. A high BEC supports an eosinophilic phenotype in clinical settings without additional measurements, whereas a low BEC requires repeated measurements because it could reflect intermittently high or predominantly low BECs.

Keywords: Asthma exacerbations; Benralizumab; Blood eosinophil count; Blood eosinophil count variability; Eosinophilic inflammation; Eosinophils; Severe asthma.

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Shaoyao-Gancao-Tang regulates the T-helper-type 1/T-helper-type 2 ratio in the lung and gut and alters gut microbiota in rats with ovalbumin-induced asthma

[Rui He](#) [1], [Sihui Wang](#) [2], [Shengxi Yang](#) [3], [Renhui Liu](#) [4], [Nan Nan](#) [5], [Xuran Lu](#) [6], [Muxin Gong](#) [7], [Jing Li](#) [8]

Affiliations expand

Abstract

Ethnopharmacological relevance: Shaoyao-Gancao Tang (SGT) is a traditional Chinese medicine formulation. It has been used to treat kinds of pain and to alleviate asthma in clinic. However, the mechanism of action is not known.

Aim of the study: To investigate the anti-asthma effect of SGT involving modulation of the T-helper type 1 (Th1) Th1/Th2 ratio in the gut-lung axis and alteration of the gut microbiota (GM) in rats with ovalbumin (OVA)-induced asthma.

Materials and methods: The main constituents of SGT were analyzed by high-performance liquid chromatography (HPLC). A model of asthma was established in rats by OVA-induced allergen challenge. Rats suffering from asthma (RSAs) were treated with SGT (2.5, 5.0 and 10.0 g/kg), dexamethasone (1 mg/kg) or physiologic saline for 4 weeks. The level of immunoglobulin (Ig)E in bronchoalveolar lavage fluid (BALF) and serum was determined by enzyme-linked immunosorbent assay. Histology of lung and colon tissues was investigated using staining (hematoxylin and eosin and periodic acid-Schiff). The Th1/Th2 ratio and levels of cytokines (interferon (IFN)-γ and interleukin (IL)-4) in the lung and colon were detected by immunohistochemistry. The GM in fresh feces was analyzed by 16 S rRNA gene sequencing.

Results: Twelve main constituents (gallic acid, albiflorin, paeoniflorin, liquiritin apioside, liquiritin, benzoic acid, isoliquiritin apioside, isoliquiritin, liquiritigenin, glycyrrhizic acid, isoliquiritigenin and glycyrrhetinic acid) of SGT were simultaneously determined by HPLC. SGT treatment (5.0 and 10.0 g/kg) was found to reduce the IgE level (a vital marker of

hyper-responsiveness) in BALF and serum, improve typical morphological changes (inflammatory-cell infiltration and goblet cell metaplasia) in the lung and colon, alleviate airway remodeling (including bronchiostenosis and basement membrane-thickening) in the lung, significantly decrease the IL-4 level and increase the IFN-γ level in the lung and colon, which led to restoration of the IFN-γ/IL-4 ratio. The dysbiosis and dysfunction of GM in RSAs were modulated by SGT. The abundance of bacteria of the genera Ethanoligenens and Harryflintia was increased in RSAs and was decreased upon SGT treatment. The abundance of Family_XIII_AD3011_group was decreased in RSAs and increased upon SGT treatment. Moreover, SGT therapy increased the abundance of bacteria of the genera Ruminococcaceae_UCG-005 and Candidatus_Sacchrimonas, and decreased that of Ruminococcus_2 and Alistipes.

Conclusions: SGT ameliorated rats with OVA-induced asthma via regulation of the Th1/Th2 ratio in the lung and gut, and modulated the GM.

Keywords: Asthma; Glycyrrhiza uralensis Fish.; Gut microbiota; Gut–lung axis; Paeonia lactiflora Pall.; Th1/Th2 balance.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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☐ 17

Asthma and Carotid Artery Plaques

Juan Carlos Cardet [1], Natalia Weare-Regales [2], Richard F Lockey [3]

Affiliations expand

No abstract available

Keywords: C reactive protein; MESA; asthma subsets; cardiovascular disease; epidemiology; inflammation; inhaled corticosteroids; interleukin-6; phenotype; type 2 inflammation.

SUPPLEMENTARY INFO

Publication typesexpand

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Editorial

Trained Immunity in Allergic Asthma

Michael Wegmann [1]

Affiliations expand

No abstract available

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Efficacy and safety of garadacimab, a factor XIIa inhibitor for hereditary angioedema prevention (VANGUARD): a global, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

Timothy J Craig [1], Avner Reshef [2], H Henry Li [3], Joshua S Jacobs [4], Jonathan A Bernstein [5], Henriette Farkas [6], William H Yang [7], Erik S G Stroes [8], Isao Ohsawa [9], Raffi Tachdjian [10], Michael E Manning [11], William R Lumry [12], Inmaculada Martinez Saguer [13], Emel Aygören-Pürsün [14], Bruce

Ritchie [15], Gordon L Sussman [16], John Anderson [17], Kimito Kawahata [18], Yusuke Suzuki [19], Petra Staubach [20], Regina Treudler [21], Henrike Feuersenger [22], Fiona Glassman [23], Iris Jacobs [23], Markus Magerl [24]

Affiliations expand

Abstract

Background: Hereditary angioedema is a rare and potentially life-threatening genetic disease that is associated with kallikrein-kinin system dysregulation. Garadacimab (CSL312), a novel, fully-human monoclonal antibody that inhibits activated factor XII (FXIIa), is being studied for the prevention of hereditary angioedema attacks. The aim of this study was to evaluate the efficacy and safety of once-monthly subcutaneous administrations of garadacimab as prophylaxis for hereditary angioedema.

Methods: VANGUARD was a pivotal, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial that recruited patients (aged ≥12 years) with type I or type II hereditary angioedema across seven countries (Canada, Germany, Hungary, Israel, Japan, the Netherlands, and the USA). Eligible patients were randomly assigned (3:2) to receive garadacimab or placebo for 6 months (182 days) by an interactive response technology (IRT) system. Randomisation was stratified by age (≤17 years vs >17 years) and baseline attack rate (1 to <3 attacks per month vs ≥3 attacks per month) for the adult group. The randomisation list and code were kept by the IRT provider during the study, with no access by site staff and funding representatives. All patients and investigational site staff, and representatives from the funder (or their delegates) with direct interaction with the study sites or patients, were masked to treatment assignment in a double-blind fashion. Randomly assigned patients received a 400-mg loading dose of subcutaneous garadacimab as two 200-mg injections or volume-matched placebo on day 1 of the treatment period, followed by five additional self-administered (or caregiver-administered) monthly doses of 200-mg subcutaneous garadacimab or volume-matched placebo. The primary endpoint was the investigator-assessed time-normalised number of hereditary angioedema attacks (number of hereditary angioedema attacks per month) during the 6-month treatment period (day 1 to day 182). Safety was evaluated in patients who received at least one dose of garadacimab or placebo. The study is registered with the EU Clinical Trials Register, 2020-000570-25 and ClinicalTrials.gov, NCT04656418.

Findings: Between Jan 27, 2021, and June 7, 2022, we screened 80 patients, 76 of whom were eligible to enter the run-in period of the study. Of 65 eligible patients with type I or type II hereditary angioedema, 39 were randomly assigned to garadacimab and 26 to placebo. One patient was randomly assigned in error and did not enter the treatment

period (no dose of study drug received), resulting in 39 patients assigned to garadacimab and 25 patients assigned to placebo being included. 38 (59%) of 64 participants were female and 26 (41%) were male. 55 (86%) of 64 participants were White, six (9%) were Asian (Japanese), one (2%) was Black or African American, one (2%) was Native Hawaiian or Other Pacific Islander, and one (2%) was listed as other. During the 6-month treatment period (day 1 to day 182), the mean number of investigator-confirmed hereditary angioedema attacks per month was significantly lower in the garadacimab group (0·27, 95% CI 0·05 to 0·49) than in the placebo group (2·01, 1·44 to 2·57; p<0·0001), corresponding to a percentage difference in means of -87% (95% CI -96 to -58; p<0·0001). The median number of hereditary angioedema attacks per month was 0 (IQR 0·00-0·31) for garadacimab and 1·35 (1·00-3·20) for placebo. The most common treatment-emergent adverse events were upper-respiratory tract infections, nasopharyngitis, and headaches. FXIIa inhibition was not associated with an increased risk of bleeding or thromboembolic events.

Interpretation: Monthly garadacimab administration significantly reduced hereditary angioedema attacks in patients aged 12 years and older compared with placebo and had a favourable safety profile. Our results support the use of garadacimab as a potential prophylactic therapy for the treatment of hereditary angioedema in adolescents and adults.

Funding: CSL Behring.

Conflict of interest statement

Declaration of interests TJC is a speaker for Pharming, CSL Behring, Takeda, Fresenius Kabi, and Grifols; has received research and consultancy grants from CSL Behring, Takeda, BioCryst, Ionis, Spark, BioMarin, Fresenius Kabi, and Grifols; and is on the medical advisory board for the US Hereditary Angioedema Association, Director of ACARE Angioedema Center at Penn State University, Hershey, and on the Board of Directors for the American Academy of Allergy, Asthma, and Immunology. AR received research grants as a principal investigator, speaker, and advisor for CSL Behring, Takeda-Shire, BioCryst, Pharming, Pharvaris, Ionis, and Shulov Innovative Science. HHL is a speaker for Pharming, CSL Behring, Takeda, and BioCryst and has received research and consultancy grants from CSL Behring, Takeda, BioCryst, Ionis, BioMarin, Pharming, and Phavaris. JSJ is a speaker for Takeda-Shire, CSL Behring, Teva, AstraZeneca, GSK, Sanofi Genzyme, and Regeneron and has received research funding or consultancy fees from CSL Behring, Takeda-Shire, BioCryst, Novartis, Genentech, AstraZeneca, Allakos, Fresenius Kabi, GSK, and Regeneron. JAB is a consultant, principal investigator, and speaker for CSL Behring, Takeda-Shire, Pharming, and BioCryst; is a consultant or principal investigator for KalVista, Biomarin, and Ionis; and is a consultant for Astria, ONO Pharmaceutical, Pharvaris, and Cycle Pharmaceuticals. HFa received research grants from CSL Behring, Takeda, and Pharming; has served as an advisor for CSL Behring, Takeda, Pharming, KalVista, ONO Pharmaceutical,

and BioCryst; and has participated in clinical trials or registries for BioCryst, CSL Behring, Pharming, KalVista, Pharvaris, and Takeda. WHY has been a speaker and advisory board member and has received honoraria from CSL Behring, Takeda-Shire, Novartis, Sanofi Genzyme, and Merck; has received research grants from CSL Behring, Takeda-Shire, BioCryst, Pharming, Aimmune, DBV Technologies, Eli Lilly, Pharvaris, AstraZeneca, Novartis, GSK, Genentech-Roche, Amgen, Sanofi Genzyme, Regeneron, Galderma, AnaptysBio, Glenmark, ALK Pharma, Dermira, Ionis, and Celgene; serves as a medical advisor (volunteer) for HAE Canada, a patient organisation; and is a member of Angioedema Centers of Reference and Excellence. ESGS has received lecturing or advertising board fees from Amgen, Sanofi, Novartis, AstraZeneca, Esperion, Ionis-Akcea, and Merck, paid to their institution. IO has received honoraria or served as a consultant or participated in advisory boards for CSL Behring, Takeda-Shire, and Torii Pharmaceutical Company. RTa is a speaker for BioCryst, CSL Behring, Pharming, AstraZeneca, Sanofi-Regeneron, GSK, and Takeda; has served as a consultant for BioCryst, CSL Behring, KalVista, Pharming, and Takeda; and has received grants or research support from BioCryst, CSL Behring, Ionis, KalVista, Pharvaris, and Takeda. MEM is a speaker for CSL Behring, Takeda, Pharming, BioCryst, GSK, Amgen, Sanofi-Regeneron, AstraZeneca, Blueprint, and Genentech; has received research grants from CSL Behring, Takeda, Pharming, BioCryst, KalVista, Pharvaris, GSK, Novartis, Merck, and Allakos; and has been a consultant for CSL Behring, Takeda, Pharming, BioCryst, KalVista, and Cycle Pharmaceuticals. WRL is a speaker for CSL Behring, Pharming, AstraZeneca, Sanofi-Regeneron, GSK, and Takeda-Shire; has served as a consultant for BioCryst, BioMarin, CSL Behring, Fresenius Kabi, Intellia, KalVista, Pharming, Pharvaris, and Takeda-Shire; is a board member of the US Hereditary Angioedema Association Medical Advisory Board; and has received grants or research support from ALK Pharma, BioCryst, CSL Behring, Ionis, Gossamer, KalVista, Kedrion, Therapure, and Takeda-Shire. IMS has received honoraria, research funding, and travel grants from BioCryst, CSL Behring, Pharming, Octapharma, KalVista, and Takeda-Shire and has served as a consultant or participated in advisory boards for these companies. EA-P has received honoraria as a speaker or advisor or grant support or clinical trial investigator support from BioCryst, BioMarin Europe, Centogene, CSL Behring, KalVista, Pharming, Pharvaris, and Takeda-Shire. BR has been a speaker and advisory board member for CSL Behring and Takeda, but has not received personal reimbursement for these activities. BR has participated in multiple clinical trials involving investigational drugs for CSL Behring, Takeda, BioCryst, Dyax, and Pharming, but does not hold patents or investments with these companies or involving this product, and serves as a volunteer Medical Scientific Advisor to HAE Canada, a patient organisation. GLS has been an advisory board member for CSL Behring and has participated in clinical trials for investigational drugs for CSL Behring, Takeda, BioCryst, Dyax, Pharming, Pharvaris, and KalVista. JA is a speaker bureau member for CSL Behring, Pharming, BioCryst, and Takeda and has received consulting fees from; is a clinical trial investigator for BioCryst, CSL Behring, Pharming, Takeda, KalVista, Pharvaris, and BioMarin; and has received consulting fees from Cycle Pharmaceuticals. KK has been a clinical trial investigator for CSL Behring. YS has received speaker fees from Novartis, AstraZeneca, Takeda-Shire, and Torii Pharmaceutical Company and has been a clinical trial investigator for CSL Behring. PS has received honoraria, research funding, travel grants, or has served as

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Electroacupuncture-induced activation of GABAergic system alleviates airway inflammation in asthma model by suppressing TLR4/MyD88/NF-κB signaling pathway

Ruisong Gong [1], Xiaowen Liu [2], Jing Zhao [1]

Affiliations expand

- PMID: 36867547

Abstract

Background: Electroacupuncture (EA) has been shown to attenuate airway inflammation in asthmatic mice; however, the underlying mechanism is not fully understood. Studies have shown that EA can significantly increase the inhibitory neurotransmitter γ-aminobutyric acid (GABA) content in mice, and can also increase the expression level of GABA type A receptor (GABAAR). Furthermore, activating GABAAR may relieve inflammation in asthma by suppressing toll-like receptor 4 (TLR4)/myeloid differentiation factor 88 (MyD88)/nuclear factor-kappa B (NF-κB) signaling pathway. Therefore, this study aimed to investigate the role of GABAergic system and TLR4/MyD88/NF-κB signaling pathway in asthmatic mice treated with EA.

Methods: A mouse model of asthma was established, and a series of methods including Western blot and histological staining assessment were employed to detect the level of GABA, and expressions of GABAAR and TLR4/MyD88/NF-κB in lung tissue. In addition, GABAAR antagonist was used to further validate the role and mechanism of GABAergic system in mediating the therapeutic effect of EA in asthma.

Results: The mouse model of asthma was established successfully, and EA was verified to alleviate airway inflammation in asthmatic mice. The release of GABA and the expression of GABAAR were significantly increased in asthmatic mice treated with EA compared with untreated asthmatic mice ($P < 0.01$), and the TLR4/MyD88/NF-κB signaling pathway was down-regulated. Moreover, inhibition of GABAAR attenuated the beneficial effects of EA in asthma, including the regulation of airway resistance and inflammation, as well as the inhibitory effects on TLR4/MyD88/NF-κB signaling pathway.

Conclusion: Our findings suggest that GABAergic system may be involved in mediating the therapeutic effect of EA in asthma, possibly by suppressing the TLR4/MyD88/NF-κB signaling pathway.

- 47 references

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Trends and Rural–Urban Differences in the Initial Prescription of Low-Value Inhaled Corticosteroids among US Veterans with COPD

Kevin I Duan[1], Lucas M Donovan[2][3], Laura J Spece[4], Laura C Feemster[5][6], Alexander D Bryant[7], Robert Plumley[8], Margaret P Collins[9], David H Au[10]

Affiliations expand

Abstract

Rationale: Guidelines recommend inhaled corticosteroids (ICS) for patients with chronic obstructive pulmonary disease (COPD) and select indications, including asthma history, high exacerbation risk, or high serum eosinophils. ICS are commonly prescribed outside of these indications despite evidence of harm. We defined "low-value" ICS prescription as receipt of an ICS without evidence of a guideline-recommended indication. ICS prescription patterns are not well characterized and could inform health system interventions to reduce low-value practices.

Objective: To evaluate the national trends in initial low-value ICS prescriptions in the Department of Veterans Affairs and determine whether rural-urban differences in low-value ICS prescribing exist.

Methods: We performed a cross-sectional study between January 4, 2010 and December 31, 2018, identifying Veterans with COPD and who were new users of inhaler therapy. We defined low-value ICS as prescription in patients with (1) no asthma, (2) low risk of future exacerbation (GOLD groups A or B), and (3) serum eosinophils <300 cells/microliter. We performed multivariable logistic regression to evaluate trends in low-value ICS prescription

over time, adjusting for potential confounders. We performed fixed effects logistic regression to assess rural-urban prescribing patterns.

Results: We identified a total of 131,009 Veterans with COPD starting inhaler therapy, of which 57,472 (44%) were prescribed low-value ICS as initial therapy. From 2010 to 2018, the probability of receiving low-value ICS as initial therapy increased by 0.42 percentage points per year (95% CI 0.31 - 0.53). Compared to urban residence, rural residence was associated with a 2.5 percentage point (95% CI 1.9 - 3.1) higher probability of receiving low-value ICS as initial therapy.

Conclusions: The prescription of low-value ICS as initial therapy is common and increasing slightly over time for both rural and urban Veterans. Given the widespread and persistent nature of low-value ICS prescribing, health system leaders should consider system-wide approaches to address this low-value prescribing practice.

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One-Year Adverse Outcomes Among US Adults With Post-COVID-19 Condition vs Those Without COVID-19 in a Large Commercial Insurance Database

Andrea DeVries [1], Sonali Shambhu [1], Sue Sloop [1], J Marc Overhage [1]

Affiliations expand

- PMID: 36867420

Abstract

Importance: Many individuals experience ongoing symptoms following the onset of COVID-19, characterized as postacute sequelae of SARS-CoV-2 or post-COVID-19 condition (PCC). Less is known about the long-term outcomes for these individuals.

Objective: To quantify 1-year outcomes among individuals meeting a PCC definition compared with a control group of individuals without COVID-19.

Design, setting, and participants: This case-control study with a propensity score-matched control group included members of commercial health plans and used national insurance claims data enhanced with laboratory results and mortality data from the Social Security Administration's Death Master File and Datavant Flatiron data. The study sample consisted of adults meeting a claims-based definition for PCC with a 2:1 matched control cohort of individuals with no evidence of COVID-19 during the time period of April 1, 2020, to July 31, 2021.

Exposures: Individuals experiencing postacute sequelae of SARS-CoV-2 using a Centers for Disease Control and Prevention-based definition.

Main outcomes and measures: Adverse outcomes, including cardiovascular and respiratory outcomes and mortality, for individuals with PCC and controls assessed over a 12-month period.

Results: The study population included 13 435 individuals with PCC and 26 870 individuals with no evidence of COVID-19 (mean [SD] age, 51 [15.1] years; 58.4% female). During follow-up, the PCC cohort experienced increased health care utilization for a wide range of adverse outcomes: cardiac arrhythmias (relative risk [RR], 2.35; 95% CI, 2.26-2.45), pulmonary embolism (RR, 3.64; 95% CI, 3.23-3.92), ischemic stroke (RR, 2.17; 95% CI, 1.98-2.52), coronary artery disease (RR, 1.78; 95% CI, 1.70-1.88), heart failure (RR, 1.97; 95% CI, 1.84-2.10), chronic obstructive pulmonary disease (RR, 1.94; 95% CI, 1.88-2.00), and asthma (RR, 1.95; 95% CI, 1.86-2.03). The PCC cohort also experienced increased mortality, as 2.8% of individuals with PCC vs 1.2% of controls died, implying an excess death rate of 16.4 per 1000 individuals.

Conclusions and relevance: This case-control study leveraged a large commercial insurance database and found increased rates of adverse outcomes over a 1-year period for a PCC cohort surviving the acute phase of illness. The results indicate a need for continued monitoring for at-risk individuals, particularly in the area of cardiovascular and pulmonary management.

Screening for asthma in preschool children with sickle cell disease

Kok Hoe Chan [1], James M Stark [2], Ricardo A Mosquera [2], Deborah L Brown [2], Neethu Menon [2], Trinh T Nguyen [3], Aravind Yadav [2]

Affiliations expand

- PMID: 36867136

- DOI: 10.1080/02770903.2023.2187305

Abstract

Background: Asthma in preschool children is poorly defined, proving to be a challenge for early detection. The Breathmobile Case Identification Survey (BCIS) has been shown to be a feasible screening tool in older SCD children and could be effective in younger children. We attempted to validate the BCIS as an asthma screening tool in preschool children with SCD.

Methods: This is a prospective, single-center study of 50 children aged 2-5 years with SCD. BCIS was administered to all patients and a pulmonologist blinded to the results evaluated patients for asthma. Demographic, clinical and laboratory data were obtained to assess risk factors for asthma and acute chest syndrome in this population.

Results: Asthma prevalence (n = 3/50; 6%) was lower than atopic dermatitis (20%) and allergic rhinitis (32%). Sensitivity (100%), specificity (85%), positive predictive value (30%) and negative predictive value (100%) of the BCIS were high. Clinical demographics, atopic dermatitis, allergic rhinitis, asthma, viral respiratory infection, hematology parameters, sickle hemoglobin subtype, tobacco smoke exposure and hydroxyurea were not different between patients with or without history of ACS, although eosinophil was significantly lower in the ACS group (p = 0.0093). All those with asthma had ACS, known viral respiratory infection resulting in hospitalization (3 RSV and 1 influenza), and HbSS (homozygous Hemoglobin SS) subtype.

Conclusion: The BCIS is an effective asthma screening tool in preschool children with SCD. Asthma prevalence in young children with SCD is low. Previously known ACS risk factors were not seen, possibly from the beneficial effects of early life initiation of hydroxyurea.

Keywords: Acute chest syndrome; RSV; allergic rhinitis; asthma; atopic dermatitis; eosinophils; hydroxyurea; screening; sickle cell disease.

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Ocular manifestations of common pulmonary diseases – A narrative review

Mamta Singh [1], Kunal Deokar [2], Bibhuti Prassn Sinha [3], Monika Keena [4], Govind Desai [5]

Affiliations expand

- PMID: 36867059

Abstract

Ocular involvement can be a comorbidity of several pulmonary disorders. A knowledge of these manifestations is essential for early diagnosis and treatment. Hence, we aimed to review the common ocular manifestations of Asthma, COPD, sarcoidosis, obstructive sleep apnea and lung cancer. The ocular manifestations of bronchial asthma include allergic keratoconjunctivitis and dry eye. The inhaled corticosteroids used in the management of asthma can lead to cataract formation. COPD is associated with ocular microvascular changes due to chronic hypoxia and spill over of systemic inflammation into the eyes. However, its clinical significance is yet to be known. Ocular involvement is very common in sarcoidosis, seen in 20% of cases of pulmonary sarcoidosis. It can involve almost any anatomical structure of the eye. Studies have shown the association of obstructive sleep apnea (OSA) with floppy eye syndrome, glaucoma, nonarteritic anterior ischemic optic neuropathy, keratoconus, retinal vein occlusion and central serous retinopathy. However, though association has been established, causality remains to be proven. The effect of positive airway pressure (PAP) therapy used in the treatment of OSA on the above ocular conditions is yet to be known. The PAP therapy can itself lead to irritation and dry eyes. Lung cancer can involve the eyes by direct invasion of nerves, ocular metastasis or as a part of paraneoplastic syndrome. The purpose of this narrative review is to raise awareness about the association between ocular and pulmonary disorders to facilitate early detection and treatment of these conditions.

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Allergy

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. 2023 Mar 3.

Factors associated with suboptimal response to monoclonal antibodies in severe asthma

Luis Pérez de Llano [1], Nuria Marina Malanda [2], Isabel Urrutia [3], Eva Martínez-Moragón [4], José Antonio Gullón-Blanco [5], Rocío Díaz-Campos [6], Mariana Muñoz Esquerre [7], Habernau Mena Alicia [8], Borja G Cosío [9], Carolina Cisneros [10], Francisco Javier Lázaro Polo [11], Daniel Laorden [12], David Dacal Rivas [1]

Affiliations expand

- PMID: 36866939

- DOI: [10.1111/all.15693](10.1111/all.15693)

No abstract available

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Postoperative Polyp Scale (POPS): Development of a New Sinonasal Polyp Grading Scale

[Arthur W Wu](#) [1] [2], [Akaber M Halawi](#) [1] [3], [Elisa A Illing](#) [1] [4], [Dennis M Tang](#) [1] [2], [Philip G Chen](#) [1] [5], [Edward C Kuan](#) [1] [6], [Jonathan Y Ting](#) [1] [4], [Daniel A Norez](#) [7], [Stacey A Kim](#) [8], [Dhruv Sharma](#) [1] [4], [Douglas D Reh](#) [1] [9], [Sanjeet V Rangarajan](#) [1] [10], [Kent K Lam](#) [1] [11], [Randall A Ow](#) [1] [12], [J Wesley Sublett](#) [1] [13], [Thomas S Higgins](#) [1] [14] [15]

Affiliations expand

Abstract

Objective: Commonly used endoscopic grading scales, such as the nasal polyp scale, inadequately describe the degree of polyposis found postoperatively in the paranasal sinus cavities. The purpose of this study was to create a novel grading system that more accurately characterizes polyp recurrence in postoperative sinus cavities, the Postoperative Polyp Scale (POPS).

Methods: A modified Delphi method was utilized to establish the POPS using consensus opinion among 13 general otolaryngologists, rhinologists, and allergists. Postoperative endoscopy videos from 50 patients with chronic rhinosinusitis with nasal polyps were reviewed by 7 fellowship-trained rhinologists and scored according to the POPS. Videos were rated again 1 month later by the same reviewers, and scores were assessed for test-retest and inter-rater reliability.

Results: Overall inter-rater reliability for the first and second reviews of the 52 videos was $K_f = 0.49$ (95% CI 0.42-0.57) and $K_f = 0.50$ (95% CI 0.42-0.57) for the POPS. Intra-rater reliability showed near-perfect test-retest reliability for the POPS with $K_f = 0.80$ (95% CI 0.76-0.84).

Conclusion: The POPS is an easy-to-use, reliable, and novel objective endoscopic grading scale that more accurately describes polyp recurrence in the postoperative state which will be useful in the future for measuring the efficacy of various medical and surgical interventions.

Level of evidence: 5 Laryngoscope, 2023.

Keywords: chronic rhinosinusitis; endoscopic grading; endoscopic sinus surgery; nasal polyps; outcomes.

- [16 references](#)

Total Reactive Isocyanate Group (TRIG) Measurement: A Commentary

Glen McConnachie[1], Paul Johnson[1]

Affiliations expand

- PMID: 36866423

- DOI: 10.1093/annweh/wxad007

Abstract

Exposure to airborne isocyanates has, for decades, been a leading cause of occupational asthma. As respiratory sensitizers, isocyanates can induce allergic respiratory diseases with symptoms persisting even without further exposure. As this cause of occupational asthma is recognized it should be almost entirely preventable. In several countries isocyanates are assigned occupational exposure limits based on the total of reactive isocyanate groups (TRIG). The measurement of TRIG has some significant advantages over the measurement of individual isocyanate compounds. This exposure metric is explicit, simplifying calculations, and comparisons across published data. It reduces the risk of underestimating exposure by 'missing' important isocyanate compounds that may be present but are not the target analytes. It allows for quantification of exposure to complex mixtures of isocyanates, di-isocyanates monomers, prepolymers, polyisocyanates, oligomers, and/or intermediate forms. This is becoming increasingly important as more complex isocyanate products are being used in the workplace. There are many methods and techniques for

measuring air concentrations/potential exposure to isocyanates. Several established methods have been standardized and published as International Organization for Standardization (ISO) methods. While some may be applied directly for determination of TRIG, others (developed for determination of individual isocyanates), require modification. This commentary aims to highlight the relative merits and limitations of those methods capable of determining TRIG and also considers potential future developments.

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Interventions to enhance medication adherence in pregnancy– a systematic review

Anna Davies [1], Sadie Mullin [2], Sarah Chapman [3], Katie Barnard [4], Danya Bakhbakhi [2], Rachel Ion [4], Francesca Neuberger [4], Judith Standing [4], Abi Merriel [2 5], Abigail Fraser [# 5 6], Christy Burden [# 2]

Affiliations expand

- PMID: 36864375

- PMCID: PMC9979410

Abstract

Background: Sub-optimal medication adherence in pregnant women with chronic disease and pregnancy-related indications has the potential to adversely affect maternal and perinatal outcomes. Adherence to appropriate medications is advocated during and when planning pregnancy to reduce risk of adverse perinatal outcomes relating to chronic disease and pregnancy-related indications. We aimed to systematically identify effective interventions to promote medication adherence in women who are pregnant or planning to conceive and impact on perinatal, maternal disease-related and adherence outcomes.

Methods: Six bibliographic databases and two trial registries were searched from inception to 28th April 2022. We included quantitative studies evaluating medication adherence interventions in pregnant women and women planning pregnancy. Two reviewers selected studies and extracted data on study characteristics, outcomes, effectiveness, intervention description (TIDieR) and risk of bias (EPOC). Narrative synthesis was performed due to study population, intervention and outcome heterogeneity.

Results: Of 5614 citations, 13 were included. Five were RCTs, and eight non-randomised comparative studies. Participants had asthma (n = 2), HIV (n = 6), inflammatory bowel disease (IBD; n = 2), diabetes (n = 2) and risk of pre-eclampsia (n = 1). Interventions included education +/- counselling, financial incentives, text messaging, action plans, structured discussion and psychosocial support. One RCT found an effect of the tested intervention on self-reported antiretroviral adherence but not objective adherence. Clinical outcomes were not evaluated. Seven non-randomised comparative studies found an association between the tested intervention and at least one outcome of interest: four found an association between receiving the intervention and both improved clinical or perinatal outcomes and adherence in women with IBD, gestational diabetes mellitus (GDM), and asthma. One study in women with IBD reported an association between receiving the intervention and maternal outcomes but not for self-reported adherence. Two studies measured only adherence outcomes and reported an association between receiving the intervention and self-reported and/or objective adherence in women with HIV and risk of pre-eclampsia. All studies had high or unclear risk of bias. Intervention reporting was adequate for replication in two studies according to the TIDieR checklist.

Conclusions: There is a need for high-quality RCTs reporting replicable interventions to evaluate medication adherence interventions in pregnant women and those planning pregnancy. These should assess both clinical and adherence outcomes.

Keywords: Adherence; Chronic disease; Maternal medicine; Medication; Perinatal outcomes; Systematic review.

Conflict of interest statement

The authors declare they have no competing interests.

- 60 references
- 2 figures

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Cluster analysis of plasma cytokines identifies two unique endotypes of children with asthma in the pediatric intensive care unit

Kirsten A Cottrill [1], Milad G Rad [2], Michael J Ripple [1][3], Susan T Stephenson [1], Ahmad F Mohammad [1], Mallory Tidwell [3], Rishikesan Kamaleswaran [1][2], Anne M Fitzpatrick [1][3], Jocelyn R Grunwell [4][5]

Affiliations expand

- PMID: 36864187

- PMCID: PMC9978291

Abstract

Children with life-threatening asthma exacerbations who are admitted to a pediatric intensive care unit (PICU) are a heterogeneous group with poorly studied inflammatory features. We hypothesized that distinct clusters of children with asthma in a PICU would be identified based on differences in plasma cytokine levels and that these clusters would have differing underlying inflammation and asthma outcomes within 1 year. Plasma cytokines and differential gene expression were measured in neutrophils isolated from children admitted to a PICU for asthma. Participants were clustered by differential plasma cytokine abundance. Gene expression differences were compared by cluster and pathway over-representation analysis was performed. We identified two clusters in 69 children with no clinical differences. Cluster 1 (n = 41) had higher cytokines compared to Cluster 2 (n = 28). Cluster 2 had a hazard ratio of 2.71 (95% CI 1.11-6.64) compared to Cluster 1 for time to subsequent exacerbation. Gene expression pathways that differed by cluster included interleukin-10 signaling; nucleotide-binding domain, leucine rich repeat containing receptor (NLR signaling); and toll-like receptor (TLR) signaling. These observations suggest that a subset of children may have a unique pattern of inflammation during PICU hospitalization that might require alternative treatment approaches.

Conflict of interest statement

The authors declare no competing interests.

- 43 references
- 4 figures

SUPPLEMENTARY INFO

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Editorial

ICS/formoterol maintenance and reliever therapy: how far beyond asthma?

Richard Beasley [1], Pepa Bruce [2], Lee Hatter [2]

Affiliations expand

- PMID: 36863775

- DOI: 10.1136/thorax-2022-219979

No abstract available

Conflict of interest statement

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Understanding the healthcare providers' perspective for bringing the assessment of burden of chronic conditions tool to practice: a protocol for an implementation study

[Danny Claessens](#)[1], [Marcia Vervloet](#)[2], [Esther Adriana Boudewijns](#)[3], [Lotte C E M Keijsers](#)[4], [Annerika H M Gidding-Slok](#)[3], [Onno C P van Schayck](#)[3], [Liset van Dijk](#)[2 5]

Affiliations expand

- PMID: 36863741

- DOI: [10.1136/bmjopen-2022-068603](#)

Abstract

Introduction: The Assessment of Burden of Chronic Conditions (ABCC) tool is developed and validated to support and facilitate a personalised approach to care for people with chronic conditions. The benefit of using the ABCC-tool greatly depends on how it is implemented. To enable a deeper understanding of when, how and by whom the ABCC-tool is used, this study protocol describes the design of an implementation study in which

the context, experiences and implementation process of the ABCC-tool by primary care healthcare providers (HCPs) in the Netherlands will be investigated.

Methods and analysis: This protocol describes an implementation study alongside an effectiveness trial, in which the ABCC-tool is evaluated in general practices. The implementation strategy of the tool in the trial confines to providing written information and an instruction video explaining the technical use of the ABCC-tool. The outcomes include a description of: (1) the barriers and facilitators of HCPs for implementation of the ABCC-tool, guided by the Consolidated Framework for Implementation Research (CFIR) and (2) the implementation outcomes guided by the Reach-Effect-Adoption-Implementation-Maintenance (RE-AIM) framework Carroll's fidelity framework. All outcomes will be gathered through individual semistructured interviews throughout 12 months of use. Interviews will be audiorecorded and transcribed. Transcripts will be analysed using content analysis for identifying barriers and facilitators (based on CFIR) and thematic analyses of HCPs' experiences (based on the RE-AIM and the fidelity frameworks).

Ethics and dissemination: The presented study was approved by the Medical Ethics Committee of Zuyderland Hospital, Heerlen (METCZ20180131). Written informed consent is mandatory prior to participation in the study. The results from the study in this protocol will be disseminated through publication in peer-reviewed scientific journals and conference presentations.

Conflict of interest statement

Competing interests: None declared.

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Respirology

[Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand](#)

[Anne B Chang](#) [1][2][3], [Scott C Bell](#) [4][5][6], [Catherine A Byrnes](#) [7][8], [Paul Dawkins](#) [9][10], [Anne E Holland](#) [11][12][13], [Emma Kennedy](#) [14][15][16], [Paul T King](#) [17], [Pamela Laird](#) [18][19][20], [Sarah Mooney](#) [9][21], [Lucy Morgan](#) [22], [Marianne Parsons](#) [23], [Betty Poot](#) [24][25], [Maree Toombs](#) [26], [Paul J Torzillo](#) [27][28], [Keith Grimwood](#) [29][30]

Affiliations expand

Abstract

This position statement, updated from the 2015 guidelines for managing Australian and New Zealand children/adolescents and adults with chronic suppurative lung disease (CSLD) and bronchiectasis, resulted from systematic literature searches by a multi-disciplinary team that included consumers. The main statements are: Diagnose CSLD and bronchiectasis early; this requires awareness of bronchiectasis symptoms and its co-existence with other respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease). Confirm bronchiectasis with a chest computed-tomography scan, using age-appropriate protocols and criteria in children. Undertake a baseline panel of investigations. Assess baseline severity, and health impact, and develop individualized management plans that include a multi-disciplinary approach and coordinated care between healthcare providers. Employ intensive treatment to improve symptom control, reduce exacerbation frequency, preserve lung function, optimize quality-of-life and enhance survival. In children, treatment also aims to optimize lung growth and, when possible, reverse bronchiectasis. Individualize airway clearance techniques (ACTs) taught by respiratory

physiotherapists, encourage regular exercise, optimize nutrition, avoid air pollutants and administer vaccines following national schedules. Treat exacerbations with 14-day antibiotic courses based upon lower airway culture results, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients with severe exacerbations and/or not responding to outpatient therapy are hospitalized for further treatments, including intravenous antibiotics and intensive ACTs. Eradicate Pseudomonas aeruginosa when newly detected in lower airway cultures. Individualize therapy for long-term antibiotics, inhaled corticosteroids, bronchodilators and mucoactive agents. Ensure ongoing care with 6-monthly monitoring for complications and co-morbidities. Undertake optimal care of under-served peoples, and despite its challenges, delivering best-practice treatment remains the overriding aim.

Keywords: adolescents; adults; bronchiectasis; children; evidence base practice; systematic review.

- [26 references]

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Hypereosinophilic syndrome in Europe: retrospective study of treatment

patterns, clinical manifestations, and healthcare resource utilization

Jeremiah Hwee [1], Lynn Huynh [2], Shawn Du [2], Namhee Kwon [3], Rupert W Jakes [4], Rafael Alfonso-Cristancho [5], Lee Baylis [6], Gema Requena [4], Anamika Khanal [2], Marc E Rothenberg [7], Mei Sheng Duh [2]

Affiliations expand

Abstract

Background: The burden of hypereosinophilic syndrome (HES) in Europe is not well characterized.

Objective: To evaluate real-world patient characteristics, treatment patterns, clinical manifestations, and healthcare resource utilization (HCRU) for patients with HES from France, Germany, Italy, Spain, and the UK.

Methods: In this retrospective non-interventional study, data for patients with a physician-confirmed diagnosis of HES were abstracted from medical chart reviews. Patients were ≥6 years of age at the time of HES diagnosis and had ≥1 year of follow-up from the index date (first clinic visit between January 2015-December 2019). Data on treatment patterns, comorbidities, clinical manifestations, clinical outcomes, and HCRU were collected from diagnosis/index date to end of follow-up.

Results: Data for 280 patients were abstracted from medical charts by 121 HES-treating physicians with multiple specialties. Most patients (55%) had idiopathic HES and 24% had myeloid HES; the median (interquartile range [IQR]) number of diagnostic tests per patient was 10 (6, 12). The most common comorbidities were asthma (45%) and anxiety/depression (36%). Most patients (89%) used oral corticosteroids (OCS), 64% used immunosuppressants/cytotoxic agents, and 44% used biologics. Patients had a median (IQR) of 3 (1, 5) clinical manifestations, most commonly constitutional (63%), lung (49%), and skin (48%). Twenty-three percent of patients experienced a flare and 40% had a complete treatment response. Some patients (30%) were hospitalized with a median (IQR) stay of 9 (5, 15) days for HES-related issues.

Conclusion: Patients with HES across five European countries had a substantial disease burden despite extensive OCS treatment, highlighting the need for additional targeted therapies.

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Lancet Gastroenterol Hepatol

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 doi: 10.1016/S2468-1253(23)00012-2. Online ahead of print.

One-food versus six-food elimination diet therapy for the treatment of eosinophilic oesophagitis: a multicentre, randomised, open-label trial

Kara L Kliewer [1], Nirmala Gonsalves [2], Evan S Dellon [3], David A Katzka [4], Juan P Abonia [1], Seema S Aceves [5], Nicoleta C Arva [6], John A Besse [1], Peter A Bonis [7], Julie M Caldwell [1], Kelley E Capocelli [8], Mirna Chehade [9], Antonella Cianferoni [10], Margaret H Collins [11], Gary W Falk [12], Sandeep K Gupta [13], Ikuo Hirano [2], Jeffrey P Krischer [14], John Leung [15], Lisa J Martin [16], Paul Menard-Katcher [17], Vincent A Mukkada [18], Kathryn A Peterson [19], Tetsuo Shoda [1], Amanda K Rudman Spergel [20], Jonathan M Spergel [10], Guang-Yu Yang [21], Xue Zhang [16], Glenn T Furuta [22], Marc E Rothenberg [23]

Abstract

Background: Empirical elimination diets are effective for achieving histological remission in eosinophilic oesophagitis, but randomised trials comparing diet therapies are lacking. We aimed to compare a six-food elimination diet (6FED) with a one-food elimination diet (1FED) for the treatment of adults with eosinophilic oesophagitis.

Methods: We conducted a multicentre, randomised, open-label trial across ten sites of the Consortium of Eosinophilic Gastrointestinal Disease Researchers in the USA. Adults aged 18-60 years with active, symptomatic eosinophilic oesophagitis were centrally randomly allocated (1:1; block size of four) to 1FED (animal milk) or 6FED (animal milk, wheat, egg, soy, fish and shellfish, and peanut and tree nuts) for 6 weeks. Randomisation was stratified by age, enrolling site, and gender. The primary endpoint was the proportion of patients with histological remission (peak oesophageal count <15 eosinophils per high-power field [eos/hpf]). Key secondary endpoints were the proportions with complete histological remission (peak count ≤1 eos/hpf) and partial remission (peak counts ≤10 and ≤6 eos/hpf) and changes from baseline in peak eosinophil count and scores on the Eosinophilic Esophagitis Histology Scoring System (EoEHSS), Eosinophilic Esophagitis Endoscopic Reference Score (EREFS), Eosinophilic Esophagitis Activity Index (EEsAI), and quality of life (Adult Eosinophilic Esophagitis Quality-of-Life and Patient Reported Outcome Measurement Information System Global Health questionnaires). Individuals without histological response to 1FED could proceed to 6FED, and those without histological response to 6FED could proceed to swallowed topical fluticasone propionate 880 μg twice per day (with unrestricted diet), for 6 weeks. Histological remission after switching therapy was assessed as a secondary endpoint. Efficacy and safety analyses were done in the intention-to-treat (ITT) population. This trial is registered on ClinicalTrials.gov, NCT02778867, and is completed.

Findings: Between May 23, 2016, and March 6, 2019, 129 patients (70 [54%] men and 59 [46%] women; mean age 37·0 years [SD 10·3]) were enrolled, randomly assigned to 1FED (n=67) or 6FED (n=62), and included in the ITT population. At 6 weeks, 25 (40%) of 62 patients in the 6FED group had histological remission compared with 23 (34%) of 67 in the 1FED group (difference 6% [95% CI -11 to 23]; p=0·58). We found no significant difference between the groups at stricter thresholds for partial remission (≤10 eos/hpf, difference 7% [-9 to 24], p=0·46; ≤6 eos/hpf, 14% [-0 to 29], p=0·069); the proportion with complete remission was significantly higher in the 6FED group than in the 1FED group (difference 13% [2 to 25]; p=0·031). Peak eosinophil counts decreased in both groups (geometric

mean ratio 0·72 [0·43 to 1·20]; p=0·21). For 6FED versus 1FED, mean changes from baseline in EoEHSS (-0·23 vs -0·15; difference -0·08 [-0·21 to 0·05]; p=0·23), EREFS (-1·0 vs -0·6; difference -0·4 [-1·1 to 0·3]; p=0·28), and EEsAI (-8·2 vs -3·0; difference -5·2 [-11·2 to 0·8]; p=0·091) were not significantly different. Changes in quality-of-life scores were small and similar between the groups. No adverse event was observed in more than 5% of patients in either diet group. For patients without histological response to 1FED who proceeded to 6FED, nine (43%) of 21 reached histological remission; for patients without histological response to 6FED who proceeded to fluticasone propionate, nine (82%) of 11 reached histological remission.

Interpretation: Histological remission rates and improvements in histological and endoscopic features were similar after 1FED and 6FED in adults with eosinophilic oesophagitis. 6FED had efficacy in just less than half of 1FED non-responders and steroids had efficacy in most 6FED non-responders. Our findings indicate that eliminating animal milk alone is an acceptable initial dietary therapy for eosinophilic oesophagitis.

Conflict of interest statement

Declaration of interests NG receives royalties from UpToDate; is a consultant for Allakos, Regeneron-Sanofi, AstraZeneca, AbbVie, Takeda, Knopp, Bristol Meyers Squibb, and Nutricia; and has received payment or honoraria for speaker's bureaus for Takeda and Regeneron-Sanofi. ESD has received research support from Ellodi (formerly Adare), Allakos, Arena, AstraZeneca, GlaxoSmithKline, Meritage, Miraca, Nutricia, Celgene (formerly Receptos and a subsidiary of Bristol Myers Squibb), Regeneron, Revolo, and Shire (a subsidiary of Takeda); is a consultant for Abbott, AbbVie, Ellodi, Aimmune, Akesobio, Allakos, Amgen, Arena, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene, Celldex, Eli Lilly, EsoCap, GlaxoSmithKline, Gossamer Bio, Invea, Landos, Lucid Diagnostics, Morphic, Nutricia, Calyx (formerly Parexel), Phathom, Regeneron, Revolo, Alimentiv (formerly Robarts), Salix, Sanofi, Shire, and Target RWE; and has education grants with Allakos, Banner, and Holoclara. DAK has received consulting fees and payments for presentations from Celgene; has served on a data and safety monitoring board at the University of North Carolina; and serves on the governing board of the American Gastroenterological Association. JPA has received research support from Cures Within Reach and Celgene; has received payment or honoraria for lectures from Takeda; and has served on a data and safety monitoring board for Octapharma USA. SSA has received research support from Implicit Biosciences and the Campaign Urging Research for Eosinophilic Disease (CURED) Foundation; has received consulting fees from Bristol Meyers Squibb, Regeneron-Sanofi, and AstraZeneca; has received payment for presentations or events from Regeneron-Sanofi; and receives patent royalties and is co-inventor of oral viscous budesonide, patented by University of California San Diego and licensed by Shire. KEC is employed by and has an equity interest in Alnylam. MC has received consulting fees from Regeneron,

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Medicine (Baltimore)

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The role of ferroptosis-related genes in airway epithelial cells of asthmatic patients based on bioinformatics

Ye Zheng[1], Jingyao Fan[2], Xiaofeng Jiang[1]

Affiliations expand

- PMID: 36862916

Abstract

It has been reported that airway epithelial cells and ferroptosis have certain effect on asthma. However, the action mechanism of ferroptosis-related genes in airway epithelial cells of asthmatic patients is still unclear. Firstly, the study downloaded the GSE43696 training set, GSE63142 validation set and GSE164119 (miRNA) dataset from the gene expression omnibus database. 342 ferroptosis-related genes were downloaded from the ferroptosis database. Moreover, differentially expressed genes (DEGs) between asthma and control samples in the GSE43696 dataset were screened by differential analysis. Consensus clustering analysis was performed on asthma patients to classify clusters, and differential analysis was performed on clusters to obtain inter-cluster DEGs. Asthma-related module was screened by weighted gene co-expression network analysis. Then, DEGs between asthma and control samples, inter-cluster DEGs and asthma-related module were subjected to venn analysis for obtaining candidate genes. The last absolute shrinkage and selection operator and support vector machines were respectively applied to the candidate genes to screen for feature genes, and functional enrichment analysis was performed. Finally, a competition endogenetic RNA network was constructed and drug sensitivity analysis was conducted. There were 438 DEGs (183 up-regulated and 255 down-regulated) between asthma and control samples. 359 inter-cluster DEGs (158 up-regulated and 201 down-regulated) were obtained by screening. Then, the black module was significantly and strongly correlated with asthma. The venn analysis yielded 88 candidate genes. 9 feature genes (NAV3, ITGA10, SYT4, NOX1, SNTG2, RNF182, UPK1B, POSTN, SHISA2) were screened and they were involved in proteasome, dopaminergic synapse etc. Besides, 4 mRNAs, 5 miRNAs, and 2 lncRNAs collectively formed competition endogenetic RNA regulatory network, which included RNF182-hsa-miR-455-3p-LINC00319 and so on. The predicted therapeutic drug network map contained NAV3-bisphenol A and other relationship pairs. The study investigated the potential molecular mechanisms of NAV3, ITGA10, SYT4, NOX1, SNTG2, RNF182, UPK1B, POSTN, SHISA2 in airway epithelial cells of asthmatic patients through bioinformatics analysis, providing a reference for the research of asthma and ferroptosis.

Conflict of interest statement

The authors have no conflicts of interest to disclose.

- 56 references
- 11 figures

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Expanded characterization of in vitro polarized M0, M1, and M2 human monocyte-derived macrophages: Bioenergetic and secreted mediator profiles

Elise Hickman [1][2], Timothy Smyth [1][2], Catalina Cobos-Uribe [1][2], Robert Immormino [1], Meghan E Rebuli [1][2][3], Timothy Moran [1][2][3], Neil E Alexis [1][2][3], Ilona Jaspers [1][2][3]

Affiliations expand

Abstract

Respiratory macrophage subpopulations exhibit unique phenotypes depending on their location within the respiratory tract, posing a challenge to in vitro macrophage model systems. Soluble mediator secretion, surface marker expression, gene signatures, and phagocytosis are among the characteristics that are typically independently measured to phenotype these cells. Bioenergetics is emerging as a key central regulator of macrophage function and phenotype but is often not included in the characterization of human monocyte-derived macrophage (hMDM) models. The objective of this study was to expand the phenotype characterization of naïve hMDMs, and their M1 and M2 subsets by measuring cellular bioenergetic outcomes and including an expanded cytokine profile. Known markers of M0, M1 and M2 phenotypes were also measured and integrated into the phenotype characterization. Peripheral blood monocytes from healthy volunteers were differentiated into hMDM and polarized with either IFN-γ + LPS (M1) or IL-4 (M2). As expected, our M0, M1, and M2 hMDMs exhibited cell surface marker, phagocytosis, and gene expression profiles indicative of their different phenotypes. M2 hMDMs however were uniquely characterized and different from M1 hMDMs by being preferentially dependent on oxidativte phosphorylation for their ATP generation and by secreting a distinct cluster of soluble mediators (MCP4, MDC, and TARC). In contrast, M1 hMDMs secreted prototypic pro-inflammatory cytokines (MCP1, eotaxin, eotaxin-3, IL12p70, IL-1α, IL15, TNF-β, IL-6, TNF-α, IL12p40, IL-13, and IL-2), but demonstrated a relatively constitutively heightened bioenergetic state, and relied on glycolysis for ATP generation. These data are similar to the bioenergetic profiles we previously observed in vivo in sputum (M1) and BAL (M2)-derived macrophages in healthy volunteers, supporting the notion that polarized hMDMs can provide an acceptable in vitro model to study specific human respiratory macrophage subtypes.

Conflict of interest statement

The authors have declared that no competing interests exist.

- 58 references
- 7 figures

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An Augmented Reality Technology to Provide Demonstrative Inhaler Technique Education for Patients With Asthma: Interview Study Among Patients, Health Professionals, and Key Community Stakeholders

Antonia O'Connor [1] [2], Kelsey Sharrad [3], Charmaine King [3], Kristin Carson-Chahhoud [1] [3] [4] [5]

Affiliations expand

- PMID: 36862496

- DOI: 10.2196/34958

Abstract

Background: Many people with asthma use incorrect inhaler technique, resulting in suboptimal disease management and increased health service use. Novel ways of delivering appropriate instructions are needed.

Objective: This study explored stakeholder perspectives on the potential use of augmented reality (AR) technology to improve asthma inhaler technique education.

Methods: On the basis of existing evidence and resources, an information poster displaying the images of 22 asthma inhaler devices was developed. Using AR technology

via a free smartphone app, the poster launched video demonstrations of correct inhaler technique for each device. In total, 21 semistructured, one-on-one interviews with health professionals, people with asthma, and key community stakeholders were conducted, and data were analyzed thematically using the Triandis model of interpersonal behavior.

Results: A total of 21 participants were recruited into the study, and data saturation was achieved. People with asthma were confident with inhaler technique (mean score 9.17, SD 1.33, out of 10). However, health professionals and key community stakeholders identified that this perception was misguided (mean 7.25, SD 1.39, and mean 4.5, SD 0.71, for health professionals and key community stakeholders, respectively) and facilitates persistent incorrect inhaler use and suboptimal disease management. Delivering inhaler technique education using AR was favored by all participants (21/21, 100%), particularly around ease of use, with the ability to visually display inhaler techniques for each device. There was a strongly held belief that the technology has the capacity for improving inhaler technique across all participant groups (mean 9.25, SD 0.89, for participants; mean 9.83, SD 0.41, for health professionals; and mean 9.5, SD 0.71, for key community stakeholders). However, all participants (21/21, 100%) identified some barriers, particularly regarding access and appropriateness of AR for older people.

Conclusions: AR technology may be a novel means to address poor inhaler technique among certain cohorts of patients with asthma and serve as a prompt for health professionals to initiate review of inhaler devices. A randomized controlled trial design is needed to evaluate the efficacy of this technology for use in the clinical care setting.

Keywords: asthma; augmented reality; disease management; inhaler technique; mobile phone; smartphone.

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Curr Opin Pediatr

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Socioeconomic determinants of asthma health

Tregony Simoneau[1], Jonathan M Gaffin

Affiliations expand

- PMID: 36861771

- DOI: 10.1097/MOP.0000000000001235

Abstract

Purpose of review: The current review provides an assessment of the recent pediatric literature evaluating socioeconomic drivers of asthma incidence and morbidity. The review addresses the specific social determinants of health related to housing, indoor and outdoor environmental exposures, healthcare access and quality, and the impact of systematic racism.

Recent findings: Many social risk factors are associated with adverse asthma outcomes. Children living in low-income, urban neighborhoods have greater exposure to both indoor and outdoor hazards, including molds, mice, second-hand smoke, chemicals, and air pollutants, all of which are associated with adverse asthma outcomes. Providing asthma education in the community - via telehealth, school-based health centers, or peer mentors - are all effective methods for improving medication adherence and asthma outcomes. The racially segregated neighborhoods created by the racist 'redlining' policies implemented decades ago, persist today as hotspots of poverty, poor housing conditions, and adverse asthma outcomes.

Summary: Routine screening for social determinants of health in clinical settings is important to identify the social risk factors of pediatric patients with asthma. Interventions targeting social risk factors can improve pediatric asthma outcomes, but more studies are needed related to social risk interventions.

- 56 references

Review

Preconception origins of asthma, allergies and lung function: The influence of previous generations on the respiratory health of our children

Cecilie Svanes [1][2], John W Holloway [3], Susanne Krauss-Etschmann [4][5]

Affiliations expand

- PMID: 36861185

- DOI: 10.1111/joim.13611

Abstract

Emerging research suggests that exposures occurring years before conception are important determinants of the health of future offspring and subsequent generations. Environmental exposures of both the father and mother, or exposure to disease processes such as obesity or infections, may influence germline cells and thereby cause a cascade of health outcomes in multiple subsequent generations. There is now increasing evidence that respiratory health is influenced by parental exposures that occur long before

conception. The strongest evidence relates adolescent tobacco smoking and overweight in future fathers to increased asthma and lower lung function in their offspring, supported by evidence on parental preconception occupational exposures and air pollution. Although this literature is still sparse, the epidemiological analyses reveal strong effects that are consistent across studies with different designs and methodologies. The results are strengthened by mechanistic research from animal models and (scarce) human studies that have identified molecular mechanisms that can explain the epidemiological findings, suggesting transfer of epigenetic signals through germline cells, with susceptibility windows in utero (both male and female line) and prepuberty (male line). The concept that our lifestyles and behaviours may influence the health of our future children represents a new paradigm. This raises concerns for future health in decades to come with respect to harmful exposures but may also open for radical rethinking of preventive strategies that may improve health in multiple generations, reverse the imprint of our parents and forefathers, and underpin strategies that can break the vicious circle of propagation of health inequalities across generations.

- 135 references

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The beneficial effects of an adenotonsillectomy upon upper

respiratory tract infections, asthma and rhinitis in children: a national database study in Korea

Mi Rye Bae [1], Kyung-Do Han [2], Sang-Hyun Park [3], Yoo-Sam Chung [4]

Affiliations expand

- PMID: 36861173

- DOI: 10.1080/00016489.2023.2181391

Abstract

Background: Adenotonsillectomy is the most commonly performed surgery in children.

Aims: To evaluate the effects of pediatric adenotonsillectomy on health care utilization.

Methods: From 2006 to 2017, age/sex-matched adenotonsillectomy participants (n = 243.396) and controls (n = 730.188) were selected (62% of male and 38% of female. 47% age≦ 6, 16% 7-9years, 8% 10-12years, 29% 13-18years). The changes in outpatient visits, hospitalization days, and drug prescriptions due to a URI, asthma, and rhinitis before and after the surgery date (from 13 months to 1 month) were compared.

Results: Outpatient visits decreased more in the surgery group than the control group (mean change, 3.24 ± 8.61 d and 1.16 ± 6.57 d for URI, 2.07 ± 8.63 d and 0.51 ± 6.47 d for rhinitis, and 0.72 ± 4.81 d and 0.42 ± 3.91 d for asthma, $p < .001$ for all). Hospitalizations also showed greater decreases in the surgery group (mean change, 0.31 ± 2.96 d and 0.04 ± 1.70 d for URI, 0.13 ± 2.40 d and 0.02 ± 1.48 d for rhinitis, 0.11 ± 2.32 d and 0.04 ± 1.83 d for asthma, $p < .001$ for all). The prescription of antihistamines, leukotriene modulators, oral antibiotics, oral steroids, and expectorants, cough suppressants and oral bronchodilators was also decreased after surgery.

Conclusions: The adenotonsillectomy group showed a greater decrease in post-operative outpatients visits, hospital days and drug prescriptions associated with URI, rhinitis and asthma than the control group.

Keywords: Adenotonsillectomy; asthma; national database; rhinitis; upper respiratory tract infection.

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It is time to end our love affair with short-acting β$_2$-agonists in asthma? Yes

Luis J Nannini[1]

Affiliations expand

- PMID: 36861059

- PMCID: PMC9969308

- DOI: 10.1183/23120541.00555-2022

Abstract

Why not directly eradicate SABA from asthma management? The time to leave behind SABA in asthma management is now. We wasted enough time identifying the key issue in asthma morbidity and mortality. Please, eradicate SABA. https://bit.ly/3DU4mmo.

Conflict of interest statement

Conflict of interest: L.J. Nannini reports the following relationships outside the submitted work: personal fees received from Novartis; consulting fees received from AstraZeneca; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca; payment for expert testimony received from AstraZeneca India; support for attending meetings and/or travel from AstraZeneca and Boehringer Ingelheim; and participation on a data safety monitoring or advisory board for AstraZeneca.

- 8 references

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The association between erosive toothwear and asthma – is it significant? A meta-analysis

Gowri Sivaramakrishnan[1], Kannan Sridharan[2], Muneera Alsobaiei[3]

Affiliations expand

- PMID: 36859415

- PMCID: PMC9977957

Abstract

Background: The association of asthma with oral conditions such as dental caries, dental erosion, periodontal diseases and oral mucosal changes has been the subject of debate among dental practitioners. Existing evidence indicates that an inhaler is the most common and effective way of delivering the asthma medications directly into the lungs. Few studies in the past attributed this association to the changes in salivary flow caused due to these medications. Considering this unclear association, the aim of the present meta-analyses is to identify the association between erosive toothwear and asthma from individual studies conducted until date.

Methodology: Electronic databases were systematically searched until 30th September 2022. Articles identified using the search strategy were imported to RAYYAN systematic review software. Data was extracted relating to study design, geographic location, year of publication, sample size, the assessment method for erosive toothwear and asthma. The Newcastle Ottawa scale was utilized to assess the quality of evidence reported from the included studies. RevMan Version 5.3 was used to perform a random-effects meta-analysis to produce pooled estimates from OR and 95% CI of included studies. The I^2 statistic was used to determine the extent of heterogeneity. A funnel plot was generated to visually assess the potential for publication bias. Sensitivity analyses were performed by excluding individual studies one at a time. GRADE approach was used for grading the evidence for key comparisons.

Results: Twelve articles were included in the final meta-analysis. A total of 1027 asthmatics and 5617 non-asthmatics were included. All studies demonstrated moderate to low risk of bias. The overall pooled estimate (OR: 2.03; 95% CI: 0.96, 4.29) and subgroup analyses in children (OR: 1.67; 95% CI: 0.63, 4.42) did not show statistically significant difference in the occurrence of dental erosion between the asthmatic and non-asthmatic group. However, asthmatic adults had significantly greater dental erosion in comparison to the control adults (OR: 2.76; 95% CI: 1.24, 6.16). Sensitivity analyses also provided inconclusive evidence. Funnel plot asymmetry indicated significant heterogeneity, changes in effect size and selective publication.

Conclusion: The association between inhalational asthmatic medication and tooth wear is inconclusive. There are a number of confounding factors that play a greater role in causing dental erosion in these patients. Dentist must pay particular attention to these factors while treating asthmatic patients. The authors produce a comprehensive checklist in order to ensure complete assessment before providing advice on their medications alone.

Conflict of interest statement

The authors declare no competing interests.

- 33 references
- 4 figures

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Improved exercise capacity results in a survival benefit after endobronchial valve treatment

Sharyn A Roodenburg [1], Dirk-Jan Slebos [2], Marlies van Dijk [2], T David Koster [2], Karin Klooster [2], Jorine E Hartman [2]

Affiliations expand

- PMID: 36858325

- DOI: 10.1016/j.rmed.2023.107175

Abstract

Background: Bronchoscopic lung volume reduction using endobronchial valves (EBV) is a treatment option for selected patients with advanced emphysema. The treatment significantly improves pulmonary function, exercise capacity, quality of life, and potentially improves survival. Our main aim was to assess whether treatment response significantly influences survival time after EBV treatment.

Methods: We evaluated treatment response at 6-week and 1-year follow-up of all patients treated with EBVs between 2008 and 2020. Survival status was retrieved on December 1, 2021. Patients were defined as responders or non-responders based on known minimal important differences for FEV1, residual volume (RV), RV/Total Lung Capacity (TLC) ratio, 6-min walk distance (6MWD), St. George's Respiratory Questionnaire (SGRQ), target lobe volume reduction (TLVR), and complete lobar atelectasis. Uni- and multivariate cox regression models were used to evaluate the effect of response on survival time.

Results: A total of 428 patients were included. EBV treatment resulted in significant improvements in pulmonary function, exercise capacity and quality of life. Median survival was 8.2 years after treatment. SGRQ and 6MWD response were independent predictors for survival (Hazard Ratio (HR) 0.50 [0.28-0.89], p = .02 and HR 0.54 [0.30-0.94], p = .03, respectively). The presence of a complete lobar atelectasis did not significantly affect survival, neither did pulmonary function improvements.

Conclusions: Our results suggest that improvement in exercise capacity and quality of life after EBV treatment are associated with a survival benefit, independent of improvements in pulmonary function, reduction in target lobe volume or the presence of complete lobar atelectasis.

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Unmet Social Needs and Pediatric Asthma Severity in an Urban Primary Care Setting

Andrew Telzak [1], Kevin P Fiori [2], Earle C Chambers [3], Jessica Haughton [4], Samantha Levano [5], Marina Reznik [6]

Affiliations expand

- PMID: 36858248

Abstract

Background and objectives: Community level social determinants of health impact asthma outcomes among children, however individual patient's priorities are not often included in designing social care interventions. Identifying connections between patient-prioritized unmet social needs and asthma severity status may allow for improved patient-centered approaches to asthma management. In this analysis, we examined the association between unmet social needs and asthma severity in an urban population of children. We hypothesized that those with a greater number of unmet social needs would report a more severe asthma status.

Methods: We conducted a secondary analysis of 4,887 patients screened for unmet social needs and asthma severity status. Bivariate associations and adjusted logistic regression modeling were used to assess the association between unmet social needs and asthma severity.

Results: Persistent asthma severity status was associated with several unmet social needs, including housing quality and stability, lack of money for food, transportation, and healthcare costs. In the multivariable analysis, having 3 or more unmet social needs was associated with a 59% greater odds of persistent asthma status (CI 1.18-2.14; P=0.002), and having two unmet social needs was associated with a 33% greater odds of persistent asthma status (CI 1.00-1.78; P=0.05).

Conclusions: Unmet social needs were associated with asthma severity status, with a greater number of unmet social needs associated with a greater odds of severe asthma status. Additional studies are warranted to further evaluate the temporal relationship between unmet social needs and how they may compound one another in their relationship with asthma severity.

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Review

Chest

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Health Disparities: Interventions for Pulmonary Disease – a narrative review

Logan J Harper [1], Pranav Kidambi [2], Jason M Kirincich [3], J Daryl Thornton [4], Sumita Khatri [5], Daniel A Culver [5]

Affiliations expand

- PMID: 36858172

- DOI: 10.1016/j.chest.2023.02.033

Abstract

Topic importance: There is an expansive literature documenting the presence of health disparities, but disproportionately few studies describing interventions to reduce disparity. In this narrative review, we categorize interventions to reduce health disparity in pulmonary disease within the United States healthcare system to support future initiatives to reduce disparity.

Review findings: We identified 211 articles describing interventions to reduce disparity in pulmonary disease related to race, income, or gender. We grouped the studies into four categories: Biologic, Educational, Behavioral, and Structural. We identified five main themes: There were few interventional trials compared to the breadth of studies describing health disparities. Trials involving patients with asthma who were Black, low income, and living in an urban setting were over represented. Race or socioeconomic status were not effective markers of individual pharmacologic treatment response. Telehealth enabled scaling of care, but more work is needed to understand how to leverage telehealth to improve outcomes in marginalized communities. Future interventions must explicitly target societal drivers of disparity, rather than focusing on individual behavior alone. Individual interventions will only be maximally effective when specifically tailored to local needs.

Summary: Much work has been done to catalog health disparities in pulmonary disease. Notable gaps in the identified literature include few interventional trials, the need for research in diseases outside of asthma, the need for high quality effectiveness trials, and an understanding of how to implement proven interventions balancing fidelity to the original protocol and the need to adapt to local barriers to care.

SUPPLEMENTARY INFO

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Review

Semin Immunol

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A major mechanism for immunomodulation: Dietary fibres and acid metabolites

Liang Xie [1], Md Jahangir Alam [2], Francine Z Marques [3], Charles R Mackay [4]

Affiliations expand

Abstract

Diet and the gut microbiota have a profound influence on physiology and health, however, mechanisms are still emerging. Here we outline several pathways that gut microbiota products, particularly short-chain fatty acids (SCFAs), use to maintain gut and immune homeostasis. Dietary fibre is fermented by the gut microbiota in the colon, and large quantities of SCFAs such as acetate, propionate, and butyrate are produced. Dietary fibre and SCFAs enhance epithelial integrity and thereby limit systemic endotoxemia. Moreover, SCFAs inhibit histone deacetylases (HDAC), and thereby affect gene transcription. SCFAs also bind to 'metabolite-sensing' G-protein coupled receptors (GPCRs) such as GPR43, which promotes immune homeostasis. The enormous amounts of SCFAs produced in the colon are sufficient to lower pH, which affects the function of proton sensors such as GPR65 expressed on the gut epithelium and immune cells. GPR65 is an anti-inflammatory $G\alpha_s$-coupled receptor, which leads to the inhibition of inflammatory cytokines. The importance of GPR65 in inflammatory diseases is underscored by genetics associated with the missense variant I231L (rs3742704), which is associated with human inflammatory bowel disease, atopic dermatitis, and asthma. There is enormous scope to manipulate these pathways using specialized diets that release very high amounts of specific SCFAs in the gut, and we believe that therapies that rely on chemically modified foods is a promising approach. Such an approach includes high SCFA-producing diets, which we have shown to decrease numerous inflammatory western diseases in mouse models. These diets operate at many levels - increased gut integrity, changes to the gut microbiome, and promotion of immune homeostasis, which represents a new and highly promising way to prevent or treat human disease.

Keywords: Dietary fibre; GPR43; GPR65; Gut microbiota/microbiome; Proton sensing; Short-chain fatty acids (SCFA).

Conflict of interest statement

Conflict of interest C.R.M is the founder of a company that produces HAMSA, HAMSP to treat human diseases.

Changes in Caregiver Mental Health and Pediatric Asthma Control during COVID-19

Katherine D Lohr [1], Robin S Everhart [1], Rachel L Holder [1], Rachel Boutté [2], Rosalie Corona [1], Suzanne E Mazzeo [1]

Affiliations expand

Abstract

Objective: This study evaluated caregivers' stress and depressive symptoms, and children's asthma control, before COVID-19 began and after its onset among families in the RVA Breathes program.

Methods: The RVA Breathes intervention, which took place in an urban city in the United States, includes asthma education delivered by a community health worker (CHW), a home assessment, and school nurse components. Participants included 125 children (5-11 years) with asthma and their caregivers (48% household income<$25,000) enrolled prior to the pandemic. Families were randomized to an active intervention arm (full intervention or intervention without school nurse component) or the control group. Caregivers completed the Center for Epidemiological Studies Depression Scale (CES-D) and the Perceived Stress Scale (PSS); children and caregivers completed the Childhood Asthma Control Test (cACT). Assessments pre-COVID-19 were compared to those completed after the pandemic's onset.

Results: Children in both intervention groups had better cACT scores after the start of COVID-19 compared to before ($t(55)=-2.131$, $p=.019$; $t(28)=-2.893$, $p=.004$). Caregivers in the intervention groups had lower PSS scores after the start of COVID-19 compared to pre-COVID-19 ($t(53)=3.928$, $p<.001$; $t(28)=2.568$, $p=.008$). Furthermore, CES-D scores improved among caregivers in the full intervention ($t(48)=1.789$, $p=.040$). Caregivers in the control condition did not report significant changes in stress or depressive symptoms.

Conclusions: Findings suggest that support from interventionists, including CHWs, might have alleviated stress and depressive symptoms during COVID-19, as well as improved asthma control during the pandemic.

Keywords: COVID-19; Pediatric asthma; caregiver mental health; disparities; family; stress.

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Review

World J Pediatr

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. 2023 Mar 1.

Risk of asthma in preterm infants with bronchopulmonary dysplasia: a systematic review and meta-analysis

Tong Sun [1], Hai-Yang Yu [2], Miao Yang [1], Yi-Fan Song [1], Jian-Hua Fu [3]

Affiliations expand

- PMID: 36857022

- DOI: 10.1007/s12519-023-00701-1

Abstract

Background: This study aimed to systematically review and meta-analyze the available literature on the association between preterm infant bronchopulmonary dysplasia (BPD) and pre-adulthood asthma.

Methods: Studies examining the association between BPD and asthma in children and adolescents were systematically reviewed, and a meta-analysis was conducted. We searched Scopus, Embase, Web of Science, PubMed, and Cochrane Library from the database inception to March 26, 2022. The pooled odds ratio (OR) estimate was used in our meta-analysis to calculate the correlation between BPD and the probability of developing asthma before adulthood. Stata 12.0 was used to conduct the statistical analysis.

Results: The correlation between asthma and BPD in preterm newborns was examined in nine studies. We used a random effect model to pool the OR estimate. Our results indicated a marked increase in the risk of subsequent asthma in preterm infants with BPD [OR = 1.73, 95% confidence interval (CI) = 1.43-2.09]. Moreover, there was no obvious heterogeneity across the studies (P = 0.617, I^2 = 0%). The pooled OR remained stable and ranged from 1.65 (95% CI = 1.35-2.01) to 1.78 (95% CI = 1.43-2.21). Regarding publication bias, the funnel plot for asthma risk did not reveal any noticeable asymmetry. We further performed Begg's and Egger's tests to quantitatively evaluate publication bias. There was no evidence of a publication bias for asthma risk (P > |Z| = 0.602 for Begg's test, and P > |t| = 0.991 for Egger's test).

Conclusions: Our findings indicate that preterm infants with BPD have a much higher risk of developing asthma in the future (OR = 1.73, 95% CI = 1.43-2.09). Preterm infants with BPD may benefit from long-term follow-up.

Keywords: Asthma; Bronchopulmonary dysplasia; Preterm infants.

- 36 references

SUPPLEMENTARY INFO

Publication types, Grant supportexpand

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Erratum: The Impact of Insulin Resistance on Loss of Lung Function and Response to Treatment in Asthma

No authors listed

- PMID: 36856563

- DOI: 10.1164/rccm.v207erratum1

No abstract available

Erratum for

- [The Impact of Insulin Resistance on Loss of Lung Function and Response to Treatment in Asthma.](#)
  Peters MC, Schiebler ML, Cardet JC, Johansson MW, Sorkness R, DeBoer MD, Bleecker ER, Meyers DA, Castro M, Sumino K, Erzurum SC, Tattersall MC, Zein JG, Hastie AT, Moore W, Levy BD, Israel E, Phillips BR, Mauger DT, Wenzel SE, Fajt ML, Koliwad SK, Denlinger LC, Woodruff PG, Jarjour NN, Fahy JV; National Heart, Lung, and Blood Institute Severe Asthma Research Program-3.Am J Respir Crit Care Med. 2022 Nov 1;206(9):1096-1106. doi: 10.1164/rccm.202112-2745OC.PMID: 35687105

SUPPLEMENTARY INFO

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J Med Food

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. 2023 Feb 28.

 doi: 10.1089/jmf.2022.K.0117. Online ahead of print.

Effects of Pear Extracts on Microbiome and Immunocytokines to Alleviate Air Pollution-Related Respiratory Hypersensitivity

Mihi Yang [1], Unjae Lee [2], Hye-Rin Cho [3], Kyung Bae Lee [3], Yun Jeoung Shin [3], Min-Jung Bae [3], Kun-Young Park [4]

Affiliations expand

Abstract

Pears are ancient functional foods for modern times. Particularly, Korean pears (*Pyrus pyrifolia cv*.) have been used as folk medicine for respiratory diseases and have strong potential for the treatment of hazardous aerosol-related diseases. Thus, the effects of pear ethanol extracts on air pollution-related respiratory hypersensitivity were studied by toxicokinetics, pro-inflammatory cytokines, and microbiomics in preclinical and randomized double-blind clinical studies. The mild-asthma subjects, who lived in the same city, Seoul, Korea, were separated into the placebo and the treatment (pear extracts, as brix 55; arbutin 5.01 mg and chlorogenic acid 0.18 mg/3 mL per day) groups for 4 weeks (*n* = 20). As results, there were positive associations between urinary 2-naphthol (NT) or 1-hydroxypyrene (OHP), exposure biomarkers for polyaromatic hydrocarbons in $PM_{2.5}$, and pro-inflammatory cytokines, interleukin (IL)-4 or IgE, respectively, in the human subjects. The pear extracts somewhat reduced 2-NT and 1-OHP levels. The proportions of fiber-degrading bacteria that stimulate growth of beneficial microflora for immune defense, that is, *Bifidobacterium* and *Eubacterium*, were significantly higher in the pear consuming group than in the placebo group. Moreover, pro-inflammatory cytokines, including IgE, IL-4, IL-5, and IL-13, were significantly suppressed by the pear extracts in the preclinical tests of the ovalbumin-induced asthma mice. Thus, we suggest that air pollution-related respiratory hypersensitivity can be alleviated by Korean pear extracts by modulation of microbiome and immunocytokines.

Keywords: Korean pears; PM2.5; cytokine; immune modulation; microbiome.

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Epithelial Barrier Hypothesis and Its Comparison with the Hygiene Hypothesis

Ayça Kıykım [1], İsmail Öğülür [2], Duygu Yazıcı [2], Haluk Çokuğraş [1], Mübeccel Akdiş [2], Cezmi A Akdiş [3]

Affiliations expand

Abstract

Chronic inflammatory conditions including allergic, autoimmune, metabolic, and neuropsychiatric disorders are constantly increasing and leading to a high burden, especially in more industrialized countries. The prevalence is still on the rise in developing countries. The start of the steep increase in asthma, atopic dermatitis, and allergic rhinitis dates to the 1960s, whereas a second wave with an increase in eosinophilic gastrointestinal disease, food allergy, and drug hypersensitivity started after the 2000s. These diseases also started to appear more with neuropsychiatric and autoimmune conditions during the last few decades. Many theories have been proposed to explain this outbreak. The hygiene hypothesis was consolidated by "old friends" and biodiversity, although some gaps remained unresolved. The introduction of the epithelial barrier hypothesis gave us a new perspective to explain the effects of industrialization without environment control and health concerns creeping into our daily lives. The present review touches on the possible explanations of why epithelial barrier hypothesis covers all previous ones, which are not contradictory but mostly complementary.

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Review

Clin Exp Allergy

Allergic rhinitis in India

Subhabrata Moitra [1], Padukudru Anand Mahesh [2], Saibal Moitra [3]

Affiliations expand

- PMID: 36856159

- DOI: 10.1111/cea.14295

Abstract

India is the home of nearly 20% of the global population with 1.35 billion people. Of all non-communicable diseases, allergic diseases such as allergic rhinitis (AR) and asthma appear to have increased in India over the past decades. Approximately 22% of adolescents currently suffer from AR in India. However, owing to the lack of adequate epidemiological studies in India, particularly in rural and suburban areas, this number may misrepresent the true burden of this disease. While the risk factors for AR are mainly environmental exposures or genetic factors, several new environmental, social, and behavioural risk factors such as the presence of dumpsters near residences, movement of vehicles near homes, and exposure to artificial light at night have been found to be associated with AR. However, despite international guidelines, the diagnosis and management of AR in India are often suboptimal, for multiple reasons such as the lack of specialized training in allergy and immunology among Indian clinicians, the lack of diagnostic facilities, and the high cost of medications. This review aims at highlighting the current scenario of AR in India and how it differs from the rest of the world. It also highlights the need for developing a strategic approach to enhance the quality of care for allergic diseases by upgrading education and training for healthcare professionals, creating awareness among clinicians and patients, and involving stakeholders and policymakers in making treatments accessible and affordable to patients.

Keywords: immunotherapy; indoor air pollution; risk factor; second-hand smoke; skin prick test.

- 104 references

Application of artificial intelligence in the diagnosis of sleep apnea

George Bazoukis [1][2], Sandeep Chandra Bollepalli [3], Cheuk To Chung [4], Xinmu Li [5], Gary Tse [4][6], Bethany L Bartley [7], Salma Batool-Anwar [7], Stuart F Quan [7][8], Antonis A Armoundas [3][9]

Affiliations expand

- PMID: 36856067

- DOI: 10.5664/jcsm.10532

Abstract

Study objectives: Machine learning (ML) models have been employed in the setting of sleep disorders. This review aims to summarize the existing data about the role of ML techniques in the diagnosis, classification, and treatment of sleep related breathing disorders.

Methods: A systematic search in MedLine, EMBASE, and Cochrane databases through January 2022 was performed.

Results: Our search strategy revealed 132 studies that were included in the systematic review. Existing data show that ML models have been successfully used for diagnostic purposes. Specifically, ML models showed good performance in diagnosing sleep apnea using easily obtained features from the electrocardiogram, pulse oximetry and sound signals. Similarly, ML showed good performance for the classification of sleep apnea into obstructive and central categories, as well as predicting apnea severity. Existing data show promising results for the ML-based guided treatment of sleep apnea. Specifically, the prediction of outcomes following surgical treatment and optimization of continuous positive airway pressure therapy, can be guided by ML models.

Conclusions: The adoption and implementation of ML in the field of sleep related breathing disorders is promising. Advancements in wearable sensor technology and ML models can help clinicians predict, diagnose and classify sleep apnea more accurately and efficiently.

Keywords: artificial intelligence; machine learning; sleep apnea.

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. 2023 Mar 1.

Comparison of ephedrine and pseudoephedrine contents in 34 Kampo extracts containing Ephedrae Herba used clinically in Japan

Mitsuhiko Nose [1], Risa Kobayashi [2], Momoka Tada [2], Shinsuke Hisaka [2], Sayaka Masada [3], Masato Homma [4], Takashi Hakamatsuka [3] [5]

Abstract

Ephedrae Herba is among the important crude drugs prescribed in Kampo medicine for the treatment of cold, flue, rhinitis, nasal congestion, cough, and asthma. The active ingredients of Ephedrae Herba, ephedrine (E) and pseudoephedrine (PE), are potent sympathomimetic compounds that stimulate α-, β1-, and β2-adrenoceptors resulting in dilatation and alleviation of nasal mucosal hyperemia. Hypertension, palpitations, insomnia, and dysuria are the main adverse effects of E and PE, which can be avoided by determining the actual contents of these alkaloids in Kampo extracts containing Ephedrae Herba. However, the extraction efficiencies of E and PE from Ephedrae Herba contained in Kampo formulas in combination with other crude drugs remain unknown. Therefore, we comprehensively determined the E and PE contents of 34 Kampo extracts containing Ephedrae Herba used clinically in Japan. The E and PE contents per daily dosage in Kampo extracts were generally proportional to the compounding amount of Ephedrae Herba. In contrast, the extraction efficiencies of E or PE were not constant and not influenced by the pH of the extracts. We assume that the extraction efficiencies of E and PE may be independently affected by other constituent crude drugs. Thus, it is necessary to investigate the cause and mechanism in the future. In conclusion, these results show that the E and PE content of each Kampo formulation can be estimated from the compounding amount of Ephedrae Herba. Therefore, the amount of Ephedrae Herba should be carefully considered to ensure the safe use of Kampo formulations containing Ephedrae Herba.

Keywords: Ephedrae Herba; Ephedrine; Kampo extracts; Pseudoephedrine.

- 23 references

SUPPLEMENTARY INFO

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Relationship Between Chronic Lung Disease Diagnosis and Susceptibility to E-Cigarette Use in Adults

Mohammed M Alqahtani [1], Abdullah M M Alanazi [2], Mark T Dransfield [3], J Michael Wells [4], Donald H Lein Jr [5], Peter S Hendricks [6]

Affiliations expand

- PMID: 36854469

- DOI: 10.4187/respcare.10071

Abstract

Background: Electronic cigarettes (e-cigarettes) are known to cause adverse pulmonary effects, yet paradoxically, the prevalence of e-cigarette use has increased among individuals with chronic lung disease. We assessed the relationship between chronic lung disease and the susceptibility to e-cigarette use in adults and determined if specific behavioral, social, and environmental factors influence this relationship.

Methods: We enrolled adults age ≥ 18 y in Alabama with chronic lung disease from university medical clinics (n = 140) and individuals without chronic lung disease (n = 123, reference group) from January 2020-March 2021. A cross-sectional design was used where we administered questionnaires to collect sociodemographic information and assessed susceptibility to e-cigarette use, exposure to social and environmental factors (ie, advertisements, warning labels, special prices, others' e-cigarette vapors, use of an e-cigarette by others in the home, and visiting a web site or online discussion), and behavioral factors (ie, alcohol and cannabis use). Moderation analyses were conducted to determine if any of these factors would modify the association between chronic lung disease and susceptibility to e-cigarette use.

Results: Susceptibility to e-cigarette use was higher among adults without chronic lung disease than among those with chronic lung disease. Noticing e-cigarette warning labels and visiting a web site or online discussion about e-cigarettes were significantly associated with an increased likelihood of susceptibility to using e-cigarettes in both groups. Exposure to e-cigarette vapor from close contacts, special pricing, living with someone who uses e-cigarettes, and cannabis use were significantly associated with an increased likelihood of susceptibility to e-cigarette use in individuals without chronic lung disease. However, our analyses did not indicate a statistically significant interaction between chronic lung disease and any social, environmental, or behavioral factors on susceptibility to e-cigarette use.

Conclusions: Individuals without chronic lung disease were more susceptible to e-cigarette use than those with chronic lung disease. Although the prevalence of some behavioral and environmental factors differed among individuals with and without chronic lung disease, these factors did not moderate the association between chronic lung disease and susceptibility to e-cigarette use. Longitudinal investigations are warranted to better test the temporal relationships between chronic lung disease, substance use, social and environmental factors, and the susceptibility to e-cigarette use among individuals with chronic lung disease to identify prevention strategies for this population.

Keywords: COPD; asthma; chronic lung disease; e-cigarettes; moderators; predictors; susceptibility.

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Review

Ann Allergy Asthma Immunol

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Update on Allergic Fungal Rhinosinusitis

Andy J Chua [1], Ali Jafar [2], Amber U Luong [3]

Affiliations expand

- PMID: 36854353

- DOI: 10.1016/j.anai.2023.02.018

Abstract

Allergic fungal rhinosinusitis (AFRS) is a unique clinical entity that falls under the broader umbrella of chronic rhinosinusitis with nasal polyps (CRSwNP) with type 2 inflammation. It is characterized by nasal polyposis, production of characteristic thick eosinophilic mucin, and expansile change of involved sinus cavities. The diagnosis is classically made using the Bent and Kuhn criteria. However, recent studies have demonstrated lack of specificity of some major criteria. The need to fulfil all five criteria before diagnosing AFRS mitigates this partially, but renders the criteria cumbersome to use, and highlights the need to develop more specific criteria. Our understanding of AFRS pathophysiology has advanced significantly, and has helped elucidate the lack of histatins contributing to the inability to clear fungal spores, consequently leading to fungi-induced disruption of the epithelial barrier and stimulation of sinonasal epithelial cells. These trigger a cascade of type 2 inflammatory cytokines driven by both the adaptive and innate immune system. While more research is needed, these findings could hypothetically point to a limited type 3 immune response at the sinus mucosa, resulting in a compensatory over-stimulation of type 2 inflammatory processes. Treatment for AFRS remains centered on surgery and topical corticosteroids. Short courses of systemic corticosteroids may be used with caution, and fungal-specific immunotherapy and systemic antifungals are options in recalcitrant disease. Biologics show early promise, as we await data from randomized controlled trials under way. Finally, new insights into AFRS pathology provide opportunities for novel therapeutic strategies.

Keywords: allergic; allergic fungal rhinosinusitis; fungal allergy; nasal polyps; rhinosinusitis.

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Publication typesexpand

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Effects of an Ocrevus Rapid Infusion Protocol: A Literature Review and Quality Improvement Project

Courtney Brandt [1][2]

Affiliations expand

Abstract

The administration of Ocrevus, an infusion therapy for the treatment of multiple sclerosis, is time and labor intensive, leading to poor patient adherence, treatment delays due to scheduling issues, and significant staff workload. This problem worsened during the COVID-19 pandemic, which created scheduling difficulties due to space restrictions. A US Food and Drug Administration-approved rapid infusion protocol for Ocrevus decreases the infusion time by 1.5 hours per patient. The purpose of this project was to complete a literature review on rapid infusion protocols and analyze the effects of the Ocrevus rapid infusion protocol on 2 outcomes of interest: total visit time and infusion reaction rates. Data were collected using retrospective chart review and analyzed by comparing the results of each outcome to the same data points prior to the implementation of the

project. Results found a statistically significant decrease in visit time, with no increase in infusion reaction rates. These findings support the implementation of this rapid Ocrevus infusion protocol in the outpatient setting with the potential to improve patient scheduling, patient satisfaction, and nursing workload, while maintaining patient safety.

- 31 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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TURKISH VALIDITY AND RELIABILITY STUDY FOR THE PERCEIVED CONTROL OF ASTHMA QUESTIONNAIRE

Ziya Koçak [1], Huri Seval Gönderen Çakmak [2]

Affiliations expand

- PMID: 36853382

- DOI: 10.1080/02770903.2023.2185156

Abstract

Rationale: The prevalence of asthma is high in Turkish people. however, there is no measurement tool that evaluates the patient's perception that affects asthma management.

Aim: In this study, the aim was to test the validity and reliability of the Perceived Control of Asthma Questionnaire (PCAQ) among adults with asthma and to investigate the psychometric features.

Method: A total of 152 people aged 18 and over, who were diagnosed with asthma at least 1 year ago by a pulmonologist and volunteered to participate in the study were included in the study. The validity of the scale was investigated with exploratory factor analysis, confirmatory factor analysis and criterion validity, while the reliability of the scale was investigated with the Cronbach alpha coefficient and test-repeat test method. Item analysis, corrected item-total point correlations and mean item points for lower-upper 27% groups were investigated.

Results: According to exploratory factor analysis results, the Turkish form of the PCAQ appeared to explain 53.093% of total variance related to the feature measured. The results of confirmatory factor analysis calculated the goodness-of-fit values for the scale as χ^2/sd = 1.507, RMSEA = 0.058, GFI = 0.928, IFI = 0.958, and NFI = 0.886. Additionally, factor loads were ranked from 0.46 to 0.79. The Cronbach alpha internal consistency coefficient was 0.85. The corrected item-total coefficient correlations varied from 0.48 to 0.69.

Conclusion: All these results show the Perceived Control of Asthma Questionnaire (PCAQ) is a valid and reliable scale tool that can be used for Turkish adults with asthma.

Keywords: asthma; perception; reliability; scale; validity.

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Allergy

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BTEX exposure and its body burden pose differential risks for asthma and its phenotypic clusters

Yuan-Ting Hsu [# 1], Chao-Chien Wu [2], Chin-Chou Wang [2 3], Wen-Yu Chung [4], Chau-Chyun Sheu [5 6], Yi-Hsin Yang [7], Ming-Yen Cheng [8], Ruay-Sheng Lai [9], Sum-Yee Leung [2], Chi-Cheng Lin [10], Yu-Feng Wei [11], Ching-Hsiung Lin [12 13 14], Sheng-Hao Lin [12 13 14], Jeng-Yuan Hsu [15], Wei-Chang Huang [16 17 18 19 20], Chia-Cheng Tseng [2], Yung-Fa Lai [21], Meng-Hsuan Cheng [5 22], Huang-Chi Chen [23], Chih-Jen Yang [5], Chian-Heng Su [5 24], Chien-Jen Wang [1], Shih-Chang Hsu [25 26], Chih-Hsing Hung [27 28], Chon-Lin Lee [3 29], Ming-Shyan Huang [5 21], Shau-Ku Huang [# 1 30]

Affiliations expand

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

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[Barriers to and Facilitators of Asthma Care For Malaysian Hajj Pilgrims: A Qualitative Study](#)

[Rizawati Ramli](#) [1], [Nik Sherina Hanafi](#) [1], [Norita Hussein](#) [1], [Ping Yein Lee](#) [2], [Sazlina Shariff Ghazali](#) [3], [Ai Theng Cheong](#) [3], [Ahmad Ihsan Abu Bakar](#) [4], [Suhazeli Abdullah](#) [5], [Azah Abdul Samad](#) [5], [Hilary Pinnock](#) [6], [Aziz Sheikh](#) [6], [Ee Ming Khoo](#) [1]

Affiliations expand

Abstract

Asthma exacerbations are among the commonest reasons for hospitalizations in Malaysian pilgrims during the Hajj. We interviewed 21 stakeholders involved in the pre-Hajj health examination at 14 primary care clinics, to explore their perceptions on barriers to and facilitators of asthma care for Hajj pilgrims. The disadvantages of the short time frame and centralized organization of the pre-Hajj health examinations were viewed as compromising clinicians' level of competencies in asthma care, which could potentially be enhanced through more training, audit, and supervision by specialists. Longer time frame to permit sufficient disease control, provision of care by a dedicated asthma team, asthma registry to support continuous care, more resources of long-acting β-agonist/inhaled corticosteroid, and provision of influenza and pneumococcal vaccines at no cost were the perceived facilitators. Delivery of asthma education, especially the asthma action plan, should be tailored to the level of the pilgrim's health literacy and facilitated by educational resources, family engagement, and regular health briefing.

Keywords: Hajj; asthma; asthma care; primary care.

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Pediatr Pulmonol

Obstructive sleep apnea screening in children with asthma

Mudiaga O Sowho [1], Rachelle Koehl [1], Rebecca Shade [1], Eliza Judge [1], Han J Woo [1], Tianshi David Wu [2], Emily P Brigham [3], Nadia N Hansel [1], Jody Tversky [4], Laura M Sterni [5], Meredith C McCormack [1]

Affiliations expand

- PMID: 36852547

- DOI: 10.1002/ppul.26375

Abstract

Rationale: Obstructive sleep apnea is highly prevalent in children with asthma, particularly in obese children. The sleep related breathing disorder screening questionnaire has low screening accuracy for obstructive sleep apnea in children with asthma. Our goal was to identify the questions on the sleep related breathing disorder survey associated with obstructive sleep apnea in children with asthma.

Methods: Participants completed the survey, underwent polysomnography and their body mass index z-score was measured. Participants with survey scores above 0.33 were considered high risk for obstructive sleep apnea and those with an apnea hypopnea index ≥ 2 events/hour classified as having obstructive sleep apnea. Logistic regression was used to examine the association of each survey question and obstructive sleep apnea. Positive and negative predictive values were calculated to estimate screening accuracy.

Results: The prevalence of obstructive sleep apnea was 40% in our sample (n=136). Loud snoring, morning dry mouth and being overweight were the survey questions associated with obstructive sleep apnea. The composite survey score obtained from all twenty-two questions had positive and negative predictive values of 51.0% and 65.5%, while the combined model of loud snoring, morning dry mouth and being overweight had positive and negative predictive values of 60.3% and 77.6%. On the other hand, the body mass index z-score alone had positive and negative predictive values of 76.3% and 72.2%.

Conclusions: The body mass index z-score is useful for obstructive sleep apnea screening in children with asthma and should be applied routinely given its simplicity and concerns that obstructive sleep apnea may contribute to asthma morbidity. This article is protected by copyright. All rights reserved.

Keywords: Asthma; Obesity; Sleep apnea screening; Sleep disordered breathing.

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Virtually supported penicillin allergy de-labelling during COVID-19

Arian Ghassemian [1], Geetanjalee Sadi [1], Raymond Mak [2][3], Stephanie Erdle [2], Tiffany Wong [2], Samira Jeimy [4]

Affiliations expand

- PMID: 36849994

- PMCID: PMC9970128

- DOI: 10.1186/s13223-023-00770-x

Free PMC article

Abstract

Background: Penicillin allergy is a commonly listed medication allergy despite rare overall incidence. Many patients erroneously have this label, which has personal, health, and societal costs. Penicillin allergy delabelling requires an oral challenge, which can be a rate limiting step in the de-labeling process; this is even more relevant with the reduction of in-person visits during the COVID-19 pandemic.

Objective: To identify the utility and broader applicability of using a virtually supported platform, initially adopted given COVID-19 restrictions, to expedite penicillin oral provocation challenge and penicillin de-labeling in patients at low to moderate risk of immediate hypersensitivity reaction and based on shared decision making.

Methods: Patients in Vancouver catchment area were referred for penicillin allergy and virtually assessed by the consulting allergist between July 2020 and April 2021. Those deemed appropriate for oral challenge based on the allergist consultant were offered the option of a virtual oral provocation challenge to oral amoxicillin in a subsequent virtual visit. Patients who agreed and were consented underwent a virtually supervised oral amoxicillin challenge during the second virtual visit. Findings are summarized in this case series.

Results: Twenty-three patients, both adult and pediatric, ranging from no to significant co-morbidities were consented and underwent the virtual challenge. One hundred percent of patients were successful with no reaction after an hour post virtual oral provocation challenge with amoxicillin.

Conclusion: Virtual medicine is likely to remain in the allergist's practice. Virtually supported penicillin allergy delabelling, based on shared decision making and risk stratification, presents another pathway for penicillin allergy delabelling.

Keywords: Antimicrobial stewardship; COVID-19; Drug allergy; Penicillin allergy; Telemedicine.

Conflict of interest statement

- 9 references
- 1 figure

DRESS syndrome due to iodinated contrast media. A case report

G Zambrano Ibarra [1], B Noguerado Mellado [2], P Tornero Molina [2], C Cuevas Bravo [2], P Rojas Pérez-Esquerra [2]

Affiliations expand

Abstract

Background: The most frequent non-immediate reactions described with iodinated contrast media (ICM) are mild to moderate, however, some cases of patients with severe non-immediate reactions, such as drug eruption with eosinophilia and systemic symptoms (DRESS) have been described.

Case presentation: An 84-year-old patient developed DRESS syndrome after administration of ICM ioversol. The patient fullfilled the RegiSCAR diagnostic criteria for DRESS (definite score = 6). He underwent intradermal skin testing (IDT) with the widest panel of ICM available at our center. IDT was positive with ioversol and iomeprol. A punch biopsy was performed on the positive IDT with the culprit drug (ioversol) and histopathology was compatible with a T-cell mediated mechanism.

Conclusion: In this case, the IDT-positive biopsy was consistent with DRESS syndrome caused by T-lymphocyte activation, supporting the clinical diagnosis.

Keywords: Drug reaction with eosinophilia and systemic symptoms; Intradermal tests; Iodinated contrast media; Non-inmediate hypersensitivity reactions.

Conflict of interest statement

The authors declares that they have no competing interests.

- 12 references
- 2 figures

FULL TEXT LINKS

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Association between Cystic Fibrosis exacerbations, lung function, T2

inflammation and microbiological colonization

[Dana Albon](#) [1], [Lijia Zhang](#) [2], [James Patrie](#) [3], [Marieke Jones](#) [3], [Z Galvin Li](#) [4], [Emily Noonan](#) [5], [Larry Borish](#) [5 6]

Affiliations expand

Abstract

Background: The Cystic Fibrosis Foundation Patient Registry (CFFPR) reports a high prevalence of asthma (34.6%) in people with Cystic Fibrosis (PwCF). While our current understanding of this relationship is limited, a type 2 inflammatory (T2) phenotype has often been identified in CF patients.

Research question: This study aimed to evaluate the relationship between the eosinophilic CF T2 inflammatory phenotype and CF-related pulmonary outcomes and microbiological data.

Study design and methods: We conducted a retrospective chart review of adult patients with CF (18 and older; n = 93) receiving their care at University of Virginia Medical Center adult program from January, 2013 through December, 2018. Data collected included demographic data, CFTR (CF transmembrane conductance regulator) mutation, CF comorbidities, medications, Absolute Eosinophil Counts (AEC) in cells/μL and Immunoglobulin E (IgE) levels in IU/mL.

Results: Of 93 patients screened for study eligibility, 74 were included in the final analysis; 19 patients were excluded due to lack of longitudinal data across the study timeline. Lung function decline correlated with increased AEC ($p < 0.001$) and IgE ($p < 0.001$) even when adjusting for covariates: age, gender, presence of Pseudomonas spp., MRSA, other bacterial spp., Aspergillus spp., and other fungi ($p < 0.001$). Univariate analysis demonstrated that people with CF who experienced more than 2 exacerbations requiring hospitalizations and/or intravenous antibiotics a year were more likely to have high AEC (p

= 0.018). Logistic regression showed that as AEC increases, the probability that the measurement was taken during a CF exacerbation increases (p = 0.0039). A linear mixed model showed that each additional annual exacerbation event increased on average the log IgE by 0.04. (p = 0.015). This finding remained stable in a multivariate model (p = 0.0145). When adjusted for atopy, log IgE increases as the number of exacerbation events increases (p = 0.022). There was no association between AEC and IgE and microbiological colonization.

Interpretation: This study has shown that in CF patients, T2 inflammation based on serum AEC and IgE correlated with pulmonary exacerbations requiring hospitalizations and/or intravenous antibiotics, independent of bacterial airway colonization. In addition, lung function decline correlated with increased IgE and AEC. Further studies are needed to explore these correlations and potential impact on treatment.

Keywords: Bacteria; Cystic fibrosis; Eosinophil; Fungi; Immunoglobulin E; Pulmonary exacerbation; Type 2 inflammation.

Conflict of interest statement

No relevant conflicts exist for Dr. Dana Albon, Dr. Lijia Zhang, James Patrie, Dr. Marieke Jones, Galvin Li, Emily Noonan, and Dr. Larry Borish.

- 17 references
- 5 figures

SUPPLEMENTARY INFO

Grant supportexpand

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Review

Inflammopharmacology

The effects of vitamin C on respiratory, allergic and immunological diseases: an experimental and clinical-based review

Mohammad Hossein Eshaghi Ghalibaf [1][2], Farzaneh Kianian [2], Sima Beigoli [1], Sepideh Behrouz [1], Narges Marefati [3], Marzie Boskabady [4][5], Mohammad Hossein Boskabady [6][7]

Affiliations expand

- PMID: 36849854

- PMCID: PMC9970132

- DOI: 10.1007/s10787-023-01169-1

Abstract

Vitamin C is used in modern medicine supplements for treatment of various disorders associated with oxidative stress, inflammation and immune dysregulation. In this review article, experimental and clinical results regarding the effects of vitamin C on respiratory immunologic, and allergic diseases are reviewed. Various databases and appropriate keywords are used to search the effect of vitamin C on respiratory diseases until the end of May 2022. Books, theses and articles were included. These studies assessed the effects of vitamin C on respiratory disorders including asthma, chronic obstructive pulmonary disease (COPD), lung infection and lung cancer. Vitamin C showed relaxant effect on tracheal smooth muscle via various mechanisms. The preventive effects of vitamin C were mediated by antioxidant, immunomodulatory and anti-inflammatory mechanisms in the experimental animal models of different respiratory diseases. Some clinical studies also indicated the effect of vitamin C on lung cancer and lung infections. Therefore, vitamin C could be used a preventive and/or relieving therapy in respiratory diseases.

Conflict of interest statement

The authors declare that there are not competing interest in this article.

- 124 references
- 4 figures

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New Concepts in Barrier Dysfunction in CRSwNP and Emerging Roles of Tezepelumab and Dupilumab

Simon Chiang [1], Stella E Lee [1]

Affiliations expand

- PMID: 36848281

Abstract

Background: Epithelial barrier disturbances in CRSwNP patients play an important role in both the innate and adaptive immune responses, contributing to chronic inflammation, olfactory dysfunction, and impairments in quality of life.

Objective: To evaluate the role of the sinonasal epithelium in disease and health, review the pathophysiology of epithelial barrier dysfunction in CRSwNP, and the immunologic targets for treatment.

Methods: Literature review.

Results: Blockade of cytokines such as thymic stromal lymphopoietin (TSLP), IL-4, and IL-13 have shown promise in barrier restoration and IL-13, specifically may be central to olfactory dysfunction.

Conclusion: The sinonasal epithelium plays a crucial role in the health and function of the mucosa and immune response. Increased understanding of the local immunologic dysfunction has led to several therapeutics that can potentially restore epithelial barrier function and olfaction. Real world and comparative effectiveness studies are needed.

Keywords: AERD; TSLP; allergic rhinitis; asthma; atopic dermatitis; barrier dysfunction; chronic rhinosinusitis; dupilumab; nasal polyps; tezepelumab.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Understanding the CRSwNP Patient as Whole

Sindhura Bandi [1], Ellen Stephen [1], Keerthi Bansal [1], Mahboobeh Mahdavinia [1]

Affiliations expand

- PMID: 36848278

- DOI: [10.1177/19458924231152671](10.1177/19458924231152671)

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a distinct inflammatory disease of the upper airways with a significant impact on the health and quality of life of affected patients. Several comorbid conditions such as allergic rhinitis, asthma, sleep disorders, and gastroesophageal reflux disease are commonly reported in patients with CRSwNP.

Objective: In this article, we intended to review the UpToDate information on how these comorbidities can impact CRSwNP patients' health and well-being.

Methods: A PUBMED search was performed to review relevant recent article on the topic.

Results: While there have been significant advances in the knowledge and management options for CRSwNP in the past few years, additional studies are needed to understand the underlying pathophysiologic mechanisms of these associations. In addition, awareness of the impact of CRSwNP on mental health, quality of life, and cognition is paramount to treating this condition.

Conclusion: Recognition and addressing CRSwNP comorbidities such as allergic rhinitis, asthma, sleep disorders, gastroesophageal reflux disease, and cognitive function impairment are important to optimally understand and manage the patient with CRSwNP as a whole.

Keywords: allergic rhinitis; asthma; chronic rhinosinusitis; cognitive function; gastroesophageal reflux disease (GERD); nasal polyps; sleep disorders.

SUPPLEMENTARY INFO

MeSH termsexpand

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Scientific Advancements That Empower Us to Understand CRS Pathophysiology

Hannan A Qureshi [1], Zechariah G Franks [1], Asiana Gurung [1], Murugappan Ramanathan Jr [1]

Affiliations expand

- PMID: 36848272

- DOI: 10.1177/19458924221148026

Abstract

Background: Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a multifactorial inflammatory condition that remains poorly understood. Over the past decade, we have witnessed impressive scientific advancements that have allowed us to better understand the molecular and cellular mechanisms that underlie the inflammatory processes in mucosal diseases including asthma, allergic rhinitis, and CRSwNP.

Objective: The present review aims to summarize and highlight the most recent scientific advancements that have enriched our understanding of CRSwNP.

Methods: A comprehensive review of the available literature on the use of new scientific techniques in CRSwNP was performed. We evaluated the most recent evidence from

studies using animal models, cell cultures, and genome sequencing techniques and their impact on our understanding of CRSwNP pathophysiology.

Results: Our understanding of CRSwNP has rapidly progressed with the development of newer scientific techniques to interrogate various pathways involved in its pathogenesis. Animal models remain powerful tools and have elucidated the mechanisms behind esinophilic inflammation in CRSwNP; however, animal models reproducing polyp formation are relatively sparse. 3D cell cultures have significant potential to better dissect the cellular interactions with the sinonasal epithelium and other cell types in CRS. Additionally, some groups are starting to utilize single-cell RNA sequencing to investigate RNA expression in individual cells with high resolution and on a genomic scale.

Conclusion: These emerging scientific technologies represent outstanding opportunities to identify and develop more targeted therapeutics for different pathways that lead to CRSwNP. An additional understanding of these mechanisms will be critical for developing future therapies for CRSwNP.

Keywords: animal models; chronic rhinosinusitis; genetic polymorphisms; nasal polyposis; organoids; single-cell sequencing.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Review

B Lineage Cells and IgE in Allergic Rhinitis and CRSwNP and the Role of Omalizumab Treatment

Junqin Bai [1], Bruce K Tan [1][2]

Affiliations expand

Abstract

Background: Allergic rhinitis (AR) and chronic rhinosinusitis (CRS) are two prevalent nasal diseases where both type 2 inflammation and immunoglobulin E (IgE) may play important roles. Although they can exist independently or comorbidly, subtle but important differences exist in immunopathogenesis.

Objective: To summarize current knowledge of pathophysiological roles of B lineage cells and IgE in AR and CRS with nasal polyps (CRSwNP).

Methods: Searched PubMed database, reviewed AR and CRSwNP-related literature, and discussed disease diagnosis, comorbidity, epidemiology, pathophysiology, and treatment. Similarities and differences in B-cell biology and IgE are compared in the 2 conditions.

Results: Both AR and CRSwNP have evidence for pathological type 2 inflammation, B-cell activation and differentiation, and IgE production. However, distinctions exist in the clinical and serological profiles at diagnosis, as well as treatments utilized. B-cell activation in AR may more frequently be regulated in the germinal center of lymphoid follicles, whereas CRSwNP may occur via extrafollicular pathways although controversies remain in these initial activating events. Oligoclonal and antigen-specific IgE maybe predominate in AR, but polyclonal and antigen-nonspecific IgE may predominate in CRSwNP. Omalizumab has been shown efficacious in treating both AR and CRSwNP in multiple clinical trials but is the only Food and Drug Administration-approved anti-IgE biologic to treat CRSwNP or allergic asthma. *Staphylococcus aureus* frequently colonizes the nasal airway and has the ability to activate type two responses including B-cell responses although the extent to which it modulates AR and CRSwNP disease severity is being investigated.

Conclusion: This review highlights current knowledge of the roles of B cells and IgE in the pathogenesis of AR and CRSwNP and a small comparison between the 2 diseases. More

systemic studies should be done to elevate the understanding of these diseases and their treatment.

Keywords: B cell; allergic rhinitis; autoantibody; chronic rhinosinusitis with nasal polyps; extrafollicular; germinal center; immunoglobulin E; omalizumab; plasma cell; type 2 inflammation.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Using Social Media Data to Investigate Public Perceptions of Cannabis as a Medicine: Narrative Review

Sedigh Khademi [1][2], Christine Mary Hallinan [1][3], Mike Conway [4], Yvonne Bonomo [1][5]

Affiliations expand

- PMID: 36848191

- DOI: 10.2196/36667

Abstract

Background: The use and acceptance of medicinal cannabis is on the rise across the globe. To support the interests of public health, evidence relating to its use, effects, and safety is required to match this community demand. Web-based user-generated data are often used by researchers and public health organizations for the investigation of consumer perceptions, market forces, population behaviors, and for pharmacoepidemiology.

Objective: In this review, we aimed to summarize the findings of studies that have used user-generated text as a data source to study medicinal cannabis or the use of cannabis as medicine. Our objectives were to categorize the insights provided by social media research on cannabis as medicine and describe the role of social media for consumers using medicinal cannabis.

Methods: The inclusion criteria for this review were primary research studies and reviews that reported on the analysis of web-based user-generated content on cannabis as medicine. The MEDLINE, Scopus, Web of Science, and Embase databases were searched from January 1974 to April 2022.

Results: We examined 42 studies published in English and found that consumers value their ability to exchange experiences on the web and tend to rely on web-based information sources. Cannabis discussions have portrayed the substance as a safe and natural medicine to help with many health conditions including cancer, sleep disorders, chronic pain, opioid use disorders, headaches, asthma, bowel disease, anxiety, depression, and posttraumatic stress disorder. These discussions provide a rich resource for researchers to investigate medicinal cannabis-related consumer sentiment and experiences, including the opportunity to monitor cannabis effects and adverse events, given the anecdotal and often biased nature of the information is properly accounted for.

Conclusions: The extensive web-based presence of the cannabis industry coupled with the conversational nature of social media discourse results in rich but potentially biased information that is often not well-supported by scientific evidence. This review summarizes what social media is saying about the medicinal use of cannabis and discusses the challenges faced by health governance agencies and professionals to make use of web-based resources to both learn from medicinal cannabis users and provide factual, timely, and reliable evidence-based health information to consumers.

Keywords: internet; medical marijuana; medicinal cannabis; public health surveillance; social media.

Effect of an Intranasal Corticosteroid on Quality of Life and Local Microbiome in Young Children With Chronic Rhinosinusitis: A Randomized Clinical Trial

Marta Latek [1], Piotr Lacwik [2], Katarzyna Molinska [1], Andrzej Blauz [3], Jakub Lach [4], Blazej Rychlik [3], Dominik Strapagiel [4], Joanna Majak [5], Joanna Molinska [1], Dorota Czech [6], Michal Seweryn [7], Piotr Kuna [1], Cezary Palczynski [2], Pawel Majak [8]

Affiliations expand

- PMID: 36848113

- PMCID: PMC9972242 (available on 2024-02-27)

Abstract

Importance: Intranasal corticosteroids (INCs) remain the first-line treatment of chronic rhinosinusitis (CRS) in both adults and children, despite the lack of evidence regarding their efficacy in the pediatric population. Similarly, their effect on the sinonasal microbiome has not been well documented.

Objective: To assess the clinical, immunological, and microbiological effects of 12 weeks of an INC in young children with CRS.

Design, setting, and participants: This open-label randomized clinical trial was performed in a pediatric allergy outpatient clinic in 2017 and 2018. Children aged 4 to 8 years with CRS diagnosed by a specialist were included. Data were analyzed from January 2022 to June 2022.

Interventions: Patients were randomized to receive intranasal mometasone in an atomizer for 12 weeks (1 application per nostril, once per day) and supplemental 3-mL sodium chloride (NaCl), 0.9%, solution in a nasal nebulizer once a day for 12 weeks (INC group) or 3-mL NaCl, 0.9%, solution in a nasal nebulizer once a day for 12 weeks (control group).

Main outcomes and measures: Measures taken both before and after treatment included the Sinus and Nasal Quality of Life Survey (SN-5), a nasopharynx swab for microbiome analysis by next-generation sequencing methods, and nasal mucosa sampling for occurrence of innate lymphoid cells (ILCs).

Results: Of the 66 children enrolled, 63 completed the study. The mean (SD) age of the cohort was 6.1 (1.3) years; 38 participants (60.3%) were male and 25 (39.7%) were female. The clinical improvement reflected by reduction in SN-5 score was significantly higher in the INC group compared with the control group (INC group score before and after treatment, 3.6 and 3.1, respectively; control group score before and after treatment, 3.4 and 3.8, respectively; mean between-group difference, -0.58; 95% CI, -1.31 to -0.19; P = .009). The INC group had a greater increase in nasopharyngeal microbiome richness and larger decrease in nasal ILC3 abundance compared with the control group. A significant interaction was observed between change in microbiome richness and the INC intervention on the prediction of significant clinical improvement (odds ratio, 1.09; 95% CI, 1.01-1.19; P = .03).

Conclusions and relevance: This randomized clinical trial demonstrated that treatment with an INC improved the quality of life of children with CRS and had a significant effect on increasing sinonasal biodiversity. Although further investigation is needed of the long-term

efficacy and safety of INCs, these data may reinforce the recommendation of using INCs as a first-line treatment of CRS in children.

Trial registration: ClinicalTrials.gov Identifier: NCT03011632.

Conflict of interest statement

SUPPLEMENTARY INFO

Associated dataexpand

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Impact of multimorbidity patterns in hospital admissions: the case study of asthma

Diana Portela [1][2][3], Pedro Pereira Rodrigues [1][3], Alberto Freitas [1][3], Elísio Costa [3][4], Jean Bousquet [5][6][7], João Almeida Fonseca [1][3], Bernardo Sousa Pinto [1][3]

Affiliations expand

- PMID: 36848045

Abstract

Most previous studies assessing multimorbidity in asthma assessed the frequency of individual comorbid diseases. We aimed to assess the frequency and clinical and economic impact of co-occurring groups of comorbidities (comorbidity patterns using the Charlson Comorbidity Index) on asthma hospitalizations. We assessed the dataset containing a registration of all Portuguese hospitalisations between 2011-2015. We applied three different approaches (regression models, association rule mining, and decision trees) to assess both the frequency and impact of comorbidities patterns in the length-of-stay, in-hospital mortality and hospital charges. For each approach, separate analyses were performed for episodes with asthma as main and as secondary diagnosis. Separate analyses were performed by participants' age group. We assessed 198340 hospitalizations in patients >18 years old. Both in hospitalizations with asthma as main or secondary diagnosis, combinations of diseases involving cancer, metastasis, cerebrovascular disease, hemiplegia/paraplegia, and liver disease displayed a relevant clinical and economic burden. In hospitalizations having asthma as a secondary diagnosis, we identified several comorbidity patterns involving asthma and associated with increased length-of-stay (average impact of 1.3-3.2 additional days), in-hospital mortality (OR range = 1.4-7.9) and hospital charges (average additional charges of 351.0 to 1025.8 Euro compared with hospitalizations without any registered Charlson comorbidity). Consistent results were observed with association rules mining and decision tree approaches. Our findings highlight the importance not only of a complete assessment of patients with asthma, but also of considering the presence of asthma in patients admitted by other diseases, as it may have a relevant impact on clinical and health services outcomes.

Keywords: asthma multimorbidity patterns; economic impact; intelligent data analysis.

Proceed to details

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Small airway disease and asthma control

Seda Beyhan Sağmen [1], Berrin Zinnet Eraslan [1], Ersin Demirer [1], Nesrin Kiral [1], Sevda Comert [1]

Affiliations expand

- PMID: 36847658

- DOI: 10.1080/02770903.2023.2185894

Abstract

Aim: Maximum mid-expiratory flow (MMEF) is one of the pulmonary function tests that report small airway disease. Our study aimed to investigate the role of MMEF values in asthma control, the prevalence of small airway disease, and their effect on asthma control in patients with asthma with normal forced expiratory volume in one second (FEV_1) values.

Material and method: Patients who presented to the Chest Diseases outpatient clinic of our hospital between 2018 and 2019 and were diagnosed as having asthma were included in the study. The characteristics of the patients, pulmonary function tests, their asthma treatment, and asthma control test (ACT) scores were recorded. Patients with FEV_1 <80 in the pulmonary function test, those with additional lung disease, those who had an attack in the last 4 weeks, and patients who smoked were excluded from the study. MMEF <65 was defined as small airway disease.

Results: The MMEF (%) and MMEF (L) values of the group with uncontrolled asthma were found to be statistically significantly lower than those of the controlled asthma group (p = 0.016 and p = 0.003, respectively). MMEF (%) and MMEF (L) values in those with wheezing were found to be significantly lower compared with those without wheezing (p = 0.025 and p = 0.049, respectively). The MMEF (%) and MMEF (L) values of the patients with nocturnal symptoms were found to be statistically significantly lower than in patients without nocturnal symptoms (p = 0.023 and p = 0.041, respectively). ACT values of patients with MMEF <65 were found to be statistically lower than those of patients with MMEF >65 (0.047).

Conclusion: Considering small airway disease in patients with asthma may be beneficial in clinical practice.

Proceed to details

Cite

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Discovery of 2-Aminopyrimidines as Potent Agonists for the Bitter Taste Receptor TAS2R14

Lukas Waterloo [1], Harald Hübner [1], Fabrizio Fierro [2], Tara Pfeiffer [1], Regine Brox [1], Stefan Löber [1], Dorothee Weikert [1], Masha Y Niv [2], Peter Gmeiner [1]

Affiliations expand

- PMID: 36847646

- DOI: 10.1021/acs.jmedchem.2c01997

Abstract

The bitter taste receptor TAS2R14 is a G protein-coupled receptor that is found on the tongue as well as in the human airway smooth muscle and other extraoral tissues. Because its activation causes bronchodilatation, TAS2R14 is a potential target for the treatment of asthma or chronic obstructive pulmonary disease. Structural variations of flufenamic acid, a nonsteroidal anti-inflammatory drug, led us to 2-aminopyridines showing considerable efficacy and potency in an IP_1 accumulation assay. In combination with an exchange of the carboxylic moiety by a tetrazole unit, a set of promising new TAS2R14 agonists was

developed. The most potent ligand **28.1** (EC$_{50}$ = 72 nM) revealed a six-fold higher potency than flufenamic acid and a maximum efficacy of 129%. Besides its unprecedented TAS2R14 activation, **28.1** revealed marked selectivity over a panel of 24 non-bitter taste human G protein-coupled receptors.

Proceed to details

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Association between polymorphisms of the *GSDMB* gene and allergic rhinitis risk in the Chinese population: a case–control study

Bilal Haider Shamsi [1], Haiyuan Chen [2], Xiong Yang [3], Mingxia Liu [4], Yonglin Liu [1]

Affiliations expand

- PMID: 36847643

Abstract

Background: Allergic rhinitis (AR) is a great risk factor for developing asthma, and its pathogenesis is affected by various factors, such as gene and environment. *GSDMB* is related to allergic diseases. Our purpose is to explore the correlation of single nucleotide polymorphisms (SNPs) in *GSDMB* and AR risk in the Chinese population.

Methods: We performed a case-control study including 1005 cases and 1004 controls. Rs2305479, rs4795400, and rs12450091 in *GSDMB* were geneotyped using Agena MassARRAY. The relationships between *GSDMB* SNPs and AR risk were assessed by logistic regression analysis in PLINK1.9.

Results: Our study showed that rs4795400 was a protective factor for AR in overall (TT vs. CC: OR = 0.66, p = 0.009; TT vs. CC/TC: OR = 0.67, p = 0.008; additive: OR = 0.87, p = 0.042 males, people with BMI ≤ 24, and living in wind-blown sand area. Rs2305479 was associated with a reduced AR risk in males (TT vs. CC: OR = 0.47, p = 0.014; TT vs. CC/TC: OR = 0.43, p = 0.004). However, rs12450091 was a risk factor for AR in people living in the loess hilly region (CC: OR = 4.75, p = 0.047). The levels of EO and EO_per in the case group were significantly higher than those in the control group (p < 0.05).

Conclusion: This study indicated thst *GSDMB* polymprphisms (rs4795400, rs2305479, and rs12450091) were associated with AR susceptibility. Further studies are required to confirm our findings and to clarify the functional relationship.

Keywords: Allergic rhinitis; Chinese population; GSDMB; Single nucleotide polymorphisms.

Proceed to details

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Predictors of success/failure in the control of asthmatic smoking patients under conditions of clinical practice

Abel Pallarés-Sanmartín [1], María Del Mar Mosteiro-Añón [2], María Macía [3], Nagore Blanco [4], David Barros-Casas [1], María Dolores Corbacho Abelaira [5], Toni Fernández-Sánchez [6], Federico Fiorentino [7]

Affiliations expand

Abstract

Background: Tobacco smoking directly affects the airway, where it triggers a very strong local inflammatory response.

Objective: To determine the predictors of improvement or worsening of asthma control in asthmatic smokers.

Methods: Observational, prospective, multicenter, single cohort study, carried out in the outpatient pulmonology departments with a follow-up period of 6 months. The treatment was adjusted according to the indications of standard clinical practice.

Results: 196 patients were included, with a mean age of 54.64 years.39% of the patients were active smokers. Interpreting an Asthma Control Questionnaire (ACQ) score of ≤ 0.75 as asthma control, this was achieved in 30.2% of the cases. Patients with greater adherence were more likely to improve their asthma symptoms ($p < 0.05$), defined as a decrease in ACQ of 0.5 points or more at the final visit, while taking concomitant medication was a negative risk factor for improvement ($p < 0.001$). An eosinophil value >300 was a predictor for achieving control ($p < 0.01$). Patients treated with fluticasone propionate/formoterol versus those receiving budesonide/formoterol or beclomethasone/formoterol had a lower ACQ score ($p < 0.01$ and $p < 0.01$, respectively).

Conclusion: Asthmatic patients with active tobacco exposure and a higher number of anti-asthma medications are more likely to have poorer control. Correct adherence to treatment is the main intervention to be performed to achieve the control. An eosinophil count greater than 300 was the main predictor for achieving control. Fluticasone propionate/formoterol FP/FORM was associated with a greater likelihood of improving ACQ score.

Keywords: Adult; asthma; bronchodilator agents; chronic disease; eosinophilia; glucocorticoids; prospective studies; quality of life; surveys and questionnaires; tobacco.

Proceed to details

Cite

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Adult asthma with symptomatic eosinophilic inflammation is accompanied by alteration in gut microbiome

Bon-Hee Gu [#1], Jun-Pyo Choi [#2], Tansol Park [3], A-Sol Kim [4], Ho Young Jung [5], Doo Young Choi [5], Sang Jin Lee [6], Yoon-Seok Chang [2], Myunghoo Kim [1 7], Han-Ki Park [5]

Affiliations expand

- PMID: 36847620

Abstract

Background: Accumulating evidence suggests that the gut microbiome is associated with asthma. However, altered gut microbiome in adult asthma is not yet well established. We aimed to investigate the gut microbiome profiles of adult asthmatic patients with symptomatic eosinophilic inflammation.

Methods: The 16s rRNA gene metagenomic analysis of feces in the symptomatic eosinophilic asthma group (EA, N=28) was compared with the healthy control (HC, N=18) and the chronic cough control (CC, N=13). A correlation analysis between individual taxa and clinical markers was performed within the EA group. Changes in the gut microbiome were examined in patients with significant symptom improvement in the EA group.

Results: The relative abundances of Lachnospiraceae and Oscillospiraceae significantly decreased and Bacteroidetes increased in the EA group. Within EA group, Lachnospiraceae was negatively correlated with indicators of type 2 inflammation and lung function decline. Enterobacteriaceae and Prevotella was positively associated with type 2 inflammation and lung function decline, respectively. The abundance of predicted genes associated with amino acid metabolism and secondary bile acid biosynthesis was diminished in the EA

group. These functional gene family alterations could be related to gut permeability, and the serum lipopolysaccharide concentration was actually high in the EA group. EA patients with symptom improvement after 1 month did not show a significant change in the gut microbiome.

Conclusions: Symptomatic eosinophilic adult asthma patients showed altered the gut microbiome composition. Specifically, a decrease in commensal clostridia was observed, and a decrease in Lachnospiraceae was correlated with blood eosinophilia and lung function decline.

Keywords: Adult; Asthma; Eosinophils; Gut Microbiome.

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Climate change and public health: The effects of global warming on the risk of allergies and autoimmune diseases: The effects of global warming on the risk of allergies and autoimmune diseases

Alexandra S Lee[1], Juan Aguilera[1], Jo Ann Efobi[1], Youn Soo Jung[1], Hana Seastedt[1], Mihir M Shah[1], Emily Yang[2], Katherine Konvinse[3], Paul J Utz[2,4], Vanitha Sampath[#,1], Kari C Nadeau[#,1,5]

Affiliations expand

Abstract

Global climate change and extreme weather events are associated with epigenetic modifications in immune cells, leading to the possible increased risk and prevalence of allergies and autoimmune diseases.

- 15 references

SUPPLEMENTARY INFO

Grant supportexpand

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☐ 79

The Sleep Environment, Napping, and Sleep Outcomes among Urban Children With and Without Asthma

[Anna J Yeo](#) [1][2][3], [Anna Cohenuram](#) [1], [Shira Dunsiger](#) [4], [Julie Boergers](#) [1][2][5], [Sheryl J Kopel](#) [1][2][5], [Daphne Koinis-Mitchell](#) [1][2][5]

Affiliations expand

Abstract

Objectives: Children with asthma living in U.S. urban neighborhoods experience increased risk for asthma morbidity and poor sleep outcomes. In addition to asthma, environmental factors (e.g. noise, uncomfortable temperature, light exposure) related to urban poverty may disturb children's sleep. This study examined the association between environmental factors and sleep outcomes among urban children with and without asthma, and whether napping underlies the environment-sleep link. Additionally, the study tested whether these associations differed by health status (i.e. asthma) or race/ethnicity.

Method: Participants included urban children aged 7-9 years with (N = 251) and without (N = 130) asthma from Latino, Black, or non-Latino White (NLW) background. Caregivers reported sleep environmental factors and naps. Sleep duration, efficiency, and nightly awakenings were assessed via actigraphy.

Results: Regardless of health status, frequent exposure to noise and light was associated with poorer sleep outcomes only among Latino children. In the full sample with and without asthma, noise exposure during nighttime sleep was related to more frequent daytime naps, which were linked to shorter nighttime sleep duration.

Conclusions: Exposure to noise and light may play a particularly influential role in shaping urban children's sleep outcomes. Racial/ethnic differences and the potential mediating role of napping in this environment-sleep association may inform tailored interventions.

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Benchmarking omics-based prediction of asthma development in children

[Xu-Wen Wang](#) [1], [Tong Wang](#) [1], [Darius P Schaub](#) [2], [Can Chen](#) [1], [Zheng Sun](#) [1], [Shanlin Ke](#) [1], [Julian Hecker](#) [1], [Anna Maaser-Hecker](#) [3], [Oana A Zeleznik](#) [1], [Roman Zeleznik](#) [4], [Augusto A Litonjua](#) [5], [Dawn L DeMeo](#) [1], [Jessica Lasky-Su](#) [1], [Edwin K Silverman](#) [1], [Yang-Yu Liu](#) [6 7], [Scott T Weiss](#) [8]

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Abstract

Background: Asthma is a heterogeneous disease with high morbidity. Advancement in high-throughput multi-omics approaches has enabled the collection of molecular assessments at different layers, providing a complementary perspective of complex diseases. Numerous computational methods have been developed for the omics-based patient classification or disease outcome prediction. Yet, a systematic benchmarking of those methods using various combinations of omics data for the prediction of asthma development is still lacking.

Objective: We aimed to investigate the computational methods in disease status prediction using multi-omics data.

Method: We systematically benchmarked 18 computational methods using all the 63 combinations of six omics data (GWAS, miRNA, mRNA, microbiome, metabolome, DNA methylation) collected in The Vitamin D Antenatal Asthma Reduction Trial (VDAART) cohort. We evaluated each method using standard performance metrics for each of the 63 omics combinations.

Results: Our results indicate that overall Logistic Regression, Multi-Layer Perceptron, and MOGONET display superior performance, and the combination of transcriptional, genomic and microbiome data achieves the best prediction. Moreover, we find that including the clinical data can further improve the prediction performance for some but not all the omics combinations.

Conclusions: Specific omics combinations can reach the optimal prediction of asthma development in children. And certain computational methods showed superior performance than other methods.

Keywords: Asthma; Disease status; Multi-omics; Prediction.

Conflict of interest statement

- 57 references
- 6 figures

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MeSH terms, Substancesexpand

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81

Monoclonal Antibodies

No authors listed

In: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012.

2023 Feb 28.

- PMID: 31644151

Excerpt

Monoclonal antibodies are immunoglobulins that have a high degree of specificity (mono-specificity) for an antigen or epitope. Monoclonal antibodies are typically derived from a clonal expansion of antibody producing malignant human plasma cells. The initial monoclonal antibodies were created by fusing spleen cells from an immunized mouse with human or mouse myeloma cells (malignant self-perpetuating antibody producing cells), and selecting out and cloning the hybrid cells (hybridomas) that produced the desired antibody reactivity. These initial monoclonal products were mouse antibodies and were very valuable in laboratory and animal research and diagnostic assays, but were problematic as therapeutic agents because of immune reactions to the foreign mouse protein. Subsequently, production of chimeric mouse-human monoclonal antibodies and means of further "humanizing" them and producing fully human recombinant monoclonal antibodies were developed. The conventions used in nomenclature of monoclonal antibodies indicate whether they are mouse dervied (-omab), chimeric (-ximab), humanized (-zumab) or fully human (-umab).

Monoclonal antibodies have broad clinical and experimental medical uses. Many of the initial monoclonal antibodies used in clinical medicine were immunomodulatory agents with activity against specific immune cells, such as CD4 or CD3 lymphocytes, which are important in the pathogenesis of rejection after solid organ transplantation. Subsequently, monoclonal antibodies were prepared against specific cytokines (anti-cytokines), which were believed to play a role in cell and tissue damage in immunologically mediated diseases such as rheumatoid arthritis, alkylosing spondylitis, inflammatory bowel disease, multiple sclerosis and psoriasis, among others. In addition, therapeutic monoclonal antibodies were developed, aimed at blocking or inhibiting the activity of specific enzymes, cell surface transporters or signaling molecules and have been used in cancer chemotherapy and to treat severe viral infections. Use of monoclonal antibodies is currently broadening to therapy of other severe, nonmalignant conditions including asthma, atopic dermatitis, migraine headaches, hypercholesterolemia, osteoporosis, bacterial diseases (such as anthrax) and viral infections (such as COVID-19). Thus, the therapeutic monoclonal antibodies do not fall into a single class and have broad therapeutic uses. As of 2022, more than 80 therapeutic monoclonal antibodies have been approved for use in the United States.

Monoclonal antibodies are generally well tolerated. Because they are large proteins (typically 150-200,000 daltons in size) they require parenteral, often intravenous, administration. Circulating proteins are metabolized by many cells, but particularly by hepatocytes. Proteins undergo hepatic uptake by endocytosis and are either degraded or

recycled to the cell surface for secretion. The hepatic metabolism of antibodies often determines their half-life. Proteins are broken down by cellular proteases into small peptides and amino acids that can used to synthesize other proteins. Metabolism of proteins does not generate toxic intermediates and, therefore, monoclonal antibodies are unlikely to induce drug induced liver injury via production of toxic metabolites. On the other hand, the peptides that are generated by the metabolism of the exogenously administered protein may ultimately be presented as foreign epitopes and generate an immune response. In addition, the primary effect of the monoclonal antibody may generate a response, either immune or otherwise, that leads to an immune mediate hepatic injury. Finally, monoclonal antibodies that suppress the immune system may cause reactivation of latent infections, including tuberculosis, herpes simplex, varicella zoster (shingles) and hepatitis B.

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Publication typesexpand

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☐ 82

Intergenerational transmission of the effects of maternal exposure to

childhood maltreatment in the USA: a retrospective cohort study

Nora K Moog [1], Peter D Cummings [2], Kathryn L Jackson [2], Judy L Aschner [3], Emily S Barrett [4], Theresa M Bastain [5], Courtney K Blackwell [2], Michelle Bosquet Enlow [6], Carrie V Breton [7], Nicole R Bush [8], Sean C L Deoni [9], Cristiane S Duarte [10], Assiamira Ferrara [11], Torie L Grant [12], Alison E Hipwell [13], Kathryn Jones [14], Leslie D Leve [15], Stephanie Lovinsky-Desir [16], Richard K Miller [17], Catherine Monk [10], Emily Oken [14], Jonathan Posner [18], Rebecca J Schmidt [19], Rosalind J Wright [20], Sonja Entringer [21], Hyagriv N Simhan [22], Pathik D Wadhwa [23], Thomas G O'Connor [24], Rashelle J Musci [25], Claudia Buss [26]; ECHO collaborators

Affiliations expand

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Abstract

Background: Childhood maltreatment is associated with adverse health outcomes and this risk can be transmitted to the next generation. We aimed to investigate the association between exposure to maternal childhood maltreatment and common childhood physical and mental health problems, neurodevelopmental disorders, and related comorbidity patterns in offspring.

Methods: We conducted a retrospective cohort study using data from the Environmental influences on Child Health Outcomes (ECHO) Program, which was launched to investigate the influence of early life exposures on child health and development in 69 cohorts across the USA. Eligible mother-child dyads were those with available data on maternal childhood maltreatment exposure and at least one child health outcome measure (autism spectrum disorder, attention-deficit hyperactivity disorder [ADHD], internalising problems, obesity, allergy, and asthma diagnoses). Maternal history of childhood maltreatment was obtained retrospectively from the Adverse Childhood Experiences or Life Stressor Checklist questionnaires. We derived the prevalence of the specified child health outcome measures in offspring across childhood and adolescence by harmonising caregiver reports and other relevant sources (such as medical records) across cohorts. Child internalising symptoms were assessed using the Child Behavior Checklist. Associations between maternal

childhood maltreatment and childhood health outcomes were measured using a series of mixed-effects logistic regression models. Covariates included child sex (male or female), race, and ethnicity; maternal and paternal age; maternal education; combined annual household income; maternal diagnosis of depression, asthma, ADHD, allergy, or autism spectrum disorder; and maternal obesity. Two latent class analyses were conducted: to characterise patterns of comorbidity of child health outcomes; and to characterise patterns of co-occurrence of childhood maltreatment subtypes. We then investigated the association between latent class membership and maternal childhood maltreatment and child health outcomes, respectively.

Findings: Our sample included 4337 mother-child dyads from 21 longitudinal cohorts (with data collection initiated between 1999 and 2016). Of 3954 mothers in the study, 1742 (44%) had experienced exposure to abuse or neglect during their childhood. After adjustment for confounding, mothers who experienced childhood maltreatment were more likely to have children with internalising problems in the clinical range (odds ratio [OR] 2·70 [95% CI 1·95-3·72], p<0·0001), autism spectrum disorder (1·70 [1·13-2·55], p=0·01), ADHD (2·09 [1·63-2·67], p<0·0001), and asthma (1·54 [1·34-1·77], p<0·0001). In female offspring, maternal childhood maltreatment was associated with a higher prevalence of obesity (1·69 [1·17-2·44], p=0·005). Children of mothers exposed to childhood maltreatment were more likely to exhibit a diagnostic pattern characterised by higher risk for multimorbidity. Exposure to multiple forms of maltreatment across all subtypes of maternal childhood maltreatment was associated with the highest risk increases for most offspring health outcomes, suggesting a dose-response relationship.

Interpretation: Our findings suggest that maternal childhood maltreatment experiences can be a risk factor for disease susceptibility in offspring across a variety of outcomes and emphasise the need for policies focusing on breaking the intergenerational transmission of adversity.

Funding: Environmental influences on Child Health Outcomes Program, Office of the Director, National Institutes of Health.

Conflict of interest statement

- 49 references
- 2 figures

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Biologika – die erste Wahl bei schwerem Asthma

[Article in German]

Dagmar Kraus[1]

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- 1 reference

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Denken Sie bei Asthma auch an die Allergenimmuntherapie!

[Article in German]

Dagmar Kraus [1]

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- 2 references

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Randomized Controlled Trial

Comparing GPs' antibiotic prescribing decisions to a clinical prediction rule: an online vignette study

Martine Nurek [1], Alastair D Hay [2], Olga Kostopoulou [1]

Affiliations expand

- PMID: 36823069

- PMCID: PMC9975984

- DOI: 10.3399/BJGP.2020.0802

Abstract

Background: The 'STARWAVe' clinical prediction rule (CPR) uses seven factors to guide risk assessment and antibiotic prescribing in children with cough (Short illness duration, Temperature, Age, Recession, Wheeze, Asthma, Vomiting).

Aim: To assess the influence of STARWAVe factors on GPs' unaided risk assessments and prescribing decisions.

Design and setting: Clinical vignettes administered to 188 UK GPs online.

Method: GPs were randomly assigned to view 32 (out of a possible 64) vignettes online depicting children with cough. The vignettes comprised the seven STARWAVe factors, which were varied systematically. For each vignette, GPs assessed risk of deterioration in one of two ways (sliding-scale versus risk-category selection) and indicated whether they would prescribe antibiotics. Finally, GPs saw an additional vignette, suggesting that the parent was concerned. Mixed-effects regressions were used to measure the influence of STARWAVe factors, risk-elicitation method, and parental concern on GPs' assessments and decisions.

Results: Six STARWAVe risk factors correctly increased GPs' risk assessments ($bs_{sliding\text{-}scale} \geq 0.66$, odds ratios [ORs]$_{category\text{-}selection} \geq 1.75$, $Ps \leq 0.001$), whereas one incorrectly reduced them (short illness duration: $b_{sliding\text{-}scale}$ -0.30, OR$_{category\text{-}selection}$ 0.80, $P \leq 0.039$). Conversely, one STARWAVe factor increased prescribing odds (temperature: OR 5.22, $P < 0.001$), whereas the rest either reduced them (short illness duration, age, and recession: ORs ≤ 0.70, $Ps < 0.001$) or had no significant impact (wheeze, asthma, and vomiting: $Ps \geq 0.065$). Parental concern increased risk assessments ($b_{sliding\text{-}scale}$ 1.29, OR$_{category\text{-}selection}$ 2.82, $P \leq 0.003$) but not prescribing odds ($P = 0.378$).

Conclusion: GPs use some, but not all, STARWAVe factors when making unaided risk assessments and prescribing decisions. Such discrepancies must be considered when introducing CPRs to clinical practice.

Keywords: STARWAVe; antimicrobial stewardship; decision support; general practice; primary care.

- 26 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Review

High inhaler resistance does not limit successful inspiratory maneuver among patients with asthma or COPD

Ville A Vartiainen [1][2], Federico Lavorini [3], Anna C Murphy [4], Klaus F Rabe [5]

Affiliations expand

- PMID: 36820500

- DOI: 10.1080/17425247.2023.2179984

Abstract

Introduction: There has been an active discussion on the sustainability of inhaler therapy in respiratory diseases, and it has cast a shadow on pMDIs which rely on propellant with high global warming potential (GWP). DPIs offer a lower GWP and effective alternative, but there has been concern whether all patients can generate sufficient inspiratory effort to

disperse the drug. This review focuses on airflow resistance of DPIs and its clinical relevance.

Areas covered: For this narrative review, we searched the literature for studies comparing flow patterns with different devices. We also included a section on clinical trials comparing reliever administration with DPI, pMDI with spacer, and nebulizer during exacerbation.

Expert opinion: The evidence supports the efficacy of DPIs irrespective of respiratory condition or age of the patient even during acute exacerbations. Air flow resistance does not limit the use of DPIs and the patients were able to generate sufficient inspiratory flow rate with almost any device studied. None of 16 identified clinical trials comparing reliever administration via DPIs to other types of devices during exacerbation or bronchial challenge showed statistically significant difference between the device types in FEV1 recovery. DPIs performed as well as other types of inhaler devices even during asthma or COPD exacerbation.

Keywords: Inhaler; dry powder inhaler; metered dose inhaler; peak inspiratory flow rate.

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Current advances in house dust mite allergen immunotherapy (AIT): Routes of administration, biomarkers and molecular allergen profiling

Thierry Batard [1], Walter G Canonica [2], Oliver Pfaar [3], Mohamed H Shamji [4], Robyn E O'Hehir [5], Menno C van Zelm [5], Laurent Mascarell [6]

Affiliations expand

Abstract

Allergy to house dust mites (HDM) is a perennial respiratory disease that affect more than half a billion people worldwide. Dermatophagoides pteronyssinus and D. farinae, two HDM species, are major sources of indoor allergens triggering allergic inflammation. Although symptomatic drugs are widely used to block the allergic reaction, allergen immunotherapy is the only curative treatment of IgE-mediated type I respiratory allergies. In this article, we review recent advances in various routes of allergen immunotherapy. We particularly focus on subcutaneous (SCIT) and sublingual (SLIT) immunotherapy, used as a reference therapy since they have transformed allergic treatments by improving symptoms (asthma and rhinitis) as well as the quality of life of patients. We also highlight recent data in more exploratory routes (i.e., oral, intralymphatic, epicutaneous and intradermal) and discuss respective advantages of various route, as well as their foreseen modes of action. Finally, we provide an update on biomarkers as well as on the relevance of the molecular profiling of allergic individuals related to treatment efficacy or asthma prediction.

Keywords: Administration routes; Allergen immunotherapy; Biomarkers; House dust mite; Molecular reactivity profiling.

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Effect of transfected induced pluripotent stem cells with Decorin gene on control of lung remodeling in allergic asthma

Ronghua Zhang [1][2], Zongxiu Yin [2], Jing Pan [2], Congying Zhai [3], Seyyed Shamsadin Athari [4], Liang Dong [5]

Affiliations expand

- PMID: 36803044

- DOI: 10.1177/10815589221140590

Abstract

Asthma is a complex respiratory disease, which is controlled by genetic and environmental factors. Type 2-dominant immune response is responsible for asthma. Decorin (Dcn) and stem cells have modulatory effect on immune system and may control tissue remodeling and asthma pathophysiology. In this study, immunomodulatory effect of transduced induced pluripotent stem cells (iPSCs) with expression of *Dcn* gene on allergic asthma pathophysiology was evaluated. After transduction of iPSCs with *Dcn* gene, allergic asthma mice were treated with iPSCs and transduced iPSCs via intrabronchial. Then, airway hyperresponsiveness (AHR), levels of interleukin (IL)-4, IL-5, IL-13, IL-33, total IgE, leukotrienes (LTs) B4, C4, hydroxyproline (HP) content, and transforming growth factor-beta (TGF-β) were measured. Also, lung histopathology study was done. AHR, levels of IL-4,

IL-5, IL-13, IL-33, total IgE, LTs B4, C4, TGF-β, HP content, mucus secretion, goblet cell hyperplasia, and eosinophilic inflammation were controlled by iPSCs and transduced iPSCs treatment. Therapeutic effect of iPSCs could control main allergic asthma symptoms and related pathophysiologic mechanisms and the effect can be increased when applied with *Dcn* expression gene.

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Cell-contact-mediated assembly of contractile airway smooth muscle rings

Jonathan Tjong [1], Stefan Pendlmayr [1], Jena Barter [1,2], Julie Chen [1], Geoffrey N Maksym [1,3], T Alexander Quinn [1,4], John P Frampton [1,2]

Affiliations expand

- PMID: 36801856

- DOI: 10.1088/1748-605X/acbd09

Abstract

Microtissues in the shape of toroidal rings provide an ideal geometry to better represent the structure and function of the airway smooth muscle present in the small airways, and to better understand diseases such as asthma. Here, polydimethylsiloxane devices consisting of a series of circular channels surrounding central mandrels are used to form microtissues in the shape of toroidal rings by way of the self-aggregation and -assembly of airway smooth muscle cell (ASMC) suspensions. Over time, the ASMCs present in the rings become spindle-shaped and axially align along the ring circumference. Ring strength and elastic modulus increase over 14 d in culture, without significant changes in ring size. Gene expression analysis indicates stable expression of mRNA for extracellular matrix-associated proteins, including collagen I and lamininsα1 andα4 over 21 d in culture. Cells within the rings respond to TGF-β1 treatment, leading to dramatic decreases in ring circumference, with increases in mRNA and protein levels for extracellular matrix and contraction-associated markers. These data demonstrate the utility of ASMC rings as a platform for modeling diseases of the small airways such as asthma.

Keywords: airway smooth muscle; contractility; soft tissue mechanics; tissue constructs; transforming growth factor beta.

SUPPLEMENTARY INFO

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A focused report on progestogen hypersensitivity

Diti H Patel [1], Lauren M Fine [1], Jonathan A Bernstein [2]

Affiliations expand

- PMID: 36800518

- DOI: 10.1080/1744666X.2023.2182292

Abstract

Introduction: Progestogen Hypersensitivity (PH) is caused by increased sensitivity to either exogenous or endogenous progestogens. It is characterized by recurrent cutaneous eruptions including erythema multiforme, eczema, urticaria, and angioedema, which may be associated with systemic symptoms including asthma and anaphylaxis.

Areas covered: Symptoms may be persistent or cyclical, coinciding with progestogen levels. With increased use of oral contraceptives and hormonal treatments for fertility, the prevalence of PH is expected to continuously increase. Several proposed immunological mechanisms, diagnostics, and treatment modalities have been proposed. Most treatments focus on suppressing ovulation and progesterone secretion or inducing tolerance through progesterone desensitization.

Expert opinion: Although there has been increased recognition both clinically and in the medical literature, there is still a general lack of knowledge of PH and its clinical features in the medical community. An improved understanding of the underlying pathophysiology as well as more available commercial testis, such as ELISA that accurately measures specific IgE to progesterone, are expected to broaden and improve opportunities for disease recognition and symptom control. It is essential for physicians across specialties to recognize how to diagnose PH and either manage this condition or refer these patients to a specialist with experience treating PH.

Keywords: Autoimmune progesterone dermatitis; IVF; Progesterone; desensitization; progestin; progestogen hypersensitivity; urticaria.

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FOXF1 attenuates TGF–β1–induced bronchial epithelial cell injury by inhibiting CDH11–mediated Wnt/β–catenin signaling

Qin Chen [1], Xing Liao [1], Ling Lin [1], Ling Wu [1], Qiuyu Tang [1]

Affiliations expand

- PMID: 36798677

- PMCID: PMC9926140

- DOI: 10.3892/etm.2023.11802

Abstract

Forkhead box F1 (FOXF1) has been reported to be associated with lung development. However, the role of FOXF1 in asthma is still not fully understood. In the present study, the biological role and the potential mechanism of FOXF1 was explored in transforming growth factor β1 (TGF-β1)-induced bronchial epithelial cell injury. Reverse transcription-quantitative PCR and western blotting were performed to detect the expression levels of

FOXF1 and cadherin (CDH) 11 in TGF-β1-induced bronchial epithelial cells. Proliferation, apoptosis and inflammation were assessed using Cell Counting Kit-8 assay, flow cytometry, western blotting and ELISA. Fibrosis and epithelial-mesenchymal transition (EMT) were evaluated using immunofluorescence and western blotting. The expression levels of the proteins involved in the Wnt/β-catenin pathway were detected by western blotting. The results indicated that FOXF1 expression was downregulated, while CDH11 expression was upregulated in TGF-β1-treated BEAS-2B cells. FOXF1 overexpression promoted proliferation, inhibited induction of apoptosis and suppressed the inflammatory response of BEAS-2B cells exposed to TGF-β1. In addition, FOXF1 overexpression restrained TGF-β1-induced bronchial epithelial fibrosis and EMT and inhibited the activation of the Wnt/β-catenin pathway. CDH11 overexpression reversed the effects of FOXF1 overexpression on proliferation, apoptosis, fibrosis, EMT and inflammation by regulating the Wnt/β-catenin pathway. Collectively, the results of the present study suggested that FOXF1 regulated TGF-β1-induced BEAS-2B cell injury by inhibiting CDH11-mediated Wnt/β-catenin signaling. This may provide a novel therapeutic strategy for the treatment of asthma.

Keywords: Wnt/β-catenin signaling; asthma; cadherin 11; forkhead box F1; transforming growth factor β1.

Conflict of interest statement

The authors declare that they have no competing interests.

- 34 references
- 6 figures

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Expert Rev Clin Immunol

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Recent insights into comorbidities in atopic dermatitis

Caroline Gewiss [1], Matthias Augustin [1]

Affiliations expand

- PMID: 36796057

- DOI: 10.1080/1744666X.2023.2181790

Abstract

Introduction: The relationship between atopic dermatitis and atopic diseases such as food allergies, asthma, and allergic rhinitis in terms of co-occurrence, underlying mechanisms, and therapy is well documented. There is increasing evidence that atopic dermatitis is associated with non-atopic comorbidities such as cardiac, autoimmune, and neuropsychological comorbidities, as well as cutaneous and extracutaneous infections, establishing atopic dermatitis as a systemic disease.

Areas covered: The authors reviewed evidence on atopic and non-atopic comorbidities of atopic dermatitis. A literature search was conducted in PubMed for peer-reviewed articles published until October 2022.

Expert opinion: Atopic and non-atopic diseases coexist with atopic dermatitis more often than would be expected by chance. The effect of biologics and small molecules on atopic and non-atopic comorbidities may contribute to a better understanding of the relationship between atopic dermatitis and its comorbidities. Their relationship needs to be explored further to dismantle the underlying mechanism and move toward an atopic dermatitis endotype-based therapeutic approach.

Keywords: Atopic dermatitis; autoimmune; cardio-metabolic; comorbidities; cutaneous; eczema; extracutaneous; infections; neuropsychological; non-atopic.

FULL TEXT LINKS

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Real-world study: drug reduction in children with allergic rhinitis and asthma receiving immunotherapy

Jorge Sánchez [1], Leidy Alvarez [2], Elizabeth García [3]

Affiliations expand

- PMID: 36789565

- DOI: 10.2217/imt-2022-0215

Abstract

Background: The reduction of pharmacological treatment after allergen immunotherapy (AIT) for house dust mites (HDMs) has been little studied in children. **Objective:** To evaluate the reduction of pharmacological treatment comparing children that receive HDM immunotherapy (AIT group) versus only pharmacotherapy. **Methods:** A historic cohort of children with rhinitis or asthma was assessed. The main outcome was the frequency of complete drug discontinuation. **Results:** 100% drug reduction was higher for rhinitis (4-year cumulative incidence: 30 vs 10.7%) and asthma (24.1 vs 10.5%) in the AIT group (n = 987) than in the pharmacotherapy group (n = 2012). **Conclusion:** Immunotherapy is associated with a significant reduction of pharmacotherapy in children. This is a marker of clinical control and could be associated with positive economic impact.

Plain language summary

The benefits of allergen immunotherapy for house dust mites has been little studied in children. The usefulness of this treatment in asthma over the use of pharmacotherapy has also not been clearly evaluated. The use of immunotherapy allowed greater reductions in pharmacological treatment in children with rhinitis and asthma. Immunotherapy is a useful treatment for childhood rhinitis and asthma and reduces the risk of adverse effects from pharmacological treatments.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

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[Remote visits for severe asthma patients after the COVID-19 pandemic: How to address the challenge?]

[Article in Spanish]

S Sánchez-García [1], L Soto-Retes [2], E Chiner [3], C Cisneros [4]; el Grupo de Trabajo onasm

Affiliations expand

- PMID: 36777238

Free PMC article

No abstract available

- 15 references
- 1 figure

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Review

Pheno-Endotyping Antrochoanal Nasal Polyposis

Octavio Garaycochea [1][2], Camilo Rodríguez Van Strahlen [3], Isam Alobid [1][4], Joaquim Mullol [1]

Abstract

Purpose of review: Antrochoanal polyps (ACPs) are benign polypoid lesions arising from the inner wall of the maxillary sinus and extending into the choana. Although the diagnosis and treatment strategies of ACP have changed since this entity was first described, the underlying pathogenic mechanism of APC is poorly understood. This article reviews the current knowledge of the etiology, inflammatory parameters, and microscopic findings of ACP.

Recent findings: The inflammatory pattern of ACP appears to center around a neutrophilic inflammation T1-dominant endotype. Apart from the inflammatory component of ACP, at the microscopic level, the presence of tissue remodeling, mostly fibrin deposition and edema, and cysts in the epithelium and lamina propria has been described. Although the origin of this T1-dominant endotype immune response of ACPs is not entirely clear, it could be related to a lymphatic obstruction mechanism. This review serves to define a phenotype of ACP with potential endotypes based on the characteristics of the inflammatory parameters, microscopic findings, and hypotheses about the pathogenesis of ACP.

Keywords: Antrochoanal polyp; Chronic sinusitis; Etiology; Inflammation; Inflammatory parameters.

- 59 references

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☐ 96

Variants in interferon gamma inducible protein 16 (IFI16) and absent in melanoma 2 (AIM2) genes that modulate inflammatory response are associated with periodontitis

Marcia Otto Barrientos [1], Álvaro A Cruz [2], Helena M P Teixeira [3], Hátilla Dos Santos Silva [3], Isaac Suzart Gomes-Filho [4], Soraya Castro Trindade [4], Kaliane Rocha Soledade [4], Jamille Souza Fernandes [5], Cinthia Vila Nova Santana [2], Gabriela Pimentel Pinheiro [2], Adelmir Souza-Machado [2], Ryan Dos Santos Costa [3], Camila A Figueiredo [3], Tatiane Teixeira Muniz Carletto Oliveira [6]

Affiliations expand

- PMID: 36758286

- DOI: 10.1016/j.archoralbio.2023.105640

Abstract

Objective: Evaluate the association of genetic variants of the interferon gamma inducible protein 16 (IFI16) and absent in melanoma 2 (AIM2) genes with periodontitis.

Methods: The study involved 117 individuals with periodontitis and 389 without periodontitis, all Brazilians, miscegenated. Individuals with periodontitis presented at least 4 teeth with ≥ 1 site with probing depth ≥ 4 mm; clinical attachment level ≥ 3 mm on the same site and bleeding upon stimulus. Genotyping was performed using the Infinium Multi-Ethnic AMR/AFR-8 Bead Chip focused on Hispanic and African American populations

with approximately 2 million markers of the human genome. Multivariate logistic regression was performed to identify associations in additive, dominant and recessive models adjusted for covariates age, obesity, mouth breathing, flossing, asthma, and ancestry.

Results: In IFI16, the rs75985579-A is positively associated with periodontitis in the additive (Odds Ratio adjusted (ORadjusted) 2.65, 95% confidence interval (CI):1.25-5.60, p value: 0.007) and dominant models (ORadjusted 2.56, 95%CI:1.13-5.81, p value: 0.017). In AIM2, the rs76457189-G, is associated negatively with periodontitis in two genetic models evaluated, additive (ORadjusted 0.21, 95%CI:0.05-0.94, p value: 0.022) and dominant (ORadjusted 0.21, 95%CI:0.05-0.94, p value: 0.022).

Conclusions: These results have shown that variants in the IFI16 and AIM2 genes are associated with periodontitis. Individuals with at least one A (adenine) allele of the rs75985579 (IFI16) are more than twice as likely to have periodontitis, while individuals with the G (guanine) allele of rs76457189 (AIM2) are less likely to be diagnosed with periodontitis, providing a negative association with periodontitis.

Keywords: AIM2; Gene; Genetic variants; IFI16; Inflammasome; Periodontitis.

Conflict of interest statement

Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

SUPPLEMENTARY INFO

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Review

Recent Updates in Understanding NSAID Hypersensitivity

Ellen Minaldi [1], Katherine Cahill [2]

Affiliations expand

- PMID: 36757490

- DOI: 10.1007/s11882-023-01064-3

Abstract

Purpose of review: To provide a review of available literature regarding nonsteroidal anti-inflammatory drug (NSAID) hypersensitivity with an emphasis on more recent findings.

Recent findings: Oral provocation tests with aspirin are important for diagnosis and management in adult and pediatric populations with reported NSAID hypersensitivity. Risk of cross-reactivity to COX-2 inhibitors varies by NSAID hypersensitivity phenotype. COX-2 inhibitors are tolerated in aspirin-exacerbated respiratory disease. Reported NSAID allergy is associated with a higher risk of a substance use disorder. Effective treatment of underlying chronic spontaneous urticaria can allow tolerance of NSAIDs in NSAID-exacerbated cutaneous disease. The pathophysiology, cross-reactivity, and appropriate diagnostic evaluation differ between the 5 distinct NSAID hypersensitivity phenotypes. Further research into the pathophysiology of NSAID hypersensitivity in patients with and without underlying disease is needed.

Keywords: Aspirin; COX-2 inhibitors; NSAID hypersensitivity; Oral provocation test; Urticaria.

- <u>46 references</u>

Evaluation of selected aspects of the hygiene hypothesis and their effect on the incidence of allergy

<u>Edyta Krzych-Fałta</u> [1], <u>Oksana Wojas</u> [2], <u>Konrad Furmańczyk</u> [2][3], <u>Diana Dziewa-Dawidczyk</u> [3], <u>Barbara Piekarska</u> [2], <u>Bolesław Samoliński</u> [2], <u>Adam Sybilski</u> [4]

Affiliations expand

- PMID: 36756848

- DOI: <u>10.13075/ijomeh.1896.01880</u>

Free article

Abstract

Objectives: The development of allergic conditions is largely dependent on the interactions between genetic (individual genetic predisposition) and environmental factors (exposure to risk factors). The aim of this study was an attempt to assess the influence of selected elements of the hygiene theory in the development of allergic diseases such as allergic rhinitis and asthma.

Material and methods: The study group consisted of 5518 women and 3868 men. The method that was used was the European Community Respiratory Health Survey II and International Study of Asthma and Allergies in Childhood questionnaire validated and adapted to Central and Eastern European conditions. The project was conducted in 8 urban areas (Gdańsk, Wrocław, Poznań, Katowice, Kraków, Lublin, Białystok, Warsaw) and 1 rural area (Krasnystaw county). This study had 2 stages; the first stage involved grouping the 22 500 respondents based on their questionnaire responses with the use of a Personal Digital Assistant (PDA); the second stage involved 7000 subjects, who underwent additional assessments: skin prick tests (birch, grasses/cereals, *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, molds [set I: *Botrytis cinerea*, *Cladosporium herbarum*, *Alternaria tenuis*, *Curvularia lunata*, *Fusarium moniliforme*, *Helminthosporium*], molds [set II: *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*], cat, dog, molds *Cladosporium herbarum*, *Alternaria tenuis*) and spirometry tests.

Results: The age at which children attend the nursery school is critical to the development of allergic diseases; in allergic rhinitis, the risk of an IgE-dependent reaction is 2 times higher in the second than in the first year of life ($p = 0.00147$, $p < 0.05$), while in asthma, having a large number of siblings increases the risk of developing obstructive disease by almost 6 times ($p = 0.00316$, $p < 0.05$).The age at which children attend the nursery school is critical to the development of allergic diseases; in allergic rhinitis, the risk of an IgE-dependent reaction is 2 times higher in the second than in the first year of life ($p = 0.00147$, $p < 0.05$), while in asthma, having a large number of siblings increases the risk of developing obstructive disease by almost 6 times ($p = 0.00316$, $p < 0.05$).

Conclusions: The hygiene theory is particularly applicable and can explain the relationship of selected habits in the development of allergic diseases. Int J Occup Med Environ Health. 2023;36(1):69-83.

Keywords: European Community Respiratory Health Survey II; International Study of Asthma and Allergies in Childhood; allergic rhinitis; allergy; asthma; hygiene hypothesis.

SUPPLEMENTARY INFO

MeSH terms, Substances, Supplementary conceptsexpand

Review

Therapeutic properties and pharmacological activities of asiaticoside and madecassoside: A review

[Shinjini Bandopadhyay](#) [1], [Sujata Mandal](#) [2], [Mimosa Ghorai](#) [2], [Niraj Kumar Jha](#) [3][4][5], [Manoj Kumar](#) [6], [Radha](#) [7], [Arabinda Ghosh](#) [8], [Jarosław Proćków](#) [9], [José M Pérez de la Lastra](#) [10], [Abhijit Dey](#) [2]

Affiliations expand

- PMID: 36756687

- PMCID: [PMC9983323](#)

- DOI: [10.1111/jcmm.17635](#)

Abstract

Centella asiatica is an ethnomedicinal herbaceous species that grows abundantly in tropical and sub-tropical regions of China, India, South-Eastern Asia and Africa. It is a popular nutraceutical that is employed in various forms of clinical and cosmetic treatments. C. asiatica extracts are reported widely in Ayurvedic and Chinese traditional medicine to boost memory, prevent cognitive deficits and improve brain functions. The major bioactive constituents of C. asiatica are the pentacyclic triterpenoid glycosides, asiaticoside and madecassoside, and their corresponding aglycones, asiatic acid and madecassic acid. Asiaticoside and madecassoside have been identified as the marker compounds of C. asiatica in the Chinese Pharmacopoeia and these triterpene compounds offer a wide range of pharmacological properties, including neuroprotective, cardioprotective, hepatoprotective, wound healing, anti-inflammatory, anti-oxidant, anti-allergic, anti-depressant, anxiolytic, antifibrotic, antibacterial, anti-arthritic, anti-tumour and immunomodulatory activities. Asiaticoside and madecassoside are also used extensively in treating skin abnormalities, burn injuries, ischaemia, ulcers, asthma, lupus, psoriasis and scleroderma. Besides medicinal applications, these phytocompounds are considered cosmetically beneficial for their role in anti-ageing, skin hydration, collagen synthesis, UV protection and curing scars. Existing reports and experimental studies on these compounds between 2005 and 2022 have been selectively reviewed in this article to provide a comprehensive overview of the numerous therapeutic advantages of asiaticoside and madecassoside and their potential roles in the medical future.

Conflict of interest statement

The authors declare no competing financial interests.

- 155 references
- 2 figures

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Variation of asthma characteristics with atopic march, gastroesophageal reflux, and ENT pathologies

[Norane Shehab](#)[1], [Jobayer Hossain](#)[2], [Ejaz Yousef](#)[3]

Affiliations expand

- PMID: 36755382

- DOI: [10.1080/02770903.2023.2174030](#)

Abstract

Background: Asthma is a significant cause of morbidity and mortality in the pediatric population. Atopic dermatitis (AD) is often the first step in the atopic march leading to the development of asthma, allergic rhinitis, and food allergies in the future.

Objective: This study aimed to evaluate the severity differences between asthmatic children with and without atopic march in addition to characteristics of asthmatic patients with GER and ear-nose-and-throat (ENT) pathologies.

Methods: A total of 616 pediatric asthmatic patients were enrolled. The study subjects were divided into two groups. Group A included asthmatic children with a history of AD. Group B had asthmatic children without a history of AD. Multiple factors were studied, including sex, race/ethnicity, family history of atopy, asthma severity, allergic rhinitis, food allergies, smoke exposure, ear-nose-and-throat (ENT) pathologies, gastroesophageal reflux (GER), frequency of systemic steroid use, and hospital admission rates.

Results: Our results revealed that patients with atopic march are at risk of developing a higher severity of asthma, resulting in increased morbidity. In contrast, asthmatic patients without atopic march had a milder asthma severity, less need for steroids, and fewer hospital admissions. A higher prevalence of ENT pathologies and/or GER existed among asthmatic children without atopic march.

Conclusion: Our findings suggest that patients with atopic march should be expected to exhibit a more severe phenotype of asthma with increased asthma morbidity. Asthmatic patients without atopic march had a milder asthma phenotype, less need for steroids, and fewer hospital admissions. A higher prevalence of ENT pathologies and/or GER existed among asthmatic children without atopic march.

Keywords: Phenotypes; morbidity and mortality; pediatrics.

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Neutrophilia in severe asthma is reduced in Ormdl3 overexpressing mice

[Briana N James](#) [1], [Cynthia Weigel](#) [1], [Christopher D Green](#) [1], [Ryan D R Brown](#) [1], [Elisa N D Palladino](#) [1], [Anuj Tharakan](#) [2], [Sheldon Milstien](#) [1], [Richard L Proia](#) [3], [Rebecca K Martin](#) [2], [Sarah Spiegel](#) [1]

Affiliations expand

Abstract

Genome-wide association studies have linked the ORM (yeast)-like protein isoform 3 (ORMDL3) to asthma severity. Although ORMDL3 is a member of a family that negatively regulates serine palmitoyltransferase (SPT) and thus biosynthesis of sphingolipids, it is still unclear whether ORMDL3 and altered sphingolipid synthesis are causally related to non-Th2 severe asthma associated with a predominant neutrophil inflammation and high interleukin-17 (IL-17) levels. Here, we examined the effects of ORMDL3 overexpression in a preclinical mouse model of allergic lung inflammation that is predominantly neutrophilic and recapitulates many of the clinical features of severe human asthma. ORMDL3 overexpression reduced lung and circulating levels of dihydrosphingosine, the product of SPT. However, the most prominent effect on sphingolipid levels was reduction of circulating S1P. The LPS/OVA challenge increased markers of Th17 inflammation with a predominant infiltration of neutrophils into the lung. A significant decrease of neutrophil infiltration was observed in the Ormdl3 transgenic mice challenged with LPS/OVA compared to the wild type and concomitant decrease in IL-17, that plays a key role in the pathogenesis of neutrophilic asthma. LPS decreased survival of murine neutrophils, which was prevented by co-treatment with S1P. Moreover, S1P potentiated LPS-induced chemotaxis of neutrophil, suggesting that S1P can regulate neutrophil survival and recruitment following LPS airway inflammation. Our findings reveal a novel connection between ORMDL3 overexpression, circulating levels of S1P, IL-17 and neutrophil recruitment into the lung, and questions the potential involvement of ORMDL3 in the pathology, leading to development of severe neutrophilic asthma.

Keywords: ORMDL3; neutropenia; severe asthma; sphingosine-1-phosphate.

- [65 references](#)

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

Review

MR imaging of the airways

Juergen Biederer [1][2][3][4]

Affiliations expand

- PMID: 36752590

- DOI: [10.1259/bjr.20220630](10.1259/bjr.20220630)

Abstract

The need for airway imaging is defined by the limited sensitivity of common clinical tests like spirometry, lung diffusion (DLCO) and blood gas analysis to early changes of peripheral airways and to inhomogeneous regional distribution of lung function deficits. Therefore, X-ray and computed tomography (CT) are frequently used to complement the standard tests.As an alternative, magnetic resonance imaging (MRI) offers radiation-free lung imaging, but at lower spatial resolution. Non-contrast enhanced MRI shows healthy airways down to the first subsegmental level/4th order (CT: eighth). Bronchiectasis can be identified by wall thickening and fluid accumulation. Smaller airways become visible, when

altered by peribronchiolar inflammation or mucus retention (tree-in-bud sign).The strength of MRI is functional imaging. Dynamic, time-resolved MRI directly visualizes expiratory airway collapse down to the lobar level (CT: segmental level). Obstruction of even smaller airways becomes visible as air trapping on the expiratory scans. MRI with hyperpolarized noble gases (^{3}He, ^{129}Xe) directly shows the large airways and peripheral lung ventilation. Dynamic contrast-enhanced MRI (DCE MRI) indirectly shows airway dysfunction as perfusion deficits resulting from hypoxic vasoconstriction of the dependent lung volumes. Further promising scientific approaches such as non-contrast enhanced, ventilation-/perfusion-weighted MRI from periodic signal changes of respiration and blood flow are in development.In summary, MRI of the lungs and airways excels with its unique combination of morphologic and functional imaging capacities for research (*e.g.,* in chronic obstructive lung disease or asthma) as well as for clinical imaging (*e.g.,* in cystic fibrosis).

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Editorial

Asthma and cardiovascular disease: A bidirectional association?

[Muhammad Adrish](#)[1], [Nicola A Hanania](#)[1]

Affiliations expand

- PMID: 36750439

Free article

No abstract available

Keywords: asthma; asthma exacerbation; cardiovascular disease; heart failure; ischemic stroke.

- 31 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Review

Management of the Pregnant Patient with Beta-Lactam Allergy

Anna R Wolfson [1][2], Michael X Schatz [3]

Affiliations expand

Abstract

Purpose of review: We review the literature and discuss the logistics of testing pregnant patients for penicillin allergy.

Recent findings: As in the general population, pregnant patients commonly report a penicillin allergy, but most patients are able to tolerate penicillin. Avoidance of beta-lactams in pregnancy is associated with increased morbidity: longer hospitalizations, more frequent infections, and more complications. Penicillin allergy testing is safe in pregnant patients, and obstetricians are eager for allergists to offer this procedure to their patients. As allergists, we can improve our patients' health outcomes by offering penicillin allergy testing in our practices. The protocols for testing both with and without skin testing in pregnant patients have been studied, and future studies will continue to clarify the safety and efficacy of penicillin allergy delabeling in pregnant patients.

Keywords: Drug allergy; Obstetric; Penicillin allergy; Pregnancy.

- 44 references

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Clinical, functional, and inflammatory characteristics of asthma among adults aged over 60 years old: a case-control study

Maria Amélia Carvalho da Silva Santos [1], Maria Marta Ferreira Amorim [2], Lilian Ballini Caetano [1], Michael Dracoulakis [1], Fernandes Ana Luisa Godoy [3]

Affiliations expand

- PMID: 36749190

- DOI: 10.1080/02770903.2023.2174029

Abstract

ObjectiveThis observational case-control study analyzed the clinical, functional, inflammatory profile, and treatment data of a cohort of patients with asthma who were followed up at the outpatient clinic of a teaching hospital.**Methods**Patients who visited the clinic between January 2008 and February 2020 and diagnosed with asthma according to the Global Initiative for Asthma (GINA) criteria were included in the study. Patients were broadly classified into two groups: age <60 or age ≥60 years. The patients were evaluated for asthma control and severity, medications used, comorbidities, smoking status, occurrence of exacerbation, spirometry at the first and last visits, sputum cytology, allergic prick test, and inflammatory cytokine levels.**Results**Patients over 60 years of age had lower asthma control test (ACT) scores, required higher doses of inhaled corticosteroids to

achieve asthma control and had worse lung function with fixed airway obstruction, higher number of comorbidities, greater exposure to tobacco, and longer outpatient follow-up than younger patients with asthma. Furthermore, older patients presented with neutrophilia and higher levels of TNFα in the induced sputum as compared to younger patients.**Conclusions**These findings suggest that patients aged ≥60 years of age had a more severe asthma profile and poorer lung function than younger patients with asthma. Furthermore, aging, long-term asthma, comorbidities, and tobacco exposure contributed to an accelerated decline in lung function.

Keywords: Asthma; functional characteristics; immunosenescence; inflammatory characteristics; older adults; phenotypes.

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Airway mucus in pulmonary diseases: Muco-adhesive and muco-penetrating particles to overcome the airway mucus barriers

Rudra Pangeni [1], Tuo Meng [1], Sagun Poudel [1], Divya Sharma [2], Hallie Hutsell [1], Jonathan Ma [3], Bruce K Rubin [4], Worth Longest [5], Michael Hindle [1], Qingguo Xu [6]

Affiliations expand

Abstract

Airway mucus is a complex viscoelastic gel that provides a defensive physical barrier and shields the airway epithelium by trapping inhaled foreign pathogens and facilitating their removal via mucociliary clearance (MCC). In patients with respiratory diseases, such as chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), non-CF bronchiectasis, and asthma, an increase in crosslinking and physical entanglement of mucin polymers as well as mucus dehydration often alters and typically reduces mucus mesh network pore size, which reduces neutrophil migration, decreases pathogen capture, sustains bacterial infection, and accelerates lung function decline. Conventional aerosol particles containing hydrophobic drugs are rapidly captured and removed by MCC. Therefore, it is critical to design aerosol delivery systems with the appropriate size and surface chemistry that can improve drug retention and absorption with the goal of increased efficacy. Biodegradable muco-adhesive particles (MAPs) and muco-penetrating particles (MPPs) have been engineered to achieve effective pulmonary delivery and extend drug residence time in the lungs. MAPs can be used to target mucus as they get trapped in airway mucus by steric obstruction and/or adhesion. MPPs avoid muco-adhesion and are designed to have a particle size smaller than the mucus network, enhancing lung retention of particles as well as transport to the respiratory epithelial layer and drug absorption. In this review, we aim to provide insight into the composition of airway mucus, rheological characteristics of airway mucus in healthy and diseased subjects, the most recent techniques to study the flow dynamics and particle diffusion in airway mucus (in particular, multiple particle tracking, MPT), and the advancements in engineering MPPs that have contributed to improved airway mucus penetration, lung distribution, and retention.

Keywords: Aerosol; Cystic fibrosis; Microrheology; Mucociliary clearance; Multiple particle tracking; Pulmonary drug delivery; Rheology.

Conflict of interest statement

Declaration of Competing Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The EEG aerosol technologies described in this publication have been filed as patent applications through Virginia Commonwealth University (VCU). Michael Hindle and Worth Longest are the co-inventors, which are subject to certain rules and restrictions under VCU policy. The terms of this arrangement are being managed by VCU in accordance with its conflict of interest policies.

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Pimecrolimus for the Treatment of Atopic Dermatitis in Infants: An Asian Perspective

Chia-Yu Chu [1], Tsung-Chieh Yao [2], I-Hsin Shih [3], Chin-Yi Yang [3][4], Chan Lee Chin [5], Sabeera Begum Binti Kader Ibrahim [6], Suganthi Thevarajah [6], Leong Kin Fon [7], Marco Hok-Kung Ho [8], Chow Chung Mo [9], Chow Pok Yu [8], Steven King-Fan Loo [10], Thomas Luger [11]

Abstract

Atopic dermatitis (AD) is a common chronic, multisystem inflammatory skin disease in pediatric patients. There has been an increase in the incidence of AD in the pediatric population of the Asia-Pacific region. Studies have shown that genetic, epigenetic, environmental and cultural factors may lead to differences in the clinical manifestation and prevalence of AD between races. Early treatment of AD is necessary to prevent the atopic march leading to comorbidities such as asthma and allergic rhinitis. Topical corticosteroids (TCS) are used as first-line therapy for the treatment of AD, but their long-term usage poses a risk to the patient's health. Pimecrolimus (1%) is a topical calcineurin inhibitor (TCI) that is indicated for the treatment of mild to moderate AD. Pimecrolimus has no apparent increase in adverse events compared to TCS, and it causes less of a burning sensation than tacrolimus. The safety and efficacy of pimecrolimus has been established through various clinical trials; yet, in many Asian countries, the use of pimecrolimus in infants is still restricted due to safety concerns. Based on the available evidence, the expert panel recommends pimecrolimus in infants between 3 months and 2 years of age in the Asian population.

Keywords: Asian population; Atopic dermatitis; Infants; Pimecrolimus; Topical calcineurin inhibitor.

- 69 references

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C-Type Lectin Receptor Mediated Modulation of T2 Immune Responses to Allergens

Alba Angelina [# 1], Leticia Martín-Cruz [# 1], Andrés de la Rocha-Muñoz [1 2], Begoña Lavín-Plaza [1], Oscar Palomares [3]

Affiliations expand

Abstract

Purpose of review: Allergic diseases represent a major health problem of increasing prevalence worldwide. In allergy, dendritic cells (DCs) contribute to both the pathophysiology and the induction of healthy immune responses to the allergens. Different studies have reported that some common allergens contain glycans in their structure. C-type lectin receptors (CLRs) expressed by DCs recognize carbohydrate structures and are crucial in allergen uptake, presentation, and polarization of T cell responses. This review summarizes the recent literature regarding the role of CLRs in the regulation of type 2 immune responses to allergens.

Recent findings: In this review, we highlight the capacity of CLRs to recognize carbohydrates in common allergens triggering different signaling pathways involved in the polarization of CD4+ T cells towards specific Th2 responses. Under certain conditions,

specific CLRs could also promote tolerogenic responses to allergens, which might well be exploited to develop novel therapeutic approaches of allergen-specific immunotherapy (AIT), the single treatment with potential disease-modifying capacity for allergic disease. At this regard, polymerized allergens conjugated to non-oxidized mannan (allergoid-mannan conjugated) are next-generation vaccines targeting DCs via CLRs that promote regulatory T cells, thus favoring allergen tolerance both in preclinical models and clinical trials. A better understanding of the role of CLRs in the development of allergy and in the induction of allergen tolerance might well pave the way for the design of novel strategies for allergic diseases.

Keywords: Allergen-specific immunotherapy (AIT); Allergens; Allergy; C-type lectin receptors (CLRs); Mannan; Type-2 immune responses.

- 72 references

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Review

An evolving perspective on novel modified release drug delivery systems for inhalational therapy

Tanvirul Hye [1], Sakib M Moinuddin [2][3], Tanoy Sarkar [2][3], Trieu Nguyen [2][3], Dipongkor Saha [2], Fakhrul Ahsan [2][3][4]

Affiliations expand

Abstract

Introduction: Drugs delivered via the lungs are predominantly used to treat various respiratory disorders, including asthma, chronic obstructive pulmonary diseases, respiratory tract infections and lung cancers, and pulmonary vascular diseases such as pulmonary hypertension. To treat respiratory diseases, targeted, modified or controlled release inhalation formulations are desirable for improved patient compliance and superior therapeutic outcome.

Areas covered: This review summarizes the important factors that have an impact on the inhalable modified release formulation approaches with a focus toward various formulation strategies, including dissolution rate-controlled systems, drug complexes, site-specific delivery, drug-polymer conjugates, and drug-polymer matrix systems, lipid matrix particles, nanosystems, and formulations that can bypass clearance via mucociliary system and alveolar macrophages.

Expert opinion: Inhaled modified release formulations can potentially reduce dosing frequency by extending drug's residence time in the lungs. However, inhalable modified or controlled release drug delivery systems remain unexplored and underdeveloped from the commercialization perspective. This review paper addresses the current state-of-the-art of inhaled controlled release formulations, elaborates on the avenues for developing newer technologies for formulating various drugs with tailored release profiles after inhalational delivery and explains the challenges associated with translational feasibility of modified release inhalable formulations.

Keywords: Control release; chemical modification of drugs; drug complexes; drug-polymer matrix; mucociliary escalator; nano-system; polymer-drug conjugates; site-specific delivery; sustained release formulations.

Prevalence of abnormal spirometry in individuals with a smoking history and no known obstructive lung disease

Thuonghien V Tran [1], Gregory L Kinney [2], Alejandro Comellas [3], Karin F Hoth [4], Arianne K Baldomero [5], A James Mamary [6], Jeffrey L Curtis [7], Nicola Hanania [8], Richard Casaburi [9], Kendra A Young [2], Victor Kim [6], Barry Make [10], Emily S Wan [11], Alejandro A Diaz [12], John Hokanson [2], James D Crapo [10], Edwin K Silverman [13], Surya P Bhatt [14], Elizabeth Regan [15], Spyridon Fortis [16]; COPDGene® Investigators – Core Units; COPDGene® Investigators – Clinical Centers

Collaborators, Affiliations expand

Abstract

Introduction: Recent evidence suggests a high prevalence of undiagnosed chronic obstructive pulmonary disease (COPD). These individuals are at risk of exacerbations and delayed treatment. We analyzed an at-risk population for the prevalence of abnormal spirometry to provide clarity into who should undergo early spirometry.

Methods: We analyzed data from the COPDGene study. Participants with ≥10 pack-years of smoking were included. Individuals with self-reported or physician-diagnosed COPD, asthma, chronic bronchitis, emphysema and/or were on inhalers were excluded. Parsimonious multivariable logistic regression models identified factors associated with abnormal spirometry, defined as either airflow obstruction (AFO) or preserved ratio impaired spirometry. Variables were selected for the final model using a stepwise backward variable elimination process which minimized Akaike information criterion (AIC). Similarly, during the 5-year follow-up period, we assessed factors associated with incident diagnosis of COPD.

Results: Of 5055 individuals, 1064 (21%) had undiagnosed AFO. Age, pack-years, current smoking and a history of acute bronchitis were associated with AFO while body mass index, female sex, and Black race were inversely associated. Among 2800 participants with 5-year follow-up, 532 (19%) had an incident diagnosis of COPD. Associated risk factors included mMRC ≥2, chronic productive cough, respiratory exacerbations during the follow-up period, and abnormal spirometry. Age was inversely associated.

Conclusions: The prevalence of undiagnosed COPD is high in at-risk populations. We found multiple factors associated with undiagnosed COPD and incident diagnosis of COPD at follow up. These results can be used to identify those at risk for undiagnosed COPD to facilitate earlier diagnosis and treatment.

Keywords: Chronic obstructive pulmonary disease; Diagnosis.

Conflict of interest statement

SUPPLEMENTARY INFO

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Review

Asthma, the central nervous system, and neurocognition: Current findings, potential mechanisms, and treatment implications

Juliet L Kroll [1], Thomas Ritz [2]

Affiliations expand

- PMID: 36708797

Abstract

Accumulating behavioral evidence suggests that asthma is associated with cognitive deficits. A number of studies have identified potential biological contributions to cognition in asthma; however, mechanistic pathways of central nervous system (CNS) involvement in asthma are yet to be established. We therefore conducted a literature review to identify studies examining potential CNS contributions to cognition in asthma. In this review, we discuss our general understanding of the CNS in asthma in the context of cognitive performance and outline a working model of mechanistic pathways linking the proposed neural influences of asthma pathology with cognition. To this extent, we incorporate neural, behavioral, psychological, social and environmental factors. Finally, we underscore the clinical significance of the CNS and neurocognitive sequelae in asthma, highlighting potential opportunities for routine monitoring, therapeutic intervention, and recommend key areas for future research.

Keywords: Asthma; Brain; Central nervous system; Cognitive function.

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Imaging-derived biomarkers in Asthma: Current status and future perspectives

[Esther Pompe](#) [1], [Anastasia Kal Kwee](#) [2], [Vickram Tejwani](#) [3], [Trishul Siddharthan](#) [4], [Firdaus Aa Mohamed Hoesein](#) [5]

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Abstract

Asthma is a common disorder affecting around 315 million individuals worldwide. The heterogeneity of asthma is becoming increasingly important in the era of personalized treatment and response assessment. Several radiological imaging modalities are available in asthma including chest x-ray, computed tomography (CT) and magnetic resonance imaging (MRI) scanning. In addition to qualitative imaging, quantitative imaging could play an important role in asthma imaging to identify phenotypes with distinct disease course and response to therapy, including biologics. MRI in asthma is mainly performed in research settings given cost, technical challenges, and there is a need for standardization. Imaging analysis applications of artificial intelligence (AI) to subclassify asthma using image analysis have demonstrated initial feasibility, though additional work is necessary to inform the role of AI in clinical practice.

Keywords: Artificial intelligence (AI); Asthma; Imaging; Quantitative.

Conflict of interest statement

Declaration of competing interest No conflicts of interest.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

Cimifugin suppresses type 2 airway inflammation by binding to SPR and regulating its protein expression in a non-enzymatic manner

Xiaoqun Gu [1], Yanyan Chen [1], Peiyao Qian [1], Ting He [1], Yameng Wu [1], Wei Lin [2], Jie Zheng [3], Min Hong [4]

Affiliations expand

Abstract

Background: Cimifugin is one of the main bioactive components of Yu-Ping-Feng-San, a well-known traditional Chinese medicine, which can effectively relieve Allergic asthma (AA) and atopic dermatitis and reduce recurrence in clinic. However, the underlying mechanism of cimifugin on AA is still unknown.

Purpose: In the present study, we aimed to investigate the effect and mechanism of cimifugin on AA.

Study design: In vivo and in vitro experimental studies were performed.

Methods: The effect of cimifugin on AA was demonstrated in vivo and in vitro. Sepiapterin reductase (SPR) was predicted as the most potent target of cimifugin in treating AA by reverse docking. Molecular docking and microscale thermophoresis (MST) were used to analyze the direct binding between cimifugin and SPR. Overexpression and interference of SPR were performed to verify whether targeting SPR is a key step of cimifugin in the treatment of AA. QM385, an inhibitor of SPR, was administrated in vivo and in vitro to evaluate the role of SPR in AA. Further, HPLC and cell-free direct hSPR enzyme activity assay were performed to research whether cimifugin regulated SPR by influencing the enzyme activity. Simultaneously, the inhibitors of protein degradation were used in vitro to explore the mechanism of cimifugin on SPR.

Results: We found cimifugin effectively alleviated AA by reducing airway hyperresponsiveness, inhibiting type 2 cytokines-mediated airway inflammation, and restoring the expression of epithelial barrier proteins. Molecular docking predicted the direct binding ability of cimifugin to SPR, which was further verified by MST. Notably, the therapeutic effect of cimifugin on AA was dampened with SPR interfering, in contrast, the phenotypic features of AA were significantly alleviated with QM385 application both in vivo and in vitro. Interestingly, cimifugin showed no effect on the enzyme activity of SPR, as the level of its substrate sepiapterin was not affected with cimifugin treatment by cell-free enzyme activity assay. Furthermore, we found cimifugin could reduce SPR protein expression without affecting its mRNA expression probably through autophagosome pathway.

Conclusions: To our knowledge, we're reporting for the first time that cimifugin can suppresses type 2 airway inflammation to alleviate AA by directly binding to SPR and regulating its protein expression in a non-enzymatic manner.

Keywords: Allergic asthma; Cimifugin; Direct bonding; Non-enzymatic manner; SPR.

Conflict of interest statement

Declaration of Competing Interest The authors declare no competing interests.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

Review

Olfactory Dysfunction in Mental Illness

Concepció Marin [1][2], Isam Alobid [3][4][5], Mireya Fuentes [3][4], Mauricio López-Chacón [3][4][5], Joaquim Mullol [6][7][8]

Affiliations expand

- PMID: 36696016

- PMCID: PMC9875195

- DOI: 10.1007/s11882-023-01068-z

Free PMC article

Abstract

Purpose of review: Olfactory dysfunction contributes to the psychopathology of mental illness. In this review, we describe the neurobiology of olfaction, and the most common olfactory alterations in several mental illnesses. We also highlight the role, hitherto underestimated, that the olfactory pathways play in the regulation of higher brain

functions and its involvement in the pathophysiology of psychiatric disorders, as well as the effect of inflammation on neurogenesis as a possible mechanism involved in olfactory dysfunction in psychiatric conditions.

Recent findings: The olfactory deficits present in anxiety, depression, schizophrenia or bipolar disorder consist of specific alterations of different components of the sense of smell, mainly the identification of odours, as well as the qualifications of their hedonic valence (pleasant or unpleasant). Epidemiological findings have shown that both environmental factors, such as air pollutants, and inflammatory disease of the upper respiratory tract, can contribute to an increased risk of mental illness, at least in part, due to peripheral inflammatory mechanisms of the olfactory system. In this review, we describe the neurobiology of olfaction, and the most common olfactory function alterations in several psychiatric conditions and its role as a useful symptom for the differential diagnosis. We also highlight the effect of inflammation on neurogenesis as a possible mechanism involved in olfactory dysfunction in these psychiatric conditions.

Conflict of interest statement

C. Marin declares that she has no conflict of interest. I. Alobid has received speaker and consultancy honoraria from Viatris, Roche, Sanofi, GSK, MSD, Menarini, Salvat and Novartis. M. Fuentes declares that she has no conflict of interest. M. López-Chacón declares that he has no conflict of interest. J. Mullol has received speaker and consultancy honoraria, and grants from Sanofi-Genzyme & Regeneron, Novartis, Viatris, Uriach Group, Mitsubishi-Tanabe, Menarini, UCB, AstraZeneca, GSK and MSD.

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- 1 figure

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Risk factors for and pregnancy outcomes after SARS-CoV-2 in pregnancy according to disease severity: A nationwide cohort study with validation of the SARS-CoV-2 diagnosis

Anna J M Aabakke [1][2][3], Tanja G Petersen [4], Karen Wøjdemann [5], Mette H Ibsen [6], Fjola Jonsdottir [7], Elisabeth Rønneberg [7], Charlotte S Andersen [8], Anne Hammer [8], Tine D Clausen [2][3], Julie Milbak [2], Lars Burmester [9], Rikke Zethner [1][7], Birgitte Lindved [10], Annette Thorsen-Meyer [11], Mohammed R Khalil [12], Birgitte Henriksen [12], Lisbeth Jønsson [13], Lise L T Andersen [14], Kamilla K Karlsen [14], Monica L Pedersen [15], Gitte Hedermann [16], Marianne Vestgaard [16], Dorthe Thisted [1][17], Agnethe N Fallesen [18], Josephine N Johansson [18], Ditte C Møller [19], Greta Dubietyte [19], Charlotte B Andersson [20][21], Richard Farlie [22], Ane-Kersti Skaarup Knudsen [22], Lea Hansen [23], Lone Hvidman [23], Anne N Sørensen [24], Sidsel L Rathcke [24], Katrine H Rubin [4][25], Lone K Petersen [14][25], Jan S Jørgensen [14], Lone Krebs [3][11], Mette Bliddal [4][25]

Affiliations expand

Abstract

Introduction: We identified risk factors and outcomes associated with SARS-CoV-2 infection in pregnancy in a universally tested population according to disease severity and validated information on SARS-CoV-2 during pregnancy in national health registers in Denmark.

Material and methods: Cohort study using data from national registers and medical records including all pregnancies between March 1, 2020 and February 28, 2021. We compared women with a validated positive SARS-CoV-2 test during pregnancy with non-infected pregnant women. Risk factors and pregnancy outcomes were assessed by Poisson and Cox regression models and stratified according to disease severity defined by hospital admission status and admission reason (COVID-19 symptoms or other). Using medical record data on actual period of pregnancy, we calculated predictive values of the SARS-CoV-2 diagnosis in pregnancy in the registers.

Results: SARS-CoV-2 infection was detected in 1819 (1.6%) of 111 185 pregnancies. Asthma was associated with infection (relative risk [RR] 1.63, 95% confidence interval [CI] 1.28-2.07). Risk factors for severe COVID-19 disease requiring hospital admission were high body mass index (median ratio 1.06, 95% CI 1.04-1.09), asthma (RR 7.47, 95% CI 3.51-15.90) and gestational age at the time of infection (gestational age 28-36 vs < 22: RR 3.53, 95% CI 1.75-7.10). SARS-CoV-2-infected women more frequently had hypertensive disorders in pregnancy (adjusted hazard ratio [aHR] 1.31, 95% CI 1.04-1.64), early pregnancy loss (aHR 1.37, 95% CI 1.00-1.88), preterm delivery before gestational age 28 (aHR 2.31, 95% CI 1.01-5.26), iatrogenically preterm delivery before gestational age 37 (aHR 1.49, 95% CI 1.01-2.19) and small-for-gestational age children (aHR 1.28, 95% CI 1.05-1.54). The associations were stronger among women admitted to hospital for any reason. The validity of the SARS-CoV-2 diagnosis in relation to pregnancy in the registers compared with medical records showed a negative predictive value of 99.9 (95% CI 99.9-100.0) and a positive predictive value of 82.1 (95% CI 80.4-83.7).

Conclusions: Women infected with SARS-CoV-2 during pregnancy were at increased risk of hypertensive disorders in pregnancy, early pregnancy loss, preterm delivery and having children small for gestational age. The validity of Danish national registers was acceptable for identification of SARS-CoV-2 infection during pregnancy.

Conflict of interest statement

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

- Cited by 1 article
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- 1 figure

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Intensive critical care and management of asthmatic and smoker patients in COVID-19 infection

Dongming Lu [1], Obaid Yaqoob [2], Manish Kumar [3 4], Ajay Singh Kushwah [2], Rahul Kumar Sharma [2], Devinder Kumar [2], Yogendra Mavai [5], Rukaiya Khan [6]

Free article

Abstract

This century's most serious catastrophe, COVID-19, has been dubbed "the most life-threatening disaster ever". Asthmatic persons are even more prone to COVID-19's complex interplay with the underlying inflammatory condition. In order to protect themselves against COVID-19, asthmatic patients must be very vigilant in their usage of therapeutic techniques and drugs (*e.g.*, bronchodilators, 5-lipoxygenase inhibitors), which may be accessed to deal with mild, moderate, and severe COVID-19 indications. People with asthma may have more severe COVID-19 symptoms, which may lead to a worsening of their condition. Several cytokines were found to be elevated in the bronchial tracts of patients with acute instances of COVID-19, suggesting that this ailment may aggravate asthma episodes by increasing inflammation. The intensity of COVID-19 symptoms is lessened in patients with asthma who have superior levels of T-cells. Several antibiotics, antivirals, antipyretics, and anti-inflammatory drugs have been suggested to suppress COVID-19 symptoms in asthmatic persons. Furthermore, smokers are more likely to have aggravated repercussions in COVID-19 infection. Being hospitalized to critical care due to COVID-19, needing mechanical breathing, and suffering from serious health repercussions, are all possible outcomes for someone who has previously smoked. Smoking damages airways and alveoli, which significantly raises the risk of COVID-19-related health complications. Patients with a previous record of smoking are predisposed to severe COVID-19 disease symptoms that essentially require a combination of bronchodilators, mucolytics, antivirals, and antimuscarinic drugs, to cope with the situation. The present review discusses the care and management of asthmatic and smoker patients in COVID-19 infection.

Keywords: COVID-19; SARS-CoV-2; asthma; critical care; smoking.

- 57 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Quantifying airway remodelling for research or clinical purposes: How should we normalize for airway size?

Graham M Donovan [1], Kimberley C W Wang [2][3], John G Elliot [3][4], Alan L James [4][5], Peter B Noble [3]

Affiliations expand

- PMID: 36691759

- DOI: 10.1111/resp.14454

Free article

No abstract available

Keywords: asthma; pathology; respiratory structure and function.

- 14 references

Real-world evaluation of asthma reliever therapy among continuous users of asthma maintenance medication in Japan: A retrospective cohort study using a claims database

Soichiro Hozawa [1], Akira Kikuchi [2], Shotaro Maeda [2]

Affiliations expand

- PMID: 36689789

- DOI: 10.1016/j.resinv.2022.12.007

Abstract

Background: The decrease in mortality rate owing to asthma has slowed in recent years. A large proportion of patients with asthma remain uncontrolled in Japan. This study aimed to

determine the prevalence of short-acting beta 2 agonists (SABA) overuse and its associated factors.

Methods: This large-scale retrospective cohort study analyzed continuously treated patients with asthma aged 15-74 years between January 2017 and December 2017 using a Japanese insurance claims database. Characteristics, disease information, and prescribed drugs were extracted from the database, and treatment steps were defined according to drug combinations based on the criteria of the Japanese asthma guidelines. SABA overuse was defined as ≥3 canisters per year. Factors associated with SABA overuse were estimated using multivariable logistic regression.

Results: Among 7,483 patients with mild-to-moderate asthma, 7,001 (93.6%) and 482 (6.4%) had low and high SABA use, respectively. Inhaled corticosteroids (ICS)/long-acting β-agonists (LABA) were the main asthma control treatments. The proportions of patients who overused SABA were 347 (9.9%) and 1,201 (5.6%) in the ICS and ICS/LABA groups, respectively. The factors associated with SABA overuse were male sex, ICS monotherapy, higher treatment steps, no history of allergic rhinitis, no history of chronic sinusitis, and no asthma management.

Conclusions: There is a relatively low prevalence of SABA overuse among asthmatic patients in Japan. ICS/LABA therapy, treatment steps, allergic rhinitis, chronic sinusitis, and asthma management are associated with a decreased risk of SABA overuse. Further studies are needed to investigate the association between SABA overuse and asthma exacerbation and mortality.

Keywords: Asthma management; Claims database; Japan; Real-world evaluation; Reliever therapy.

Conflict of interest statement

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[mRNA COVID-19 Vaccine Anaphylaxis: Epidemiology, Risk Factors, and Evaluation](#)

[Jordon Jaggers](#) [1][2], [Anna R Wolfson](#) [3][4][5]

Affiliations expand

- PMID: 36689047

- PMCID: [PMC9869308](#)

- DOI: [10.1007/s11882-023-01065-2](#)

Free PMC article

Abstract

Purpose of review: The COVID-19 vaccines have proved essential in our defense against the COVID-19 pandemic. However, concerns regarding allergic reactions to the vaccines persist to this day. Herein, we review the data regarding the frequency of allergic reactions

to the COVID-19 vaccines, the epidemiology, and the management of patients reporting vaccine allergic reactions.

Recent findings: Although initial reports emphasized a high risk of anaphylaxis to the COVID-19 vaccines, more recent data demonstrate similar rates of anaphylaxis to the COVID-19 vaccines as to other vaccines. Alternative explanations for increased rates of apparent allergic reactions are discussed, including the role for stress-related and nocebo responses. COVID-19 vaccines and mRNA vaccine technology are overwhelmingly safe and well-tolerated by most patients. Careful history and case review will enable the discerning physician to safely vaccinate most patients. Rare patients with objective signs and symptoms of anaphylaxis may be candidates for alternatives to vaccination including monoclonal antibodies.

Conflict of interest statement

Dr. Jaggers has nothing to declare. Dr. Wolfson has nothing to declare.

- 48 references

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Respir Investig

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. 2023 Mar;61(2):149-152.

Cardiovascular safety of genetically proxied interleukin-5 inhibition: A mendelian randomization study

Philip Alton [1], David M Hughes [2], Sizheng Steven Zhao [3]

Affiliations expand

- PMID: 36682083

- DOI: 10.1016/j.resinv.2022.12.004

Abstract

Interleukin-5 (IL-5) inhibitors have revolutionized the management of eosinophilic asthma. However, IL-5 is thought to play a protective role in atherosclerosis, and cardiovascular safety data for IL-5i are scarce. We used population-level data to examine the association between genetically proxied IL-5i and the risk of cardiovascular diseases. Genetic instruments for IL-5i were selected from a genome-wide association study of eosinophil count in 563,946 individuals. Genetic association data for coronary artery disease were obtained from 60,801 cases, 40,585 stroke cases, 7988 venous thromboembolism cases, and up to 406,111 controls. We used the inverse-variance weighted method and a series of sensitivity analyses. Nine genetic variants were selected to instrument IL-5i. Genetically proxied IL-5i was not associated with the risk of coronary heart disease (OR 0.82, 95%CI 0.65-1.03), stroke (OR 1.10; 0.95-1.27), or venous thromboembolism (OR 0.87; 0.64-1.17). We found no genetic evidence to suggest that IL-5i affects the risk of adverse cardiovascular and thromboembolic events.

Keywords: Asthma; Cardiovascular safety; Genetic instrumental variable; IL-5; Mepolizumab.

Conflict of interest statement

Conflict of Interest The authors have no conflicts of interest.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

Multimorbidity increased the risk of urinary incontinence in community-dwelling adults: Results from the English Longitudinal Study On Ageing

Mario Barbagallo [1], Lee Smith [2], Ai Koyanagi [3], Ligia J Dominguez [4], Anna Fazzari [1], Eliana Marrone [1], Stefania Maggi [5], Giovanni Ruotolo [6], Alberto Castagna [6], Nicola Veronese [7]

Affiliations expand

- PMID: 36669309

- DOI: 10.1016/j.maturitas.2022.12.007

Abstract

Multimorbidity (MM) is common in older people. Recent evidence, largely from cross-sectional studies, suggests that MM could be a risk factor for urinary incontinence (UI). For

this reason, we aimed to explore the association between MM at baseline and incident UI, and which individual chronic medical conditions/factors might explain the association between MM and UI, using data from the English Longitudinal Study on Ageing, during ten years of follow-up. MM was defined as having two or more chronic medical conditions; the presence of UI was assessed using self-reported information. A logistic regression analysis, adjusted for baseline potential confounders, was used to assess the association between MM and UI, reporting the data as odds ratios (ORs) with their 95 % confidence intervals (CIs). Of 9432 initial participants, 6742 (mean age: 64.8 years; 53.2 % females) without UI at baseline were included in the analysis. MM was present at baseline in 48.8 % of the participants. People with MM had a significantly higher cumulative incidence of UI than their counterparts, leading to a significantly higher risk of UI also after adjusting for potential confounders at baseline (OR = 1.30; 95 % CI: 1.14-1.48). Among the medical conditions, only three were significantly associated with incident UI, namely asthma, Parkinson's disease, and psychiatric disorders. In conclusion, MM at baseline was associated with an increased risk of UI during ten years of follow-up, suggesting that UI is more likely to be present in people with several chronic medical conditions.

Conflict of interest statement

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SSM Popul Health

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Determinants and health outcomes of trajectories of social mobility in Australia

Mithilesh Dronavalli [1], Andrew Page [1], Sandro Sperandei [1], Gabriela Uribe [2], Carmen Huckel Schneider [2], John Eastwood [3]

Affiliations expand

- PMID: 36660174

- PMCID: PMC9843487

- DOI: 10.1016/j.ssmph.2023.101336

Free PMC article

Abstract

Objectives: To investigate trajectories in socio-economic position (SEP) and the onset of a range of physical and mental health outcomes and commencement of treatment.

Methods: The Household Income and Labour Dynamics Australia (HILDA) study, a nationally representative prospective cohort study over the period 2001 to 2020 was used to define trajectories of SEP. Trajectories of low, low-middle, upper-middle and high SEP and decreasing (low-middle to upper-middle SEP) or increasing (upper-middle to lower-middle SEP) SEP were identified using k-longitudinal means. Cox-regression was used to assess SEP trajectories and physical (arthritis or osteoporosis, any cancer, asthma, chronic bronchitis or emphysema, Type 1 diabetes, Type 2 diabetes, hypertension or high blood pressure, and coronary heart disease), and mental health (depression or anxiety) outcomes, and treatment commencement. Predictors of SEP trajectories were also investigated using multinomial logistic regression and random forests.

Results: Decreasing SEP had a higher relative risk of new onset illness than increasing SEP for all health outcomes. Increasing SEP had relative risk estimates that were more

consistent with upper-middle income groups and decreasing SEP had a relative risk consistent with lower-middle income groups. In contrast, there was no socio-economic gradient in treatment commencement for physical health outcomes, or depression or anxiety, with the exception of arthritis or osteoporosis.

Conclusion: Decreasing SEP was associated with poor health outcomes, and increasing SEP with better health outcomes. A range of socio-demographic and psychosocial determinants of SEP trajectories were identified to inform policy responses that could modify trajectories of health inequalities in the Australian context.

Conflict of interest statement

None declared.

- 39 references
- 4 figures

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Incorporating Dynamic Pricing in Cost-Effectiveness Analysis: Are Known Unknowns Valuable?

R Brett McQueen [1], Kelly E Anderson [2], Joseph F Levy [3], Josh J Carlson [4]

Affiliations expand

Abstract

Background: Current practice in health technology assessment (HTA) of pharmaceuticals conducts cost-effectiveness analyses (CEAs) based on a static price or the estimated price at market launch. Recent publications suggest incorporating dynamic pricing. To test the feasibility and importance of including dynamic pricing, we compared the standard static approach to four dynamic scenarios by replicating US-based HTA evaluations with dynamic pricing inputs.

Methods: The four case examples included omalizumab (Xolair®) for the treatment of allergic asthma, elagolix (Orilissa®) for the treatment of endometriosis, ocrelizumab (Ocrevus®) for the treatment of primary progressive multiple sclerosis (PPMS), and dupilumab (Dupixent®) for the treatment of atopic dermatitis (AD). The primary outcome was the relative percentage change in incremental cost-effectiveness ratios (ICERs) per quality-adjusted life-year (QALY) for two dynamic pricing scenarios versus static pricing. Secondary outcomes included the absolute difference in ICERs versus base-case and an assessment of decision uncertainty.

Results: Base-case ICERs were $327,000, $102,000, $700,000, and $102,000 for allergic asthma, endometriosis, PPMS, and AD, respectively. Across scenarios and case examples, the range of ICERs versus base-case varied from decreases of 56% to increases of 232%. The absolute difference in ICERs versus base-case ranged from decreases of $120,000 to increases of $758,000. Conclusions on cost effectiveness were altered in 2/16 scenarios across the four case examples.

Conclusions: Given the decision context that US payers face, with prices varying over time, findings suggest further research to reduce uncertainty around price trajectories, as well as conducting or updating multiple assessments over the lifecycle of pharmaceutical products.

- 24 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

Severe asthma, more than that?

Fanny Wai San Ko[1]

Affiliations expand

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No abstract available

Keywords: asthma; comorbidities; inducible laryngeal obstruction; treatment.

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Maternal human papillomavirus infection during pregnancy and preterm delivery: A mother-child cohort study in Norway and Sweden

Johanna Wiik [1][2][3], Magdalena R Vaernesbranden [1][4], Christine M Jonassen [5][6], Anne Cathrine Staff [4][7], Karin C L Carlsen [4][8], Berit Granum [9], Guttorm Haugen [4][7], Gunilla Hedlin [10][11], Katarina Hilde [4][7], Bo Jacobsson [2][3][12], Staffan Nilsson [13][14], Björn Nordlund [10][11], Anbjørg Rangberg [6], Eva Maria Rehbinder [4][15], Verena Sengpiel [2][3], Håvard Skjerven [4][8], Birgitte K Sundet [4][7], Cilla Söderhäll [10][11], Riyas Vettukattil [4][8], Katrine Sjøborg [1]

Affiliations expand

Abstract

Introduction: Human papillomavirus (HPV) infection is common in women of reproductive age. Infection and inflammation are leading causes for preterm delivery (PTD), but the role of HPV infection in PTD and prelabor rupture of membranes (PROM) is unclear. We aimed to explore whether HPV infection during pregnancy in general, and high-risk-HPV (HR-HPV) infection specifically, increased the risk of PTD, preterm prelabor rupture of membranes (PPROM), PROM at term, and/or chorioamnionitis.

Material and methods: In pregnant women, who were participating in a prospective multicenter cohort study from a general population in Norway and Sweden (PreventADALL, ClinicalTrials.gov NCT02449850), HPV DNA was analyzed in available urine samples at mid-gestation (16-22 weeks) and at delivery, and in the placenta after delivery with Seegene Anyplex II HPV28 PCR assay. The risk of PTD, PPROM, PROM, and chorioamnionitis was analyzed using unadjusted and adjusted logistic regression analyses for any 28 HPV genotypes, including 12 HR-HPV genotypes, compared with HPV-negative women. Further, subgroups of HPV (low-risk/possibly HR-HPV, HR-HPV-non-16 and HR-HPV-16), persistence of HR-HPV from mid-gestation to delivery, HR-HPV-viral load, and presence of multiple HPV infections were analyzed for the obstetric outcomes. Samples for HPV analyses were available from 950 women with singleton pregnancies (mean age 32 years) at mid-gestation and in 753 also at delivery.

Results: At mid-gestation, 40% of women were positive for any HPV and 24% for HR-HPV. Of the 950 included women, 23 had PTD (2.4%), nine had PPROM (0.9%), and six had chorioamnionitis (0.6%). Of the term pregnancies, 25% involved PROM. The frequency of PTD was higher in HR-HPV-positive women (8/231, 3.5%) than in HPV-negative women (13/573, 2.3%) at mid-gestation, but the association was not statistically significant (odds ratio 1.55; 95% confidence interval 0.63-3.78). Neither any HPV nor subgroups of HPV at mid-gestation or delivery, nor persistence of HR-HPV was significantly associated with increased risk for PTD, PPROM, PROM, or chorioamnionitis. No HPV DNA was detected in placentas of women with PTD, PPROM or chorioamnionitis.

Conclusions: HPV infection during pregnancy was not significantly associated with increased risk for PTD, PPROM, PROM, or chorioamnionitis among women from a general population with a low incidence of adverse obstetric outcomes.

Keywords: HPV; delivery; infections; preterm birth; rupture of membranes.

Conflict of interest statement

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

- 30 references
- 2 figures

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Apigenin ameliorates non-eosinophilic inflammation, dysregulated immune homeostasis and mitochondria-mediated airway epithelial cell apoptosis in chronic obese asthma via the ROS-ASK1-MAPK pathway

Hang Yu [1], Xi Huang [1], Hua-He Zhu [1], Na Wang [1], Cong Xie [1], Yao-Long Zhou [1], Han-Lin Shi [1], Meng-Meng Chen [1], Yue-Ren Wu [1], Zhen-Hui Ruan [1], Yu-Bao Lyu [1], Qing-Li Luo [2], Jing-Cheng Dong [3]

Abstract

Background: Obese asthma is one of the important asthma phenotypes that have received wide attention in recent years. Excessive oxidative stress and different inflammatory endotypes may be important reasons for the complex symptoms, frequent aggravation, and resistance to traditional treatments of obese asthma. Apigenin (API), is a flavonoid natural small molecule compound with good anti-inflammatory and antioxidant activity in various diseases and proved to have the potential efficacy to combat obese asthma.

Methods: In vivo, this study fed C57BL/6 J mice with high-fat diets(HFD)for 12 weeks and then stimulated them with OVA for 6 weeks to establish a model of chronic obese asthma, while different doses of oral API or dexamethasone were used for therapeutic interventions. In vitro, this study used HDM to stimulate human bronchial cells (HBEs) to establish the model and intervened with API or Selonsertib (SEL).

Results: This study clarified that OVAinduced a type of mixed granulocytic asthma with elevated neutrophils and eosinophils in obese male mice fed with long-term HFD, which also exhibited mixed TH17/TH1/TH2 inflammation. Apigenin effectively suppressed this complex inflammation and acted as a regulator of immune homeostasis. Meanwhile, apigenin reduced AHR, inflammatory cell infiltration, airway epithelial cell apoptosis, airway collagen deposition, and lung oxidative stress via the ROS-ASK1-MAPK pathway in an obese asthma mouse model. In vitro, this study found that apigenin altered the binding status of TRAF6 to ASK1, inhibited ASK1 phosphorylation, and protected against ubiquitin-dependent degradation of ASK1, suggesting that ROS-activated ASK1 may be an important target for apigenin to exert anti-inflammatory and anti-apoptotic effects. To further verify the intervention mechanism, this study clarified that apigenin improved cell viability and mitochondrial function and inhibited apoptosis by interfering with the ROS-ASK1-MAPK pathway.

Conclusions: This study demonstrates for the first time the therapeutic effect of apigenin in chronic obese asthma and further clarifies its potential therapeutic targets. In addition, this study clarifies the specificity of chronic obese asthma and provides new options for its treatment.

Keywords: ASK1; Apigenin; Apoptosis; Chronic obese asthma; Inflammation; ROS.

Conflict of interest statement

Declaration of Competing Interest The manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. We have read and understood your journal's policies, and we believe that neither the manuscript nor the study violates any of these. The are no conflicts of interest to declare.

SUPPLEMENTARY INFO

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Interactions between microbiome and underlying mechanisms in asthma

Purevsuren Losol [1], Milena Sokolowska [2], Yoon-Seok Chang [3]

Affiliations expand

- PMID: 36641058

Abstract

Microbiome primes host innate immunity in utero and play fundamental roles in the development, training, and function of the immune system throughout the life. Interplay between the microbiome and immune system maintains mucosal homeostasis, while alterations of microbial community dysregulate immune responses, leading to distinct phenotypic features of immune-mediated diseases including asthma. Microbial imbalance within the mucosal environments, including upper and lower airways, skin, and gut, has consistently been observed in asthma patients and linked to increased asthma exacerbations and severity. Microbiome research has increased to uncover hidden microbial members, function, and immunoregulatory effects of bacterial metabolites within the mucosa. This review provides an overview of environmental and genetic factors that modulate the composition and function of the microbiome, and the impacts of microbiome metabolites and skin microbiota on immune regulation in asthma.

Keywords: Asthma; Diet; Immunity; Metabolite; Microbiome.

Conflict of interest statement

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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The role of CopA in Streptococcus pyogenes copper homeostasis and virulence

Tina H Dao [1], Amy Iverson [1], Stephanie L Neville [2], Michael D L Johnson [3], Christopher A McDevitt [2], Jason W Rosch [4]

Affiliations expand

- PMID: 36639322

- DOI: 10.1016/j.jinorgbio.2023.112122

Free article

Abstract

Maintenance of intracellular metal homeostasis during interaction with host niches is critical to the success of bacterial pathogens. To prevent infection, the mammalian innate immune response employs metal-withholding and metal-intoxication mechanisms to limit bacterial propagation. The first-row transition metal ion copper serves critical roles at the host-pathogen interface and has been associated with antimicrobial activity since antiquity. Despite lacking any known copper-utilizing proteins, streptococci have been reported to accumulate significant levels of copper. Here, we report that loss of CopA, a copper-specific exporter, confers increased sensitivity to copper in Streptococcus pyogenes strain HSC5, with prolonged exposure to physiological levels of copper resulting in reduced viability during stationary phase cultivation. This defect in stationary phase survival was rescued by supplementation with exogeneous amino acids, indicating the pathogen had altered nutritional requirements during exposure to copper stress. Furthermore, S. pyogenes HSC5 ΔcopA was substantially attenuated during murine soft-tissue infection, demonstrating the importance of copper efflux at the host-pathogen interface. Collectively, these data indicate that copper can severely reduce the viability of stationary

phase S. pyogenes and that active efflux mechanisms are required to survive copper stress in vitro and during infection.

Keywords: CopA; Copper; GAS; Group A streptococcus; P-type ATPase.

Conflict of interest statement

Declaration of Competing Interest None.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Review

In vitro human cell-based models to study airway remodeling in asthma

Ying Zhou [1], Qirui Duan [1], Dong Yang [2]

Affiliations expand

Abstract

Airway remodeling, as a predominant characteristic of asthma, refers to the structural changes that occurred both in the large and small airways. These pathological changes not only contribute to airway hyperresponsiveness and airway obstruction, but also predict poor outcomes of patients. In vitro models are the alternatives to animal models that facilitate airway remodeling research. Current approaches to mimic airway remodeling in vitro include mono cultures of cell lines and primary cells that are derived from the respiratory tract, and co-culture systems that consist of different cell subpopulations. Moreover, recent advances in microfluid chips and organoids show promise in simulating the complex architecture and functionality of native organs. According, they enable highly physiological-relevant investigations of human diseases in vitro. Here we aim to detail the current human cell-based models regarding their key pros and cons, and to discuss how they may be used to facilitate our understanding of airway remodeling in asthma.

Keywords: Airway remodeling; Asthma; In vitro models; Microfluid chip; Tissue engineering.

Conflict of interest statement

Conflict of interest statement Ying Zhou, Qirui Duan, and Dong Yang declare that they have no conflict of interest.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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[Association of helminth infestation with childhood asthma: a nested case-control study](#)

[Chamara V Senaratna](#) [1], [Piyumali K Perera](#) [2], [Segarajasingam Arulkumaran](#) [3], [Nirupama Abeysekara](#) [4], [Pramodya Piyumanthi](#) [5], [Garun S Hamilton](#) [6], [Gillian M Nixon](#) [7], [Rupika S Rajakaruna](#) [2], [Shyamali C Dharmage](#) [8]

Affiliations expand

- PMID: 36632894

Free article

Abstract

Objectives: The association between helminthiasis and asthma remains inconclusive but can only be investigated in counties where helminthiasis is transitioning from a high to low burden. We investigated this association using data from a childhood respiratory cohort in Sri Lanka.

Methods: A case-control study was nested within a population-based cohort of children aged 6-14 years in Sri Lanka. The stool samples of 190 children with asthma and 190 children without asthma were analyzed to assess the burden of helminth infestation. Logistic regression models were fitted to investigate the association of gastrointestinal helminth species with asthma.

Results: Helminthiasis in children with and without asthma was 23.3% (n = 44) and 15.3% (n = 23), respectively. Those with asthma were more likely to have helminthiasis (odds ratio 3.7; 95% confidence interval 1.7, 7.7; P = 0.001), particularly with Trichiuris trichura (odds ratio 4.5; 95% confidence interval 1.6, 12.3; P = 0.004). Helminth eggs per gram of feces were not associated with asthma (P >0.05).

Conclusion: Our findings demonstrate a positive association between T. trichura infestation and asthma and point to the need to fully characterize this association to understand the likely immunological mechanism that drives it. This association highlights an important public health intervention in countries where these infestations are still prevalent, affecting 24% of the population worldwide.

Keywords: Asthma; Child; Gastrointestinal; Helminthiasis; Parasitic infestation.

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The effect of COVID-19 on patients recieving omalizumab treatment

N Sayaca [1], K A Cansız [1], E Yıldırım [1], B Öztürk [2], C Kırmaz [1]

Abstract

in English, French

Background and aim: Although exposure during drug administration and susceptibility to coronavirus disease-19 (COVID-19) infection secondary to immunomodulatory effects constitute potential risks for patients with chronic spontaneous urticaria (CSU) or asthma on omalizumab (OMZ), there is a risk of loss of response following discontinuation of OMZ. There are few studies describing the clinical course of COVID-19 in patients receiving OMZ.

Materials and methods: A total of 103 patients on OMZ were included in the study between February 2021 and January 2022.

Results: Fourteen (13.6%) of the patients participating in the study had SARS-CoV-2 infection, of whom 3 (21.4%) required hospitalization and 11 (78.6%) were treated in an outpatient clinic. During the pandemic, 17 (16.5%) of the patients interrupted their OMZ treatment. Patients on OMZ for six months or less had a lower rate of interruption (2.5%) than those on OMZ for more than 6 months (25.4%). Patients interrupted treatment for the following reasons: 3 (17.6%) had COVID-19, 10 (58.9%) did not attend the hospital visit due to concern about contamination with SARS-CoV-2, and 4 (23.5%) thought that OMZ treatment would facilitate contamination with SARS-CoV-2. After interrupting OMZ, 3 (25%) female patients and 5 (100%) male patients presented no worsening of their symptoms. Three (13%) of the patients on OMZ for asthma and 11 (13.8%) of those on the drug for urticaria had COVID-19 infection. Patients presenting CSU and severe asthma are completely different, with different potential consequences of OMZ interruption. Nine (52.9%) patients had aggravated symptoms following interruption of OMZ treatment. Three of them described worsening of asthma symptoms and a need to increment their maintenance therapy due to asthma exacerbation after nearly three weeks of interruption, and 6 of them had hives and pruritus as urticaria exacerbation nearly four weeks after interruption of OMZ. The asthma patients did not stop their other treatments, including inhaled corticosteroids.

Conclusion: Use of OMZ does not increase the risk of SARS-CoV-2 infection, COVID-19-related pneumonia, or COVID-19-related hospitalization. We advise patients not to interrupt OMZ treatment during the COVID-19 pandemic unless advised to do so by their doctors, and we recommend that they receive instruction concerning self-administration of OMZ to avoid visiting hospitals in the event of a pandemic.

Keywords: Asthma; COVID-19; Omalizumab; Urticaria.

- 24 references

Utility of chest radiograph severity scoring in emergency department for predicting outcomes in COVID-19: A study of 1275 patients

Anirudh Venugopalan Nair [1], Devendra Kumar [2], Matthew McInnes [3], Ahmed Akram Hadi [2], Hanee Subair Valiyakath Subair [2], Omar Ammar Khyatt [2], Mohammed Atea Almashhadani [2], Bamil Jacob [2], Anu Vasudevan [4], Mohammad Zaya Ashruf [2], Mahmoud Al-Heidous [2], Deepak Kuttikatt Soman [5]

Affiliations expand

- PMID: 36623355

Abstract

Objective: To measure the reliability and reproducibility of a chest radiograph severity score (CSS) in prognosticating patient's severity of disease and outcomes at the time of disease presentation in the emergency department (ED) with coronavirus disease 2019 (COVID-19).

Materials and methods: We retrospectively studied 1275 consecutive RT-PCR confirmed COVID-19 adult patients presenting to ED from March 2020 through June 2020. Chest radiograph severity score was assessed for each patient by two blinded radiologists. Clinical and laboratory parameters were collected. The rate of admission to intensive care unit, mechanical ventilation or death up to 60 days after the baseline chest radiograph were collected. Primary outcome was defined as occurrence of ICU admission or death. Multivariate logistic regression was performed to evaluate the relationship between clinical parameters, chest radiograph severity score, and primary outcome.

Results: CSS of 3 or more was associated with ICU admission (78 % sensitivity; 73.1 % specificity; area under curve 0.81). CSS and pre-existing diabetes were independent predictors of primary outcome (odds ratio, 7; 95 % CI: 3.87, 11.73; p < 0.001 & odds ratio, 2; 95 % CI: 1-3.4, p 0.02 respectively). No significant difference in primary outcome was observed for those with history of hypertension, asthma, chronic kidney disease or coronary artery disease.

Conclusion: Semi-quantitative assessment of CSS at the time of disease presentation in the ED predicted outcomes in adults of all age with COVID-19.

Keywords: COVID-19; Chest radiograph; SARS-CoV-2; X-ray.

Conflict of interest statement

Declaration of competing interest Authors have no disclosure or no relevant relationships.

- 42 references
- 3 figures

Review

Recent advances predict a bright future for nebulizers

Michael Troy [1], Joseph Van Vleet [2], Donald Tashkin [1], Igor Barjaktarevic [1]

Affiliations expand

- PMID: 36621855

- DOI: 10.1097/MCP.0000000000000941

Abstract

Purpose of review: With the improvement in device technology and delivery methods of inhaled medications, along with development of novel compounds and recognition of the

importance of personalized approach in the management of chronic airway diseases, nebulizers have not only maintained their place in the treatment hierarchy of airway disease but have also proven a vital platform for the development of new classes of drugs.

Recent findings: This short review explores recent advances in nebulized drug delivery in chronic obstructive pulmonary disease and other chronic airway diseases, emphasizing the progress in nebulizer technology, physiologic advantages of nebulized drug delivery and the high versatility of currently available and developing nebulizer-delivered pharmacotherapies.

Summary: Versatility and efficiency of nebulizers allows for a broad spectrum of existing and novel therapies to be clinically studied, facilitating the progress in phenotype-targeted pharmacotherapies in the management of chronic airway diseases.

- 77 references

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Review

J Oral Biol Craniofac Res

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Onco-immunity and therapeutic application of amygdalin: A review

[Ahmed Mohammed Alwan](#) 1, [Dinesh Rokaya](#) 2, [Goma Kathayat](#) 3, [Jalil Tavakol Afshari](#) 1

Affiliations expand

Free PMC article

Abstract

Background: Amygdalin is known as a chemical compound derived from various fruits. The glycosides existing in this plant have been historically utilized as an anticancer agent. This review presented an overview of amygdalin and its onco-immunity and other therapeutic medical applications.

Method: A literature search for studies relating to amygdalin and cancer treatment was carried out using PubMed and Google Scholar. Combinations of the following terms were used in the search strategies: "amygdalin," "rhodanese," "cyanide," "cyanogenic," "hypothiocyanite," "mandelonitrile," "glucosides," "cancer," "apoptosis," and "cytotoxicity," combined with a cancer term such as "seed," "almond," or "apricot," "cancer + cell line, antiproliferation or inhibition," "BAX From the March 3, 1981 until the April 15, 2021, all of the English-language papers were evaluated based on the inclusion criteria. Publications included reviews, chapters from books, and original research papers.

Results: The FDA prohibits Amygdalin from medical usage as an anticancer treatment due to a lack of proof of cure in cancer cases. When this natural-based compound is used with conditional chemotherapeutic medicines causes synergistic effects. Besides, amygdalin is used to manage asthma, improve the immune system, induce apoptosis in human renal fibroblasts, and inhibit hyperglycemia.

Conclusion: Various medical uses of amygdalin have been found such as managing asthma, improving the immune system, inducing apoptosis in human renal fibroblasts, and inhibiting hyperglycemia. More effective in vitro and review studies are required to elucidate the exact role of this herb in medical applications.

Conflict of interest statement

The authors declare no conflicts of interest.

- 94 references
- 5 figures

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Job and exposure intensity among hospital cleaning staff adversely affects respiratory health

Nana Happiness Ndlela [1][2], Rajen N Naidoo [2]

Affiliations expand

Abstract

Background: Occupational exposure to various types of cleaning agents may increase the risk of adverse respiratory health among cleaners. This study investigated the relationship between exposure to cleaning and disinfecting agents, using a job-task and exposure intensity metric, and respiratory outcomes among cleaners.

Methods: A sample of 174 cleaners was selected from three public hospitals in Durban. A questionnaire was used to collect demographic and occupational information, and spirometry, including post-bronchodilator measures, was conducted according to the American Thoracic Society guidelines and skin prick testing were performed. Exposure metrics for job tasks and chemical exposures were created using frequency and employment-lifetime duration of exposure. Multivariate analysis regression models used job task and exposure intensity metrics.

Results: Doctor-diagnosed asthma prevalence was 9.8%. Breathlessness with wheeze (22.4%) was the prevalent respiratory symptom. Positive responses to skin prick testing were seen in 74 (43.2%). There was a statistically significant increased risk for shortness of breath with exposure to quaternary ammonium compounds (odds ratio [OR]: 3.44; 95% confidence interval [CI]: 1.13-10.5) and breathlessness with exposure to multipurpose cleaner (OR: 0.34; CI: 0.12-0.92). The losses in percent-predicted forced expiratory volume in 1 s (FEV1) ranged from 0.3%-6.7%. Results among the bronchodilator-positive (8.6%) showed lung function losses twofold greater when compared to the total study population with percentage predicted FEV1 (-22.6 %; $p < 0.000$).

Conclusion: Exposure to certain cleaning and disinfectant agents adversely affects respiratory health, particularly lung function. This effect, while seen generally among cleaning workers, is more pronounced among those with pre-existing reversible obstructive lung disease.

Keywords: allergy; asthma; cleaners; cleaning agents; occupational exposures; respiratory.

- 38 references

SUPPLEMENTARY INFO

Comparing self-reported obstructive airway disease in firefighters with and without World Trade Center exposure

Alexandra K Mueller [1][2], Ankura Singh [1][2], Mayris P Webber [1][3], Charles B Hall [3], David J Prezant [1][2][3], Rachel Zeig-Owens [1][2][3]

Affiliations expand

- PMID: 36597815

- DOI: 10.1002/ajim.23455

Abstract

Background: The degree to which routine, non-World Trade Center (WTC) firefighting exposures contribute to the WTC exposure-obstructive airway disease (OAD) relationship is unknown. Our objective was to compare the frequency of self-reported OAD diagnoses in WTC-exposed firefighters from the Fire Department of the City of New York (FDNY)

compared with non-WTC-exposed firefighters from other cities and the general population.

Methods: A total of 9792 WTC-exposed male FDNY firefighters and 3138 non-WTC-exposed male firefighters from Chicago, Philadelphia, and San Francisco who were actively employed on 9/11/01 and completed a health questionnaire were included. Logistic regression estimated odds ratios of self-reported asthma and COPD diagnoses in firefighters (WTC-exposed vs. non-WTC-exposed; all firefighters vs. general population), adjusting for age, race, smoking status, and last medical visit.

Results: WTC-exposed firefighters were, on average, younger on 9/11 (mean ± SD = 40.2 ± 7.4 vs. 44.1 ± 9.1) and less likely to report ever-smoking (32.9% vs. 41.8%) than non-WTC-exposed firefighters. Odds of any OAD and asthma were 4.5 and 6.3 times greater, respectively, in WTC-exposed versus non-WTC-exposed. Odds of COPD were also greater in WTC-exposed versus non-WTC-exposed, particularly among never-smokers. Compared with the general population, WTC-exposed firefighters had greater odds of both asthma and COPD, while the nonexposed had lower odds of asthma and greater odds of COPD.

Conclusions: Odds ratios for OAD diagnoses were greater in WTC-exposed firefighters versus both non-WTC-exposed and the general population after adjusting for covariates. While asthma and other OADs are known occupational hazards of firefighting, WTC exposure significantly compounded these adverse respiratory effects.

Keywords: COPD; World Trade Center; asthma; firefighters; obstructive airway disease.

- 41 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Military deployment–related respiratory problems: an update

Eric Garshick [1], Paul D Blanc [2]

Affiliations expand

Abstract

Purpose of review: Military personnel deployed to Southwest Asia and Afghanistan were potentially exposed to high levels of fine particulate matter and other pollutants from multiple sources, including dust storms, burn pit emissions from open-air waste burning, local ambient air pollution, and a range of military service-related activities that can generate airborne exposures. These exposures, individually or in combination, can have adverse respiratory health effects. We review exposures and potential health impacts, providing a framework for evaluation.

Recent findings: Particulate matter exposures during deployment exceeded U.S. National Ambient Air Quality Standards. Epidemiologic studies and case series suggest that in postdeployment Veterans with respiratory symptoms, asthma is the most commonly diagnosed illness. Small airway abnormalities, most notably particularly constrictive bronchiolitis, have been reported in a small number of deployers, but many are left without an established diagnosis for their respiratory symptoms. The Promise to Address

Comprehensive Toxics Act was enacted to provide care for conditions presumed to be related to deployment exposures. Rigorous study of long-term postdeployment health has been limited.

Summary: Veterans postdeployment to Southwest Asia and Afghanistan with respiratory symptoms should undergo an exposure assessment and comprehensive medical evaluation. If required, more advanced diagnostic considerations should be utilized in a setting that can provide multidisciplinary expertise and long-term follow-up.

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Respirology

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Cardiovascular and cerebrovascular mortality in patients with preceding asthma exacerbation

Soojoung Yu [1], Sang Chul Lee [2], Jung Hwa Hong [3], Chang Hoon Han [2], Seon Cheol Park [2], Ji Ye Jung [4]

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Differential remodeling in small and large murine airways revealed by novel whole lung airway analysis

Amanda L Tatler [1], Christopher J Philp [1], Michael R Hill [2], Sam Cox [3], Andrew M Bullock [2], Anthony Habgood [1], Alison John [1], Robert Middlewick [1], Katherine E Stephenson [1], Amanda T Goodwin [1], Charlotte K Billington [1], Reuben D O'Dea [2], Simon R Johnson [1], Bindi S Brook [2]

Abstract

Airway remodeling occurs in chronic asthma leading to increased airway smooth muscle (ASM) mass and extracellular matrix (ECM) deposition. Although extensively studied in murine airways, studies report only selected larger airways at one time-point meaning the spatial distribution and resolution of remodeling are poorly understood. Here we use a new method allowing comprehensive assessment of the spatial and temporal changes in ASM, ECM, and epithelium in large numbers of murine airways after allergen challenge. Using image processing to analyze 20-50 airways per mouse from a whole lung section revealed increases in ASM and ECM after allergen challenge were greater in small and large rather than intermediate airways. ASM predominantly accumulated adjacent to the basement membrane, whereas ECM was distributed across the airway wall. Epithelial hyperplasia was most marked in small and intermediate airways. After challenge, ASM changes resolved over 7 days, whereas ECM and epithelial changes persisted. The new method suggests large and small airways remodel differently, and the long-term consequences of airway inflammation may depend more on ECM and epithelial changes than ASM. The improved quantity and quality of unbiased data provided by the method reveals important spatial differences in remodeling and could set new analysis standards for murine asthma models.

Keywords: airway smooth muscle; asthma; extracellular matrix; heterogeneity.

Conflict of interest statement

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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A compilation answering 50 questions on monkeypox virus and the current monkeypox outbreak

Beatriz Cabanillas [1], Giuseppe Murdaca [2], Amir Guemari [3], Maria Jose Torres [4], Ahmet Kursat Azkur [5], Emel Aksoy [5], Joana Vitte [3] [6], Leticia de Las Vecillas [7], Mattia Giovannini [8] [9], Ruben Fernández-Santamaria [10], Riccardo Castagnoli [11] [12], Andrea Orsi [13], Rosa Amato [13], Irene Giberti [13], Alba Català [14], Dominika Ambrozej [15] [16], Bianca Schaub [17] [18], Gerdien A Tramper-Stranders [19], Natalija Novak [20], Kari C Nadeau [21], Ioana Agache [22] [23], Mubeccel Akdis [24], Cezmi A Akdis [24] [25]

Affiliations expand

- PMID: 36587287

- DOI: 10.1111/all.15633

Abstract

The current monkeypox disease (MPX) outbreak constitutes a new threat and challenge for our society. With more than 55,000 confirmed cases in 103 countries, World Health

Organization declared the ongoing MPX outbreak a Public Health Emergency of International Concern (PHEIC) on July 23, 2022. The current MPX outbreak is the largest, most widespread, and most serious since the diagnosis of the first case of MPX in 1970 in the Democratic Republic of the Congo (DRC), a country where MPX is an endemic disease. Throughout history, there have only been sporadic and self-limiting outbreaks of MPX outside Africa, with a total of 58 cases described from 2003 to 2021. This figure contrasts with the current outbreak of 2022, in which more than 55,000 cases have been confirmed in just 4 months. MPX is, in most cases, self-limiting; however, severe clinical manifestations and complications have been reported. Complications are usually related to the extent of virus exposure and patient health status, generally affecting children, pregnant women, and immunocompromised patients. The expansive nature of the current outbreak leaves many questions that the scientific community should investigate and answer in order to understand this phenomenon better and prevent new threats in the future. In this review, 50 questions regarding monkeypox virus (MPXV) and the current MPX outbreak were answered in order to provide the most updated scientific information and to explore the potential causes and consequences of this new health threat.

- 156 references

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J Affect Disord

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. 2023 Mar 1;324:162-169.

Cognitive impairments among patients in a long–COVID clinic: Prevalence, pattern and relation to illness severity, work function and quality of life

K W Miskowiak [1], J K Pedersen [2], D V Gunnarsson [3], T K Roikjer [2], D Podlekareva [4], H Hansen [5], C H Dall [3], S Johnsen [4]

Affiliations expand

Free PMC article

Abstract

Background: A considerable proportion of people experience lingering symptoms after Coronavirus Disease 2019 (COVID-19). The aim of this study was to investigate the frequency, pattern and functional implications of cognitive impairments in patients at a long-COVID clinic who were referred after hospitalisation with COVID-19 or by their general practitioner.

Methods: Patients underwent cognitive screening and completed questionnaires regarding subjective cognition, work function and quality of life. Patients' cognitive performance was compared with that of 150 age-, sex-, and education-matched healthy controls (HC) and with their individually expected performance calculated based on their age, sex and education.

Results: In total, 194 patients were assessed, on average 7 months (standard deviation: 4) after acute COVID-19.44-53 % of the patients displayed clinically relevant cognitive impairments compared to HC and to their expected performance, respectively. Moderate to large impairments were seen in global cognition and in working memory and executive function, while mild to moderate impairments occurred in verbal fluency, verbal learning

and memory. Hospitalised (n = 91) and non-hospitalised (n = 103) patients showed similar degree of cognitive impairments in analyses adjusted for age and time since illness. Patients in the cognitively impaired group were older, more often hospitalised, had a higher BMI and more frequent asthma, and were more often female. More objective cognitive impairment was associated with more subjective cognitive difficulties, poorer work function and lower quality of life.

Limitations: The study was cross-sectional, which precludes causality inferences.

Conclusions: These findings underscore the need to assess and treat cognitive impairments in patients at long-COVID clinics.

Keywords: COVID-19; Cognitive impairment; Quality of life; Work function.

Conflict of interest statement

Conflict of interest The authors report no conflicts of interest in relation to the current manuscript. Outside of the present work, KWM reports having received consultancy fees from Janssen-Cilag and Lundbeck; JKP, DVG, DP, HH, CHD and SJ report no conflicts of interest outside of the present work.

- 46 references
- 3 figures

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Ann Allergy Asthma Immunol

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Unique ulcerative undefined autoinflammatory disease mistaken for factitious disorder

Nicolas Tcheurekdjian [1], Nareen Tenbelian [2], Carlos M Isada [3], Kord Honda [4], Glenn Treisman [5], Haig Tcheurekdjian [6]

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Allergy

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IL-5 receptor expression in lung fibroblasts: Potential role in airway remodeling in asthma

Khuloud Bajbouj [1] [2], Rola AbuJabal [1] [2], Lina Sahnoon [2], Ronald Olivenstein [3], Bassam Mahboub [4], Qutayba Hamid [1] [2] [3]

Affiliations expand

No abstract available

Keywords: IL-5 receptor; airway fibroblasts; asthma; fibrosis.

- 11 references

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Publication types, Grant supportexpand

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Review

Pulm Ther

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Utility of Hypoglycemic Agents to Treat Asthma with Comorbid Obesity

Derek Ge [1], Dinah Foer [2], Katherine N Cahill [3]

Affiliations expand

Abstract

Adults with obesity may develop asthma that is ineffectively controlled by inhaled corticosteroids and long-acting beta-adrenoceptor agonists. Mechanistic and translational studies suggest that metabolic dysregulation that occurs with obesity, particularly hyperglycemia and insulin resistance, contributes to altered immune cell function and low-grade systemic inflammation. Importantly, in these cases, the same proinflammatory cytokines believed to contribute to insulin resistance may also be responsible for airway remodeling and hyperresponsiveness. In the past decade, new research has emerged assessing whether hypoglycemic therapies impact comorbid asthma as reflected by the incidence of asthma, asthma-related emergency department visits, asthma-related hospitalizations, and asthma-related exacerbations. The purpose of this review article is to discuss the mechanism of action, preclinical data, and existing clinical studies regarding the efficacy and safety of hypoglycemic therapies for adults with obesity and comorbid asthma.

Keywords: Body mass index; DPP-4 inhibitors; GLP-1R agonists; Incretins; Insulin; Metformin; SGLT-2 inhibitors; Sulfonylureas; Thiazolidinediones; Type 2 diabetes.

- 119 references
- 2 figures

SUPPLEMENTARY INFO

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De novo discovery of traits co-occurring with chronic obstructive pulmonary disease

Evgeniia Golovina [1], Tayaza Fadason [1][2], Rachel K Jaros [1], Haribalan Kumar [3], Joyce John [3], Kelly Burrowes [3], Merryn Tawhai [3], Justin M O'Sullivan [4][2][5][6][7]

Affiliations expand

- PMID: 36574990

- PMCID: PMC9795035

Abstract

Chronic obstructive pulmonary disease (COPD) is a heterogeneous group of chronic lung conditions. Genome-wide association studies have identified single-nucleotide polymorphisms (SNPs) associated with COPD and the co-occurring conditions, suggesting common biological mechanisms underlying COPD and these co-occurring conditions. To identify them, we have integrated information across different biological levels (i.e., genetic variants, lung-specific 3D genome structure, gene expression and protein-protein interactions) to build lung-specific gene regulatory and protein-protein interaction networks. We have queried these networks using disease-associated SNPs for COPD, unipolar depression and coronary artery disease. COPD-associated SNPs can control genes involved in the regulation of lung or pulmonary function, asthma, brain region volumes, cortical surface area, depressed affect, neuroticism, Parkinson's disease, white matter microstructure and smoking behaviour. We describe the regulatory connections, genes and biochemical pathways that underlay these co-occurring trait-SNP-gene associations. Collectively, our findings provide new avenues for the investigation of the underlying biology and diverse clinical presentations of COPD. In so doing, we identify a collection of genetic variants and genes that may aid COPD patient stratification and treatment.

Conflict of interest statement

The authors declare that they have no conflict of interest.

- 63 references
- 11 figures

SUPPLEMENTARY INFO

MeSH termsexpand

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Systemic contact dermatitis to peanut ingestion

[Katelyn H Wong](#) [1], [Mehek Mehta](#) [2], [Agnieszka Matczuk](#) [3], [Stephanie Leeds](#) [2]

Affiliations expand

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Preliminary study of the exploration patients' experiences of chronic respiratory experiences during the COVID-19 pandemic using interpretative phenomenological analysis

Edina Tomán [1 2], Judit Nóra Pintér [2], Rita Hargitai [3]

Affiliations expand

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Abstract

During the first period of coronavirus pandemic, respiratory patients may have been more vulnerable to mental health problems in addition to their physical vulnerability. The aim was to explore and deepen our understanding of the experiences of chronic respiratory patients at risk of pandemic COVID-19 using interpretative phenomenological analysis. The study involved 8 participants with asthma, COPD or cystic fibrosis. Three main themes emerged: 1. respiratory illness as a defining experience in everyday life, 2. the impact of the COVID-19 pandemic on the self and identity organisation, and 3. adaptation to experiencing vulnerability. Breathlessness as the most frightening feature of progressive lung disease, can be linked to fear and anxiety in different ways. The experience of vulnerability is a fundamental part of their lives. The potentially contagious nature of COVID-19 draws a sharp line between the endangered Self and the dangerous Other. In terms of their adaptation, we observe essentially self-defense mechanisms and emotion-focused strategies.

Keywords: COVID-19; Coronavirus; Interpretative phenomenological analysis; Qualitative research; Respiratory disease.

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- 50 references
- 1 figure

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Urinary metabolites of polycyclic aromatic hydrocarbons and short-acting beta agonist or systemic corticosteroid asthma medication use within NHANES

Stephen P Uong [1], Haider Hussain [2], Erin Thanik [2], Stephanie Lovinsky-Desir [3], Jeanette A Stingone [4]

Affiliations expand

- PMID: 36572332

Abstract

Background: Within cross-sectional studies like the U.S. National Health and Nutritional Examination Survey (NHANES), researchers have observed positive associations between polycyclic aromatic hydrocarbon (PAH) exposure and asthma diagnosis. It is unclear whether similar relationships exist for measures of acute asthma outcomes, including short-term asthma medication use to alleviate symptoms. We examined the relationship between markers of recent PAH exposure and 30-day short-acting beta agonist (SABA) or systemic corticosteroid use, an indicator for recent asthma symptoms.

Materials and methods: For 16,550 children and adults across multiple waves of NHANES (2005-2016), we fit quasi-Poisson multivariable regression models to describe the association between urinary 1-hydroxypyrene (a metabolite of PAH) and SABA or systemic corticosteroid use. We assessed for effect modification by age group and asthma controller medication use. All models were adjusted for urinary creatinine, age, female/male designation, race/ethnicity, poverty, insurance coverage, and serum cotinine.

Results: After controlling for confounding, an increase of one standard deviation of 1-hydroxypyrene was associated with greater prevalence of recent SABA or systemic corticosteroid use (PR: 1.06, 95% CI: 1.03-1.10). The results were similar among those with ever asthma diagnosis and across urine creatinine dilution methods. We did not observe effect modification by age group (p-interaction = 0.22) or asthma controller medication use (p-interaction = 0.73).

Conclusion: Markers of recent PAH exposure was positively associated with SABA or systemic corticosteroid use, across various urine dilution adjustment methods. It is important to ensure appropriate temporality between exposures and outcomes in cross-sectional studies.

Keywords: Asthma exacerbations; Asthma medications; Asthma symptoms; Indoor and outdoor air pollution; Polycyclic aromatic hydrocarbons; Urine dilution adjustment.

Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The Influence of US Drug Price Dynamics on Cost-Effectiveness Analyses of Biologics

Stephen J Kogut [1], Jon D Campbell [2], Steven D Pearson [2]

Affiliations expand

- PMID: 36566884

- DOI: 10.1016/j.jval.2022.12.010

Abstract

Objectives: This study aimed to evaluate the influence of drug price dynamics in cost-effectiveness analyses.

Methods: We evaluated scenarios involving typical US drug price increases during the exclusivity period and price decreases after the loss of exclusivity (LOE). Worked examples are presented using the Institute for Clinical and Economic Review's assessments of tezepelumab for the treatment of severe asthma and targeted immune modulators for rheumatoid arthritis.

Results: Tezepelumab case: yearly 2% price increases during the period of exclusivity and a post-LOE price decrease of 25% yielded an incremental cost per quality-adjusted life-year (QALY) gained that increased over the base case from $430 300 to $444 600 (+3.2%). Yearly 2% price increases followed by a steeper post-LOE price reduction of 40% resulted in a cost per QALY gained of $401 400 (6.8% reduction vs the base case). Rheumatoid arthritis case: incorporating post-LOE price reductions for etanercept (intervention) and adalimumab (comparator) ranging from 25% to 40% yielded an incremental cost per QALY of $121 000 and $122 300, respectively (< 3% increase from the base case of $119 200/QALY). Including a 2% yearly price increase during the projected exclusivity periods of both intervention and comparator increased the cost per QALY gained by > 60%.

Conclusion: Two biologic treatment cases incorporating price dynamics in cost-effectiveness analyses had varied impacts on the cost-effectiveness ratio depending on the magnitude of pre-LOE price increase and post-LOE price decrease and whether the LOE also affected the comparator. Yearly price increase magnitude during the period of exclusivity, among other factors, may counterbalance the effects of lower post-LOE intervention prices.

Keywords: cost-effectiveness analysis; dynamic; exclusivity; pricing.

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. 2023 Mar;112(3):496-504.

Loss of control in preschoolers with asthma is a risk factor for disease persistency

Adam Holm-Weber [1], Louise Aarestrup [1], Julie Prahl [1], Mette Hermansen [1], Kirsten Skamstrup Hansen [1,2], Bo Chawes [1,3]

Affiliations expand

- PMID: 36565166

- DOI: 10.1111/apa.16630

Abstract

Aim: To describe the relationship between loss of control events in preschoolers with asthma and persistence of disease.

Methods: We reviewed medical records of children <6 years diagnosed with asthma in 2018 to assess loss of control events during three years of follow-up. Asthma persistency was defined by redeem of short-acting β2-agonist or asthma controllers within one year after the end of follow-up. Logistic regression models were applied to analyse the association between loss of control events and persistence of asthma.

Results: We included 172 patients (median age 1.8 years), whereof 126 (73.3%) experienced a loss of control event and 87 (50.6%) had asthma one year after the end of follow-up. Any loss of control event was associated with persistence of asthma adjusted for controller treatment at inclusion, prior exacerbations, atopic comorbidity and caesarean section: aOR, 10.9 (95% CI, 3.9-34.6), p < 0.001. This was also significant restricted to events in the first year of follow-up: 3.52 (1.50-8.67), p < 0.01 and among children only experiencing one event: 6.4 (1.7-27.3), p = 0.01.

Conclusion: Loss of control events during a 3-year period among preschoolers with asthma are closely related to disease persistency, which may aid clinicians to assess risk of persistent asthma in young children.

Keywords: asthma; children; loss of control; persistence; remission.

- <u>Cited by 1 article</u>
- <u>30 references</u>

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Does maternal fermented dairy products consumption protect against cow's milk protein allergy in toddlers?

<u>Zeynep Gulec Koksal</u>[1], <u>Pinar Uysal</u>[2], <u>Adnan Mercan</u>[2], <u>Simge Atar Bese</u>[2], <u>Duygu Erge</u>[2]

Affiliations expand

- PMID: 36563745

- DOI: <u>10.1016/j.anai.2022.12.024</u>

Abstract

Background: Cow's milk protein allergy (CMPA) is the most common immunoglobulin E-mediated food allergy in childhood.

Objective: To investigate the potential impact on the disease of the frequency, amount, and diversity of maternal consumption of fermented dairy products (FDP) during pregnancy and lactation in children with immunoglobulin E-mediated CMPA.

Methods: One hundred sixty toddlers (80 with physician-diagnosed CMPA and 80 healthy controls) and their mothers participated in this case-control study. The data were collected using a structured questionnaire and were compared between the 2 groups.

Results: The most commonly consumed FDP were cheese, yogurt, and tarhana. The amounts of maternal yogurt, tarhana, and kefir consumed during pregnancy (P < .001, P < .001, and P = .04, respectively) in addition to yogurt and tarhana consumption during lactation (P < .001 and P = .001, respectively) were lower in toddlers with CMPA. The frequency of maternal consumption of yogurt, cheese, and tarhana during lactation (P = .001, P = .003, and P = .02, respectively) and the diversity of FDP were also lower in toddlers with CMPA (P = .001). At multivariate logistic regression analysis, maternal weight gain during pregnancy (odds ratio [OR], 1.11; 95% confidence interval [CI], 1.04-1.18; P = .001), maternal age (OR, 1.20; 95% CI, 1.09-1.31; P < .001), and gestational age at birth (OR, 1.23; 95% CI, 1.03-1.48; P = .02) increased the odds of the baby having CMPA. The diversity of FDP consumed during lactation was protective against CMPA (OR, 0.439; 95% CI, 0.272-0.711; P = .001).

Conclusion: Weekly maternal consumption of FDP was low during pregnancy and lactation in toddlers with CMPA. Although the diversity of FDP consumed during lactation may reduce the risk of CMPA, this effect was not observed during pregnancy.

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Unconventional interactions of the TRPV4 ion channel with beta-adrenergic receptor ligands

Miguel Benítez-Angeles [1], Emmanuel Juárez-González [1], Ariela Vergara-Jaque [2][3], Itzel Llorente [1], Gisela Rangel-Yescas [4], Stéphanie C Thébault [5], Marcia Hiriart [1], León D Islas [4], Tamara Rosenbaum [6]

Affiliations expand

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Abstract

The transient receptor potential vanilloid 4 (TRPV4) ion channel is present in different tissues including those of the airways. This channel is activated in response to stimuli such as changes in temperature, hypoosmotic conditions, mechanical stress, and chemicals from plants, lipids, and others. TRPV4's overactivity and/or dysfunction has been associated with several diseases, such as skeletal dysplasias, neuromuscular disorders, and lung pathologies such as asthma and cardiogenic lung edema and COVID-19-related respiratory malfunction. TRPV4 antagonists and blockers have been described; nonetheless, the mechanisms involved in achieving inhibition of the channel remain scarce, and the search for safe use of these molecules in humans continues. Here, we show that the widely used bronchodilator salbutamol and other ligands of β-adrenergic receptors inhibit TRPV4's activation. We also demonstrate that inhibition of TRPV4 by salbutamol is achieved through interaction with two residues located in the outer region of the pore and that salbutamol leads to channel closing, consistent with an allosteric mechanism. Our study

provides molecular insights into the mechanisms that regulate the activity of this physiopathologically important ion channel.

Conflict of interest statement

The authors declare that they have no conflict of interest.

- 120 references
- 11 figures

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MeSH terms, Substances, Associated dataexpand

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Review

Anti-inflammatory effects of medications used for viral infection-induced respiratory diseases

Mutsuo Yamaya [1], Akiko Kikuchi [2], Mitsuru Sugawara [3], Hidekazu Nishimura [4]

Affiliations expand

Abstract

Respiratory viruses like rhinovirus, influenza virus, respiratory syncytial virus, and coronavirus cause several respiratory diseases, such as bronchitis, pneumonia, pulmonary fibrosis, and coronavirus disease 2019, and exacerbate bronchial asthma, chronic obstructive pulmonary disease, bronchiectasis, and diffuse panbronchiolitis. The production of inflammatory mediators and mucin and the accumulation of inflammatory cells have been reported in patients with viral infection-induced respiratory diseases. Interleukin (IL)-1β, IL-6, IL-8, tumor necrosis factor-α, granulocyte-macrophage colony-stimulating factor, and regulated on activation normal T-cell expressed and secreted are produced in the cells, including human airway and alveolar epithelial cells, partly through the activation of toll-like receptors, nuclear factor kappa B and p44/42 mitogen-activated protein kinase. These mediators are associated with the development of viral infection-induced respiratory diseases through the induction of inflammation and injury in the airway and lung, airway remodeling and hyperresponsiveness, and mucus secretion. Medications used to treat respiratory diseases, including corticosteroids, long-acting β_2-agonists, long-acting muscarinic antagonists, mucolytic agents, antiviral drugs for severe acute respiratory syndrome coronavirus 2 and influenza virus, macrolides, and Kampo medicines, reduce the production of viral infection-induced mediators, including cytokines and mucin, as determined in clinical, in vivo, or in vitro studies. These results suggest that the anti-inflammatory effects of these medications on viral infection-induced respiratory diseases may be associated with clinical benefits, such as improvements in symptoms, quality of life, and mortality rate, and can prevent hospitalization and the exacerbation of chronic obstructive pulmonary disease, bronchial asthma, bronchiectasis, and diffuse panbronchiolitis.

Keywords: Airway epithelial cells; Inhaled corticosteroid; Muscarinic antagonist; Viral infection; β(2)-agonist.

Conflict of interest statement

- 158 references
- 1 figure

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Supplementary conceptsexpand

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Allergy

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. 2023 Mar;78(3):855-858.

 doi: 10.1111/all.15624. Epub 2022 Dec 30.

The second COVID-19 mRNA vaccine dose enhances the capacity of Spike-

specific memory B cells to bind Omicron BA.2

Gemma E Hartley [1], Emily S J Edwards [1], Nirupama Varese [1], Irene Boo [2], Pei M Aui [1], Scott J Bornheimer [3], P Mark Hogarth [1 4 5], Heidi E Drummer [2 6 7], Robyn E O'Hehir [1 8], Menno C van Zelm [1 8]

Affiliations expand

- PMID: 36541822

- PMCID: PMC9877979

- DOI: 10.1111/all.15624

Free PMC article
No abstract available

Conflict of interest statement

MCvZ, REO'H, and PMH are inventors on a patent application related to this work. SJB is an employee of and owns stock in BD Biosciences. All the other authors declare no conflict of interest.

- 6 references
- 2 figures

SUPPLEMENTARY INFO

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Proposed solutions by the American College of Allergy, Asthma, and Immunology and advocacy experts to address racial disparities in atopic dermatitis and food allergy

Mark Corbett [1], Abby Allen [2], Nichole Bobo [3], Michael B Foggs [4], Luz S Fonacier [5], Ruchi Gupta [6], Rachel Kowalsky [7], Erin Martinez [8], Wendy Smith Begolka [9], Cherie Zachary [10], Michael S Blaiss [11]

Affiliations expand

- PMID: 36538973

- DOI: 10.1016/j.anai.2022.12.017

Abstract

Atopic dermatitis (AD) and food allergies are more prevalent and more severe in people with skin of color than White individuals. The American College of Allergy, Asthma, and Immunology (ACAAI) sought to understand the effects of racial disparities among patients with skin of color with AD and food allergies. The ACAAI surveyed its members (N = 200 completed), conducted interviews with health care providers and advocacy leaders, and hosted a roundtable to explore the challenges of diagnosis and management of AD and food allergies in people with skin of color and to discuss potential solutions. Most of the survey respondents (68%) agreed that racial disparities make it difficult for people with skin of color to receive adequate treatment for AD and food allergies. The interviews and roundtable identified access to care, burden of costs, policies and infrastructure that limit access to safe foods and patient education, and inadequate research involving people with skin of color as obstacles to care. Proposed solutions included identifying ways to recruit more people with skin of color into clinical trials and medical school, educating health care

providers about diagnosis and treating AD and food allergy in people with skin of color, improving access to safe foods, creating and disseminating culturally appropriate materials for patients, and working toward longer appointment times for patients who need them. Challenges in AD and food allergy in persons with skin of color were identified by the ACAAI members. Solutions to these challenges were proposed to inspire actions to mitigate racial disparities in AD and food allergy.

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Anaphylaxis to pickled chili pepper (Capsicum frutescens): Role of pickling processing in the allergic reactivity

Celine Galleani [1], Rafael Valdelvira [2], M Carmen Diéguez [2], Jesús F Crespo [2], Beatriz Cabanillas [2]

Affiliations expand

- PMID: 36538971

- DOI: 10.1016/j.anai.2022.12.020

No abstract available

Association of Childhood Respiratory Status with Adult Occupational Exposures in a Birth Cohort

Philip Harber [1 2], Melissa Furlong [1], Debra A Stern [2], Wayne J Morgan [2 3], Anne L Wright [2 3], Stefano Guerra [2], Fernando D Martinez [2]

Affiliations expand

- PMID: 36538681

- DOI: 10.1513/AnnalsATS.202204-293OC

Abstract

Rationale: People with better early-life respiratory health may be more likely to work in occupations with high workplace exposures in adult life compared with people with poor respiratory health. This may manifest as a healthy worker effect bias, potentially confounding the analysis of environmental exposure studies. **Objectives:** To evaluate associations between lung function in adolescence and occupational exposures at initial adult employment. **Methods:** The TCRS (Tucson Children's Respiratory Study) is a long-

term prospective study of respiratory health beginning at birth. Associations between respiratory function at age 11 years and occupational exposures at first job at age 26 years were evaluated with logistic regression. We calculated percentage predicted values for forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1:FVC ratio, and forced expiratory flow from 25% to 75% of vital capacity at age 11. At the 26-year visit, participants self-reported occupational exposures to dust, smoke, and fumes/gas at first job in a standardized interview. **Results:** Forced expiratory flow from 25% to 75% of vital capacity and FEV_1:FVC ratio at age 11 were positively associated with dust workplace exposures at the first job. Each 10% increase in percentage predicted prebronchodilator FEV_1:FVC ratio was associated with 30% higher odds of workplace dust exposure (odds ratio for a 1% increase, 1.03 [95% confidence interval, 1.00-1.06; P = 0.045]). Similar associations were observed for FEV_1 and FVC with workplace smoke exposures. We also observed modification by time at job: associations were stronger for those who remained in their jobs longer than 12 months. In addition, those with better function at age 11 were more likely to stay in their jobs longer than 12 months if their first jobs involved exposure to dust. **Conclusions:** Childhood lung function affects initial career choice. This study supports the premise of the healthy worker effect.

Keywords: childhood lung function; healthy worker effect; job choice; occupation; spirometry.

SUPPLEMENTARY INFO

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Review

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Which Endoscopic Procedure to Use and in What Patient? Valves, Coils, Foam, and Heat in COPD and Asthma

Andrew Li [1][2][3], Pyng Lee [4][5]

Affiliations expand

- PMID: 36534323

- PMCID: PMC9931990

- DOI: 10.1007/s41030-022-00208-6

Abstract

Despite the latest developments in therapeutic agents targeting airway endotypes, a significant proportion of patients with asthma and chronic obstructive pulmonary disease (COPD) remain symptomatic. Endoscopic therapies have a complementary role in the management of these airway diseases. The sustained efficacy of bronchial thermoplasty (BT) among patients with asthma over 10 years has been encouraging, as it has been shown to improve symptom control and reduce hospital admissions and exacerbations. Studies suggest that BT helps ameliorate airway inflammation and reduce airway smooth muscle thickness. While studies suggest that it is as effective as biologic agents, its role in the management of severe asthma has yet to be clearly defined and GINA 2022 still suggests limiting its use to patients with characteristics of the various populations studied. Conversely, bronchoscopic lung volume reduction has shown promise among patients with advanced COPD. Rigorous patient selection is important. Patients with minimal collateral ventilation (CV) and higher heterogeneity index have shown to benefit the most from endobronchial valve (EBV) therapy. For those with ongoing CV, endobronchial coils would be more appropriate. Both therapeutic modalities have demonstrated improved quality of life, effort tolerance, and lung function indices among appropriately selected patients. The emerging evidence suggests that endoscopic procedures among airway disease still have a substantial role to play despite the development of new therapeutic options.

- 94 references
- 1 figure

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An observational multi-centric COVID-19 sequelae study among health care workers

Ajay Kumar Shukla [1], Shubham Atal [1], Aditya Banerjee [1], Ratinder Jhaj [1], Sadasivam Balakrishnan [1], Preeta Kaur Chugh [2], Denis Xavier [3], Atiya Faruqui [3], Aakanksha Singh [3], Ramasamy Raveendran [4], Jayanthi Mathaiyan [4], Jeevitha Gauthaman [4], Urwashi I Parmar [5], Raakhi K Tripathi [5], Sandhya K Kamat [5], Niyati Trivedi [6], Prashant Shah [6], Janki Chauhan [6], Harihar Dikshit [7], Hitesh Mishra [7], Rajiv Kumar [7], Dinesh Kumar Badyal [8], Monika Sharma [9], Mamta Singla [10], Bikash Medhi [11], Ajay Prakash [11], Rupa Joshi [11], Nabendu S Chatterjee [12], Jerin Jose Cherian [12], Ved Prakash Kamboj [12], Nilima Kshirsagar [12]

Abstract

Background: India has seen more than 43 million confirmed cases of COVID-19 as of April 2022, with a recovery rate of 98.8%, resulting in a large section of the population including the healthcare workers (HCWs), susceptible to develop post COVID sequelae. This study was carried out to assess the nature and prevalence of medical sequelae following COVID-19 infection, and risk factors, if any.

Methods: This was an observational, multicenter cross-sectional study conducted at eight tertiary care centers. The consenting participants were HCWs between 12 and 52 weeks post discharge after COVID-19 infection. Data on demographics, medical history, clinical features of COVID-19 and various symptoms of COVID sequelae was collected through specific questionnaire.

Finding: Mean age of the 679 eligible participants was 31.49 ± 9.54 years. The overall prevalence of COVID sequelae was 30.34%, with fatigue (11.5%) being the most common followed by insomnia (8.5%), difficulty in breathing during activity (6%) and pain in joints (5%). The odds of having any sequelae were significantly higher among participants who had moderate to severe COVID-19 (OR 6.51; 95% CI 3.46-12.23) and lower among males (OR 0.55; 95% CI 0.39-0.76). Besides these, other predictors for having sequelae were age (≥45 years), presence of any comorbidity (especially hypertension and asthma), category of HCW (non-doctors vs doctors) and hospitalisation due to COVID-19.

Interpretation: Approximately one-third of the participants experienced COVID sequelae. Severity of COVID illness, female gender, advanced age, co-morbidity were significant risk factors for COVID sequelae.

Funding: This work is a part of Indian Council for Medical Research (ICMR)- Rational Use of Medicines network. No additional financial support was received from ICMR to carry out the work, for study materials, medical writing, and APC.

Conflict of interest statement

All other authors declare no competing interests.

- 35 references

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J Ethnopharmacol

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. 2023 Mar 1;303:116047.

 doi: 10.1016/j.jep.2022.116047. Epub 2022 Dec 14.

The extract from Hyssopus cuspidatus Boriss. Prevents bronchial airway remodeling by inhibiting mouse

bronchial wall thickening and hASMC proliferation and migration

Xiaocui Cai [1], Yan Mao [2], Xiaoli Shen [3], Haifang Li [4], Jinhua He [5], Mingjun Zhang [6]

Affiliations expand

- PMID: 36528211

- DOI: 10.1016/j.jep.2022.116047

Abstract

Ethnopharmacological relevance: Bronchial asthma, a non-communicable chronic respiratory disease, affects people of all ages. An important pathological feature of bronchial asthma is airway remodeling. Hyssopus cuspidatus Boriss. has been used to treat bronchial asthma for over 100 years in Uygur medicine. The ethanol extract of Hyssopus cuspidatus Boriss.(JAX2) can improve airway inflammation in asthma. However, the anti-asthmatic airway-remodeling effect of JAX2 is unclear.

Aim of the study: The current study investigated the anti-airway remodeling effect of JAX2 and elucidated its mechanism of action.

Materials and methods: The present study established an ovalbumin-induced mouse model of asthma and platelet-derived growth factor-BB-induced human airway smooth muscle cells (hASMCs) proliferation model, with dexamethasone (DEX) and feining tablets (FNP) designated as positive control drugs. Pathological changes in lung tissues were observed using hematoxylin and eosin staining. Interleukin (IL)-5, IL-10, IL-13, and IL-33 levels in the bronchoalveolar lavage fluid (BALF) and serum of mice were determined using enzyme-linked immunosorbent assay (ELISA). Changes in the expression and distribution of TGF-β1, p-ERK1/2, Smad2/3, and p-Smad3 in lung tissues were determined using immunohistochemistry. Western blotting (WB) was used to determine the protein levels of p-ERK1/2 in lung tissues and cells. MTS assay was used to determine the effects of JAX2 on cell proliferation. IL-5, IL-10, IL-13, MMP-2, and MMP-9 levels in the cell supernatant were determined using ELISA. HASMCs migration was observed using the scratch and transwell methods. The effect of JAX2 on the hASMCs cycle was determined using flow cytometry.

Results: JAX2 significantly improved the pathological status of lung tissues in asthmatic mice. It could also significantly reduce IL-5, IL-13, and IL-33 levels in the BALF and serum of asthmatic mice in a dose-dependent manner and significantly increase IL-10 levels. TGF-β1, p-ERK1/2, Smad2/3, and p-Smad3 expression in lung tissues were decreased in a dose-dependent manner. The protein level of p-ERK1/2 in lung tissues was also reduced. JAX2

could significantly inhibit the proliferation and migration of PDGF-BB-induced hASMCs. IL-5, IL-13, MMP-9, and MMP-2 levels decreased significantly, and IL-10 levels increased significantly in a dose-dependent manner in the cell supernatant. JAX2 could block hASMCs in the G0/G1 phase, thereby inhibiting cell proliferation. p-ERK1/2 protein levels were found to decrease in a dose-dependent manner.

Conclusions: JAX2 significantly inhibits airway remodeling in asthma. Its mechanism of action may be inhibiting the proliferation and migration of hASMCs, releasing inflammatory factors and metalloproteinases, activating the ERK1/2 signal pathway, and promoting the secretion of anti-inflammatory factors.

Keywords: Airway remodeling; Bronchial Asthma; Hyssopus cuspidatus Boriss..

Conflict of interest statement

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Yardstick for managing cough, part 1: In adults and adolescent patients older than 14 years of age

Richard S Irwin [1], John J Oppenheimer [2], Whitney Dunlap [3], Jay A Lieberman [4], Anne B Chang [5]

Affiliations expand

- PMID: 36526233

- DOI: 10.1016/j.anai.2022.12.008

Abstract

Nationwide statistics in the United States and Australia reveal that cough of undifferentiated duration is the most common complaint for which patients of all ages seek medical care in the ambulatory setting. Management of chronic cough is one of the most common reasons for new patient visits to pulmonologists. Because symptomatic cough is such a common problem and so much has been learned about how to diagnose and treat cough of all durations but especially chronic cough, this 2-part yardstick has been written to review in a practical way the latest evidence-based guidelines most of which have been developed from recent high quality systematic reviews on how best to manage cough of all durations in adults, adolescents, and children. In this manuscript, part 1 of the 2-part series, we provide evidence-based, and expert opinion recommendations on the management of chronic cough in adult and adolescent patients (>14 years of age).

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Fixed drug eruption to aripiprazole, cetirizine, and hydroxyzine hydrochloride

Nicole Diaz-Ramos [1], Sylvette Nazario [2], Iona Malinow-Maceo [2]

Affiliations expand

- PMID: 36521786

- DOI: 10.1016/j.anai.2022.12.007

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A confirmed fosfomycin-induced mast cell activation with anaphylaxis

Michiel Beyens[1], Dorien Pint[2], Alessandro Toscano[3], Didier Ebo[4], Vito Sabato[4]

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Clinical guidance for the use of dupilumab in eosinophilic esophagitis: A yardstick

Seema S Aceves[1], Evan S Dellon[2], Matthew Greenhawt[3], Ikuo Hirano[4], Chris A Liacouras[5], Jonathan M Spergel[6]

Affiliations expand

Abstract

The Joint Task Force for the American Academy of Allergy Asthma Immunology and American College of Allergy Asthma Immunology and the American Gastroenterology Association recently published guidelines for the management of eosinophilic esophagitis (EoE). Because the guideline was published, dupilumab became the first and only medication to gain regulatory approval for the treatment of EoE. This expert opinion document provides a framework for how the clinician can consider using dupilumab in the treatment strategy for patients with EoE.

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Exploring the anti-inflammatory potential of Colocasia esculenta root

extract in in-vitro and in-vivo models of inflammation

Momita Rani Baro [1], Manas Das [2], Anuradha Kalita [3], Bhabajyoti Das [4], Kishore Sarma [5]

Affiliations expand

Abstract

Ethnopharmacological relevance: Colocasia esculenta (CE) (L.) Schott is an annual herbaceous tropical plant from the family of Araceae which has been traditionally used for the healing of various ailments such as asthma, arthritis, internal hemorrhage, diarrhea, and neurological disorders. The plant is reported to have potential anti-microbial, anti-fungal, antimetastatic, anti-hepatotoxic, and anti-lipid peroxidative activities.

Aim of the study: The present study is designed to explore the potential anti-inflammatory property of Colocasia esculenta methanolic root extract (CEMRE) on carrageenan-induced rat paw edema and lipopolysaccharide (LPS) stimulated RAW264.7 cells.

Materials and methods: Carrageenan-induced rat paw edema model was used to investigate the in vivo anti-inflammatory action of CEMRE. Adult male Wistar rats (180-220 g; n = 6) were pre-treated with CEMRE (100, 200, and 400 mg/kg BW) orally before 1 h of injection of 1% carrageenan. Indomethacin (10 mg/kg BW) was given orally as the standard drug. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), nitric oxide (NO), prostaglandinE2 (PGE2), and cytokines levels were measured. Liquid chromatography-mass spectrometry (LC-MS) was done to identify the phytoconstituents present in CEMRE. The inhibitory activity of CEMRE was investigated against cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in in vitro assessment of LPS-stimulated RAW264.7 cells. The RAW 264.7 cells were pre-treated with Indomethacin (5 μM and 10 μM) and CEMRE (17 μg/ml and 34 μg/ml) followed by induction of LPS (1 μg/ml) for 24 h. Docking analyses were also performed to explore the interaction of important phytoconstituents (Sinapic acid, Acetylsalicylic acid, L-fucose, Salicylic acid, Quinic acid, Zingerone, and Gingerol) of CEMRE with COX-2 and iNOS.

Results: Pre-treatment with CEMRE (400 mg/kg) could inhibit the paw inflammation significantly which was elevated due to carrageenan induction. The inhibition is comparable to that of the standard drug Indomethacin. The concentration of serum AST,

ALT, ALP, NO, PGE2 and cytokines were also considerably lowered in the CEMRE-treated group as compared to the carrageenan-induced group. CEMRE (34 μg/ml) inhibited the LPS-stimulated relative expression of mRNA of COX-2 and iNOS and significantly reduced the expression of nitric oxide and prostaglandin E2. Docking analyses revealed promising interaction with low binding energies between Sinapic acid with both the target proteins COX-2 and iNOS.

Conclusion: Collectively, our results suggested that CEMRE exhibited effective anti-inflammatory actions on carrageenan-induced rat paw edema and LPS-treated RAW 264.7 cells by reducing the in vivo paw edema inhibition, inhibiting the serum NO, PGE2, cytokines and also reduced the in vitro production of NO, PGE2 along with expressions of mRNA COX-2 and iNOS. Molecular docking demonstrated good binding affinities among the target proteins and ligand Sinapic acid. Thus the bioactive compound from CE need to be isolated and purified.

Keywords: Colocasia esculenta; Inflammation; LPS-Stimulated RAW264.7cells; Nitric oxide; Rat paw edema.

Conflict of interest statement

Declaration of competing interest Authors declare no conflicts of interest. The funder had no role in the design of the study; collection, analyses or interpretation of data; writing of the manuscript, or decision to publish the results. The manuscript has not been submitted for possible publication to another journal or that the work has not previously been published elsewhere.

SUPPLEMENTARY INFO

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Ann Allergy Asthma Immunol

Worsening hypereosinophilia with use of dupilumab

Sonia Mathew [1], Timothy Kubal [2], Farnaz Tabatabaian [3]

Affiliations expand

- PMID: 36513222

- DOI: 10.1016/j.anai.2022.12.005

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A case of rare splice-site Bruton's tyrosine kinase mutation with atypical X-linked agammaglobulinemia

Sanghwa E Park [1], Brittanie I Neaves [2], Karla Adams [3]

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Factors associated with home epinephrine-treated reactions during peanut and tree-nut oral immunotherapy

Liat Nachshon [1], Naama Schwartz [2], Michael B Levy [3], Michael R Goldberg [4], Naama Epstein-Rigbi [4], Yitzhak Katz [4], Arnon Elizur [4]

Affiliations expand

Abstract

Background: Home reactions requiring epinephrine administration, a marker of their severity, restrict the widespread use of oral immunotherapy (OIT), but their risk factors are largely not known.

Objective: To identify risk factors for such reactions during OIT to most allergenic foods.

Methods: All patients who began OIT for peanut, tree nuts, sesame, or egg allergy at the Shamir Medical Center between April 2010 and January 2020 were enrolled. The patients were instructed to use their epinephrine autoinjectors during reactions consisting of severe abdominal pain, significant shortness of breath, or lethargy, or whenever in uncertainty of reaction severity. Patients with and without home epinephrine-treated reactions (HETRs) were compared.

Results: A total of 757 OIT treatments for peanut (n = 346), tree nuts (n = 221; walnut n = 147, cashew n = 57, hazelnut n = 16, almond n = 1), sesame (n = 115), and egg (n = 75) allergies were administered to 644 patients. Eighty-three (10.9%) patients experienced HETRs. The highest rate of HETRs was experienced during walnut (20.4%) or hazelnut (25%) OIT, followed by peanut (9.8%), sesame (6.1%), egg (6.7%), and cashew (5.3%) OIT. Risk factors for HETRs included a reaction treated in an emergency department (ER) (P = .005) before starting OIT and a reaction treated with epinephrine during in-clinic induction (P < .001). Significantly fewer patients with (73.6%) than without (88.3%) HETRs achieved full desensitization (P = .001), but only a few patients with HETRs (8.4%) failed treatment.

Conclusion: Previous reaction severity is the main predictor for HETRs during OIT. These reactions are more frequent during walnut and hazelnut OIT than during OIT for other foods studied. Most patients experiencing HETRs achieved desensitization.

FULL TEXT LINKS

ELSEVIER
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Review

The epidemiology of food allergy in adults

[Christopher Warren](#)[1], [Sai R Nimmagadda](#)[2], [Ruchi Gupta](#)[3], [Michael Levin](#)[4]

Affiliations expand

- PMID: 36509408

- DOI: [10.1016/j.anai.2022.11.026](#)

Abstract

The prevalence and awareness of food allergy (FA) among US adults is arguably at a historical high, both with respect to primary immunoglobulin E-mediated food hypersensitivity and other food-triggered conditions that operate through a variety of immunologic mechanisms (eg, pollen-FA syndrome, alpha-gal syndrome, food protein-induced enterocolitis syndrome, eosinophilic esophagitis). Worryingly, not only are many adults retaining childhood-onset food allergies as they age into adulthood, it seems that many adults are experiencing adult-onset allergies to previously tolerated foods, with correspondingly adverse physical, and psychological health impacts. Consequently, this review aims to summarize what is currently known about the epidemiology and population-level burden of FA among adult populations in North America and around the

globe. This article also provides insights into the natural history of these conditions and what we need to know as we look to the future to support effective care and prevent FA.

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The long-term effect of dupilumab on dyspnea, sleep, and activity in oral corticosteroid-dependent severe asthma

Lawrence D Sher [1], Giovanni Passalacqua [2], Camille Taillé [3], Lauren Cohn [4], Nadia Daizadeh [5], Nami Pandit-Abid [6], Xavier Soler [7], Angela Khodzhayev [7], Juby A Jacob-Nara [6], Yamo Deniz [7], Paul J Rowe [6], Arpita Nag [5], Yi Zhang [7]

Affiliations expand

- PMID: 36509407

Free article

Abstract

Background: Severe asthma impacts quality of life (QoL), including dyspnea, sleep, and activity limitation. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukins-4 and -13, which are key and central drivers of type 2 inflammation. Phase 3 LIBERTY ASTHMA VENTURE ([NCT02528214](NCT02528214)) and LIBERTY ASTHMA TRAVERSE open-label extension ([NCT02134028](NCT02134028)) evaluated dupilumab 300 mg vs placebo every 2 weeks for 24 weeks (VENTURE) and dupilumab only for an additional 48 to 96 weeks (TRAVERSE) in patients with oral corticosteroid (OCS)-dependent severe asthma.

Objective: To assess dupilumab's impact on Asthma QoL Questionnaire (AQLQ) items related to breathing symptoms, sleep, and activity limitation, and on OCS reduction.

Methods: The proportion of patients with AQLQ scores of 6 or 7 for breathing symptoms-, sleeping-, and activity-related items in VENTURE and TRAVERSE, together with OCS dose reductions in VENTURE.

Results: In VENTURE, significantly greater proportions of dupilumab- vs placebo-treated patients achieved scores of 6 or 7 by week 24 in breathing symptoms-related (42.7%-60.2% vs 22.4%-39.3%), sleeping-related (45.6%-65.0% vs 27.1%-47.7%), and activity-related (44.7%-51.5% vs 22.4%-34.6%) AQLQ items. Improvements were maintained through TRAVERSE in the dupilumab/dupilumab group and increased to dupilumab treatment levels in the placebo/dupilumab group. Significant OCS dose reductions were observed in VENTURE; up to 90% and 60% of dupilumab-treated vs 65% and 41% of placebo-treated patients with AQLQ scores of 6 or 7 in breathing symptoms-, sleeping-, and activity-related items achieved greater than or equal to 50% dose reduction and eliminated OCS at week 24, respectively.

Conclusion: In patients with severe OCS-dependent asthma, dupilumab improved QoL related to breathing symptoms, sleep, and activity limitation, and reduced OCS use.

Trial registration: ClinicalTrials.gov Identifiers: [NCT02528214](NCT02528214) and [NCT02134028](NCT02134028).

SUPPLEMENTARY INFO

Associated dataexpand

FULL TEXT LINKS

Impact of vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the atopic dermatitis serum proteome

[Madeline Kim](#) [1], [Benjamin Ungar](#) [1], [Yeriel Estrada](#) [1], [Ana B Pavel](#) [1], [Emma Guttman-Yassky](#) [2]

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Free PMC article

No abstract available

- [10 references](#)
- [1 figure](#)

-
-
-

A prediction model for asthma exacerbations after stopping asthma biologics

Jonathan W Inselman [1], Molly M Jeffery [1], Jacob T Maddux [2], Regina W Lam [3], Nilay D Shah [4], Matthew A Rank [5], Che G Ngufor [1]

Affiliations expand

Abstract

Background: Little is known regarding the prediction of the risks of asthma exacerbation after stopping asthma biologics.

Objective: To develop and validate a predictive model for the risk of asthma exacerbations after stopping asthma biologics using machine learning models.

Methods: We identified 3057 people with asthma who stopped asthma biologics in the OptumLabs Database Warehouse and considered a wide range of demographic and clinical risk factors to predict subsequent outcomes. The primary outcome used to assess success after stopping was having no exacerbations in the 6 months after stopping the biologic. Elastic-net logistic regression (GLMnet), random forest, and gradient boosting machine models were used with 10-fold cross-validation within a development (80%) cohort and validation cohort (20%).

Results: The mean age of the total cohort was 47.1 (SD, 17.1) years, 1859 (60.8%) were women, 2261 (74.0%) were White, and 1475 (48.3%) were in the Southern region of the United States. The elastic-net logistic regression model yielded an area under the curve (AUC) of 0.75 (95% confidence interval [CI], 0.71-0.78) in the development and an AUC of 0.72 in the validation cohort. The random forest model yielded an AUC of 0.75 (95% CI, 0.68-0.79) in the development cohort and an AUC of 0.72 in the validation cohort. The gradient boosting machine model yielded an AUC of 0.76 (95% CI, 0.72-0.80) in the development cohort and an AUC of 0.74 in the validation cohort.

Conclusion: Outcomes after stopping asthma biologics can be predicted with moderate accuracy using machine learning methods.

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Sex-specific differences in T-cell immune dysregulation and aberrant response to inflammatory stimuli in offspring exposed to maternal chronic inflammation

Jin Liu [1], Yang Liu [1], Gregory Kirschen [1], Anguo Liu [1], Jun Lei [1], Irina Burd [2]

Affiliations expand

Abstract

Problems: Maternal chronic inflammation (MI) can adversely affect offspring's immune development resulting in dysregulation of splenic T cells. Interleukin 1 beta (IL-1β) contributes to mediating inflammation in the placenta to induce fetal toxicity and cause long-term postnatal sequelae. In this study, we investigated how MI affects the T-cell immune development from the fetal to the neonatal period and how offspring responded to postnatal IL-1β challenge when exposed to an adverse intrauterine environment. We also extend these studies to examine the sex-specific differences.

Methods of study: Time-pregnant CD1 dams were administrated with four consecutive injections of mouse recombinant Interleukin-1β (rIL-1β) or phosphate-buffered saline (PBS) from embryonic day (E)14 to E17. Pups were treated with rIL-1β or PBS at postnatal day (PND)11 (pre-weaning) or PND24 (post-weaning). Pups' splenic immune cells were isolated and then characterized using flow cytometry.

Results: At PND12, no differences were observed either in Ctrl or MI offspring. At PND25, we observed elevated amount of CD8+ T cells, descending CD4+ /CD8+ and Treg/Teff ratio in MI offspring. Pre-weaning rIL-1β administration did not affect T-cell subpopulation in Ctrl pups while post-weaning rIL-1β administration increased T cells and CD8+ T cells and decreased CD4+ /CD8+ and Treg/Teff ratio in Ctrl offspring. Furthermore, pre-weaning rIL-1β administration decreased the frequency of T cells and Treg/Teff ratio in MI pups while post-weaning rIL-1β administration increased Tregs and Treg/Teff in MI pups. Regarding sex-specific changes, we observed that at PND12, MI females exhibited higher CD4+ /CD8+ and Treg/Teff ratio than Ctrl females. At PND25, we observed elevated amount

of CD8+ T cells, descending CD4+ /CD8+ and Treg/Teff ratio in MI Females, while MI males did not show any changes in T-cell population. Pre-weaning rIL-1β administration decreased T-cell frequency in both MI males and females and decreased Treg/Teff ratio only in MI females. Post-weaning rIL-1β administration increased Tregs and Treg/Teff ratio, and decreased CD4+ /CD8+ ratio in MI females.

Conclusions: Prenatal-inflammation-exposed offspring exhibited dysfunctional T-cell immunity and regulatory immune responses to postnatal challenges, showing both sex-specific and age-dependent differences. It could be speculated from our results that experiencing environmental challenges or adverse stimuli during the vulnerable intrauterine period, such as maternal chronic inflammation, stress, preterm birth, and chronic infections, might induce fetal immune reprogramming and potentially cause long-term adverse immune consequences, such as a predisposition to allergic diseases, autoimmune diseases, asthma and pediatric mortality of unknown etiology.

Keywords: T-cell immunity development; Treg/Teff balance; maternal chronic inflammation.

- 57 references

SUPPLEMENTARY INFO

MeSH termsexpand

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Clinical characteristics of the asthma bronchiectasis phenotype

Rory Chan [1], Chary Duraikannu [2], Brian Lipworth [3]

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Metabarcoding airborne pollen from subtropical and temperate eastern Australia over multiple years reveals

pollen aerobiome diversity and complexity

B C Campbell [1], S Van Haeften [1], K Massel [2], A Milic [1], J Al Kouba [3], B Addison-Smith [1], E K Gilding [4], P J Beggs [3], J M Davies [5]

Affiliations expand

Abstract

eDNA metabarcoding is an emergent tool to inform aerobiome complexity, but few studies have applied this technology with real-world environmental pollen monitoring samples. Here we apply eDNA metabarcoding to assess seasonal and regional differences in the composition of airborne pollen from routine samples collected across successive years. Airborne pollen concentrations over two sampling periods were determined using a continuous flow volumetric impaction air sampler in sub-tropical (Mutdapilly and Rocklea) and temperate (Macquarie Park and Richmond), sites of Australia. eDNA metabarcoding was applied to daily pollen samples collected once per week using the rbcL amplicon. Composition and redundancy analysis of the sequence read counts were examined. The dominant pollen families were mostly consistent between consecutive years but there was some heterogeneity between sites and years for month of peak pollen release. Many more families were detected by eDNA than counted by light microscopy with 211 to 399 operational taxonomic units assigned to family per site from October to May. There were 216 unique and 119 taxa shared between subtropics (27°S) and temperate (33°S) latitudes, with, for example, Poaceae, Myrtaceae and Causurinaceae being shared, and Manihot, Vigna and Aristida being in subtropical, and Ceratodon and Cerastium being in temperate sites. Certain genera were observed within the same location and season over the two years; Chloris at Rocklea in autumn of 2017-18 (0.625, $p \leq 0.004$) and 2018-19 (0.55, $p \leq 0.001$), and Pinus and Plantago at Macquarie Park in summer of 2017-18 (0.58, $p \leq 0.001$ and 0.53, $p \leq 0.003$, respectively), and 2018-19 (0.8, $p \leq 0.003$ and 0.8, $p \leq 0.003$, respectively). eDNA metabarcoding is a powerful tool to survey the complexity of pollen aerobiology and distinguish spatial and temporal profiles of local pollen to a far deeper level than traditional counting methods. However, further research is required to optimise the metabarcode target to enable reliable detection of pollen to genus and species level.

Keywords: Aerobiome; Environmental DNA; Metabarcoding; Pollen monitoring; Sub-tropics; Temperate.

Conflict of interest statement

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MeSH terms, Substancesexpand

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Arch Gerontol Geriatr

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. 2023 Mar;106:104892.

 doi: 10.1016/j.archger.2022.104892. Epub 2022 Dec 5.

Association between multimorbidity patterns and catastrophic health expenditure among Chinese older adults living alone

Xinjia Zhai [1], Quan Zhang [2], Xinxuan Li [3], Xinyi Zhao [4]

Affiliations expand

Abstract

Background: Multimorbidity is prevalent among older adults and may result in catastrophic health expenditures (CHEs) on older adults' households. However, whether older adults living alone suffer such a financial burden is unknown. We aimed to investigate the association between multimorbidity patterns and CHE in Chinese older adults living alone.

Methods: We included 884 participants aged 60 years and over and living alone from the 2018 wave of the China Health and Retirement Longitudinal Study (CHARLS). Latent class analysis was performed to identify multimorbidity patterns based on 14 self-reported chronic diseases. The logit model and Tobit model were adopted to analyze the association of multimorbidity patterns with the incidence and intensity of CHE, respectively.

Results: Approximately 20.2% of the older adults living alone experienced CHE. Among the four multimorbidity groups (minimal disease, cardiovascular, lung and asthma, and multisystem), the multisystem group and cardiovascular group had significantly higher incidence and intensity of CHE than the minimal disease group.

Conclusions: Older adults living alone had high risks of CHE, especially those belonging to the multisystem pattern and cardiovascular pattern. Integrated care should be adopted in the treatment of multimorbidity to reduce health costs. More elder services and social assistance should be provided to solitary older adults with certain patterns of multimorbidity.

Keywords: Catastrophic health expenditure; China; Multimorbidity patterns; Older adults living alone.

Conflict of interest statement

Declarations of Competing Interest All the authors have no financial or any other kind of personal conflicts with this manuscript.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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Physiologically-Based Pharmacokinetic Modeling of Omalizumab to Predict the Pharmacokinetics and Pharmacodynamics in Pediatric Patients

[Guimu Guo](#) [#1], [Xiang You](#) [#1], [Wanhong Wu](#) [1], [Jiarui Chen](#) [1], [Meng Ke](#) [1], [Rongfang Lin](#) [1], [Pinfang Huang](#) [1], [Cuihong Lin](#) [1]

Affiliations expand

- PMID: 36495063

- DOI: [10.1002/cpt.2815](#)

Abstract

Omalizumab is widely used in clinical practice; however, knowledge gaps in the dosage of omalizumab for children aged 2-6 years with moderate-to-severe persistent allergic asthma have been identified. The aim of this study was to explore dosing regimens for moderately-to-severely allergic pediatric patients aged 2-6 years. The physiologically-based pharmacokinetic (PBPK) model of omalizumab was developed and verified in adult patients, extrapolated to pediatric patients, and simulated for omalizumab by adding two observation chambers (free IgE and total IgE). The simulation results showed that the fold errors of the predicted and observed values of the area under the curve (AUC) and peak plasma concentration (C_{max}) were between 0.5 and 2.0, and the average folding error and the absolute average folding error values for all concentration-time data points were 1.09 and 1.48, respectively. The PBPK model combined with pharmacokinetic/pharmacodynamic analysis of omalizumab demonstrated that both the model-derived dose and the original dose could control the average free IgE of 2-6-year-old children with moderate-to-severe allergic asthma below 25 ng/mL, and some of the model-derived doses were lower. This conclusion provides a basis for the selection of dosage in clinical practice reference.

- 51 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Scoping Review of Pulmonary Telemedicine Consults: Current Knowledge and Research Gaps

Brandon Li [1], Kari R Gillmeyer [2], Brianne Molloy-Paolillo [3], Varsha G Vimalananda [4][3], A Rani Elwy [3][5], Renda Soylemez Wiener [2][6], Seppo T Rinne [2][3]

Affiliations expand

Abstract

Rationale: Telemedicine consults, including video consults, telephone consults, electronic consults, and virtual conferences, may be particularly valuable in the management of chronic pulmonary diseases, but there is limited guidance on best practices for pulmonary telemedicine consults. **Objectives:** This scoping review aims to identify, characterize, and analyze gaps in the published literature on telemedicine consults health providers use to manage patients with chronic pulmonary diseases. **Methods:** We searched PubMed, Embase, Web of Science, and Cochrane Library from database origin through July 10, 2021. We included manuscripts describing applications of telemedicine consults for patients with chronic pulmonary diseases (asthma, chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, and interstitial lung disease). We restricted our review to full-length articles published in English about provider-led (as opposed to nurse-led) telemedicine consults. **Results:** Our search yielded 3,118 unique articles; 27 articles met the

inclusion criteria. All telemedicine consult modalities and chronic pulmonary conditions were well represented in the review except for pulmonary hypertension and interstitial lung disease, which were represented by one and no articles, respectively. Most articles described a small, single-center, observational study that focused on the acceptability, feasibility, use, and/or clinical effectiveness of the telemedicine consult. Few studies had objectively measured clinical outcomes or included a comparator group, and none compared telemedicine consult modalities against one another. **Conclusions:** Our scoping review identified limited literature describing pulmonary telemedicine consults and highlighted several gaps in the literature that warrant increased attention. Providers treating chronic pulmonary diseases are left with limited guidance on best practices for telemedicine consults.

Keywords: chronic pulmonary diseases; telemedicine.

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Myocd regulates airway smooth muscle cell remodeling in response to chronic asthmatic injury

Qin Yang [1][2], Qing Miao [1], Hui Chen [1][3], Duo Li [1], Yongfeng Luo [1], Joanne Chiu [1], Hong-Jun Wang [1][3], Michael Chuvanjyan [1], Michael S Parmacek [4], Wei Shi [1][3]

Affiliations expand

Abstract

Abnormal growth of airway smooth muscle cells is one of the key features in asthmatic airway remodeling, which is associated with asthma severity. The mechanisms underlying inappropriate airway smooth muscle cell growth in asthma remain largely unknown. Myocd has been reported to act as a key transcriptional coactivator in promoting airway-specific smooth muscle development in fetal lungs. Whether Myocd controls airway smooth muscle remodeling in asthma has not been investigated. Mice with lung mesenchyme-specific deletion of Myocd after lung development were generated, and a chronic asthma model was established by sensitizing and challenging the mice with ovalbumin for a prolonged period. Comparison of the asthmatic pathology between the Myocd knockout mice and the wild-type controls revealed that abrogation of Myocd mitigated airway smooth muscle cell hypertrophy and hyperplasia, accompanied by reduced peri-airway inflammation, decreased fibrillar collagen deposition on airway walls, and attenuation of abnormal mucin production in airway epithelial cells. Our study indicates that Myocd is a key transcriptional coactivator involved in asthma airway remodeling. Inhibition of Myocd in asthmatic airways may be an effective approach to breaking the vicious cycle of asthmatic progression, providing a novel strategy in treating severe and persistent asthma. © 2022 The Authors. The Journal of Pathology published by John Wiley & Sons Ltd on behalf of The Pathological Society of Great Britain and Ireland.

Keywords: Myocd; airway fibrillar collagen; airway inflammation; airway mesenchymal epithelial interaction; airway remodeling; airway smooth muscle cells; asthma.

- 53 references

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

FULL TEXT LINKS

Modeling the Natural Course of Atopic Multimorbidity: Correlates of Early-Life States and Exposures

Arthur H Owora[1]

Affiliations expand

- PMID: 36480962

- DOI: 10.1164/rccm.202211-2062LE

No abstract available

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

Proceed to details

Dasatinib attenuates airway inflammation of asthma exacerbation in mice induced by house dust mites and dsRNA

[Yuki Nishimoto](#)[1], [Daiki Ando](#)[1], [Kosuke Irie](#)[1], [Ikumi Kainuma](#)[1], [Yuki Katayama](#)[1], [Shiori Sato](#)[1], [Tomohiro Suzuki](#)[1], [Mai Harada](#)[1], [Tsubasa Yoshida](#)[1], [Kazuhiro Ito](#)[2], [Yasuo Kizawa](#)[1]

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Abstract

Asthma exacerbation is a significant clinical problem that causes resistance to corticosteroid therapy and elevated hospitalization risk. Src family kinases (SFKs) contribute to various steps of the immune response, such as airway inflammation in viral or bacterial infections and allergic asthma. Therefore, we determined the effects of dasatinib (DAS), a

typical Src inhibitor, on a murine asthma exacerbation model induced by house dust mites (HDM) and synthetic analog of double-stranded RNA, poly(I:C). A/J mice were sensitized to intrapreneurial HDM twice every seven days and challenged with intranasal HDM once every second day for a total of six exposures, and/or exposed to poly(I:C) twice daily for three consecutive days. Drug treatments were performed twice daily for three days, starting one day after the last HDM challenge or 2 h before each poly(I:C) exposure. DAS improved poly(I:C)-induced acute inflammation dose-dependently. Both DAS and fluticasone propionate (FP) attenuated HDM-induced allergic airway inflammation. However, in HDM and poly(I:C) induced-asthma exacerbated mice, DAS significantly improved inflammatory cells in bronchoalveolar lavage fluid and histological changes in the lungs, whereas FP did not. Therefore, SFKs are important targets for controlling severe asthma refractory to conventional therapies.

Keywords: Asthma; Corticosteroid resistance; Exacerbation; Src family kinase.

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Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- 34 references
- 4 figures

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Pediatr Pulmonol

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Preventive therapy for childhood asthma and wheezing: Should we change our approach due to disrupted seasonality in viral circulation?

Cristina De Rose [1], Stefano Miceli Sopo [1][2], Danilo Buonsenso [1][3][4]

Affiliations expand

- PMID: 36478418

- DOI: 10.1002/ppul.26250

No abstract available

Comment on

- [Influenza and respiratory syncytial virus during the COVID-19 pandemic: Time for a new paradigm?](#)
  Binns E, Koenraads M, Hristeva L, Flamant A, Baier-Grabner S, Loi M, Lempainen J, Osterheld E, Ramly B, Chakakala-Chaziya J, Enaganthi N, Simó Nebot S, Buonsenso D.Pediatr Pulmonol. 2022 Jan;57(1):38-42. doi: 10.1002/ppul.25719. Epub 2021 Oct 13.PMID: 34644459 **Free PMC article.**

- 17 references

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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The Human Respiratory Microbiome: Current Understandings and Future Directions

[Lan Zhao](#) [1][2][3], [Jun-Li Luo](#) [4], [Mohammed Khadem Ali](#) [1][2], [Edda Spiekerkoetter](#) [1][2], [Mark R Nicolls](#) [1][2][3]

Affiliations expand

- PMID: 36476129

- DOI: [10.1165/rcmb.2022-0208TR](#)

Abstract

Microorganisms colonize the human body. The lungs and respiratory tract, previously believed to be sterile, harbor diverse microbial communities and the genomes of bacteria (bacteriome), viruses (virome), and fungi (mycobiome). Recent advances in amplicon and shotgun metagenomic sequencing technologies and data-analyzing methods have greatly aided the identification and characterization of microbial populations from airways. The respiratory microbiome has been shown to play roles in human health and disease and is an area of rapidly emerging interest in pulmonary medicine. In this review, we provide updated information in the field by focusing on four lung conditions, including asthma, chronic obstructive pulmonary disease, cystic fibrosis, and idiopathic pulmonary fibrosis. We evaluate gut, oral, and upper airway microbiomes and how they contribute to lower airway flora. The discussion is followed by a systematic review of the lower airway microbiome in health and disease. We conclude with promising research avenues and implications for evolving therapeutics.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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School lives of adolescent school students living with chronic physical health conditions: a qualitative evidence synthesis

Bethan K C Spencer [1], Judy Wright [1], Kate Flemming [2], David Cottrell [1], Simon Pini [3]

Affiliations expand

- PMID: 36460338

- DOI: 10.1136/archdischild-2022-324874

Free article

Abstract

Objective: Assess the existing evidence base in order to synthesise the current qualitative findings for the impact of chronic health conditions on the school lives of young people.

Design: Qualitative evidence synthesis using thematic synthesis.

Patients: Young people aged 11-18 years with a chronic health condition from one of the following groups: oncology, cystic fibrosis, diabetes, asthma, rheumatology, neuromuscular, colorectal, chronic pain, allergies and dermatology.

Outcome measure: Qualitative findings and discussions present in included studies formed the data for the thematic synthesis.

Results: From a search identifying 19 311 records, a sample of 35 papers were included. The included papers represented 15 countries and primarily employed interviews as part of data collection. Thematic synthesis resulted in six themes: 'keeping up/catching up/missing out/looking forward'; 'identity'; 'relationship with peers'; 'normality and difference'; 'autonomy'; 'relationships with staff'.

Conclusions: Thematic synthesis highlighted the commonalities, rather than divergence, of issues for young people across different chronic conditions. Policies need to be based on the experiences of the people they aim to provide for, and while attendance and attainment remain important, there is clearly more that needs to be considered when gathering data, designing interventions and developing policies to support this population. It may also be advisable for clinical professionals to include the broader psychosocial aspects of school life in discussions and plans to support young people with long-term conditions.

Prospero registration number: CRD42021278153.

Keywords: adolescent health; qualitative research.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

Responsiveness of Inhaled Corticosteroid Treatment in Children with Asthma: The Role of rs242941 Polymorphism of CRHR1 Gene

Hanh Nguyen-Thi-Bich[1], Thuy Nguyen-Thi-Dieu[2], Le Nguyen-Ngoc-Quynh[1], Huong Le-Thi-Minh[3], Sy Duong-Quy[4][5][6][7]

Affiliations expand

Free PMC article

Abstract

Introduction: Inhaled corticosteroid (ICS) is the most widely used and effective treatment of asthma. However, some patients do not respond to ICS, which might be due to various genetic factors. Hence, understanding the genetic factors involved in the ICS response could help physicians to individualize their treatment decision and action plans for given patients. This study aimed to analyze the characteristics of corticotropin-releasing hormone receptor 1 (CRHR1) genotypes in children with asthma and the correlation between rs242941 polymorphism of CRHR1 gene and ICS responsiveness.

Methods: This prospective study included children with uncontrolled asthma, assessing their eosinophil count, IgE concentration, lung function, and fractional concentration of nitric oxide in exhaled breath (FENO) and performing CRHR1 polymorphism sequencing. The level of asthma control was assessed by asthma control test (ACT); the responsiveness of asthma treatment with ICS was evaluated by measuring the change of ACT and forced expiratory volume in 1 s (FEV_1) after treatment versus at inclusion.

Results: In total, 107 patients were analyzed for CRHR1 at rs242941. Among these, 86 (80.3%) had homozygous wild-type GG, 20 (18.7%) had heterozygous GT genotypes, and 1 (1.0%) had a homozygous variant for TT. Children with personal and family history of atopy were more likely to have GT and TT genotypes. The severity of asthma was similar between children with asthma in the three groups of GG, GT, and TT genotypes of CRHR1 at rs242941. FENO level, total IgE concentration, and eosinophilic count in children with asthma were not significantly different between GG and GT genotypes. The patient with a TT homozygous variant genotype had a higher level of FENO. There was no correlation between CRHR1 polymorphism at rs242941 and asthma control evaluated by asthma control test and lung function parameters.

Conclusion: TT genotype of rs242941 in the CRHR1 gene is not frequent. Clinical and functional characteristics of children with asthma with rs242941 polymorphism of CRHR1 gene remain homogeneously similar. There is no correlation between rs242941 polymorphism and ACT or FEV_1.

Keywords: Asthma; CRHR1; Children; FENO; ICS; rs242941.

- [24 references](#)
- [2 figures](#)

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Cardiopulmonary fitness in children with asthma versus healthy children

Johan Moreau [# 1 2], Floriane Socchi [# 1 3], Marie Catherine Renoux [1], Anne Requirand [1], Hamouda Abassi [1 2], Sophie Guillaumont [1 3], Stefan Matecki [1 2], Helena Huguet [4], Martina Avesani [5], Marie-Christine Picot [4 6], Pascal Amedro [7 8]

Affiliations expand

Abstract

Objectives: To evaluate, with a cardiopulmonary exercise test (CPET), the cardiopulmonary fitness of children with asthma, in comparison to healthy controls, and to identify the clinical and CPET parameters associated with the maximum oxygen uptake (VO_{2max}) in childhood asthma.

Design: This cross-sectional controlled study was carried out in CPET laboratories from two tertiary care paediatric centres. The predictors of VO_{2max} were determined using a multivariable analysis.

Results: A total of 446 children (144 in the asthma group and 302 healthy subjects) underwent a complete CPET. Mean VO_{2max} was significantly lower in children with asthma than in controls (38.6±8.6 vs 43.5±7.5 mL/kg/min; absolute difference (abs. diff.) of -4.9 mL/kg/min; 95% CI of (-6.5 to -3.3) mL/kg/min; p<0.01) and represented 94%±9% and 107%±17% of predicted values, respectively (abs. diff. -13%; 95% CI (-17 to -9)%; p<0.01). The proportion of children with an impaired VO_{2max} was four times higher in the asthma

group (24% vs 6%, p<0.01). Impaired ventilatory efficiency with increased VE/VCO_2 slope and low breathing reserve (BR) were more marked in the asthma group. The proportion of children with a decreased ventilatory anaerobic threshold (VAT), indicative of physical deconditioning, was three times higher in the asthma group (31% vs 11%, p<0.01). Impaired VO_{2max} was associated with female gender, high body mass index (BMI), FEV1, low VAT and high BR.

Conclusion: Cardiopulmonary fitness in children with asthma was moderately but significantly altered compared with healthy children. A decreased VO_{2max} was associated with female gender, high BMI and the pulmonary function.

Trial registration number: NCT04650464.

Keywords: cardiology; child health; paediatrics; respiratory medicine.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

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Allergy

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IgG memory B cells expressing IL4R and FCER2 are associated with atopic diseases

Carlos J Aranda [1][2], Edgar Gonzalez-Kozlova [3], Sean P Saunders [4], Weslley Fernandes-Braga [1][2], Miyo Ota [1][2], Sriram Narayanan [5], Jin-Shu He [5], Ester Del Duca [6], Bose Swaroop [6], Sacha Gnjatic [2][7], Gail Shattner [4], Joan Reibman [4], Nicholas A Soter [8], Emma Guttman-Yassky [6], Maria A Curotto de Lafaille [1][2]

Affiliations expand

- PMID: 36445014

Abstract

Background: Atopic diseases are characterized by IgE antibody responses that are dependent on cognate CD4 T cell help and T cell-produced IL-4 and IL-13. Current models of IgE cell differentiation point to the role of IgG memory B cells as precursors of pathogenic IgE plasma cells. The goal of this work was to identify intrinsic features of memory B cells that are associated with IgE production in atopic diseases.

Methods: Peripheral blood B lymphocytes were collected from individuals with physician diagnosed asthma or atopic dermatitis (AD) and from non-atopic individuals. These samples were analyzed by spectral flow cytometry, single cell RNA sequencing (scRNAseq), and in vitro activation assays.

Results: We identified a novel population of IgG memory B cells characterized by the expression of IL-4/IL-13 regulated genes FCER2/CD23, IL4R, IL13RA1, and IGHE, denoting a history of differentiation during type 2 immune responses. CD23+ IL4R+ IgG+ memory B cells had increased occurrence in individuals with atopic disease. Importantly, the frequency of CD23+ IL4R+ IgG+ memory B cells correlated with levels of circulating IgE. Consistently, in vitro stimulated B cells from atopic individuals generated more IgE+ cells than B cells from non-atopic subjects.

Conclusions: These findings suggest that CD23+ IL4R+ IgG+ memory B cells transcribing IGHE are potential precursors of IgE plasma cells and are linked to pathogenic IgE production.

Keywords: IgE; atopic diseases; high-dimensional flow cytometry; memory IgG; single-cell sequencing.

- 63 references

SUPPLEMENTARY INFO

Grant supportexpand

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Randomized Controlled Trial

Association of adenotonsillectomy with wheezing episodes in childhood: A secondary analysis of the Childhood Adenotonsillectomy Trial

Jose A Castro-Rodriguez [1], Fiorella Biancardi [2], Oslando Padilla [3], Andrea A Beckhaus [1], Ignacio E Tapia [4]

Affiliations expand

Abstract

Background: Observational studies suggest that asthma/wheezing improves after adenotonsillectomy (AT). However, there is a paucity of randomized clinical trial (RCT) specifically studying the effects of AT in asthma/wheezing. Therefore, we conducted a post-hoc analysis of the Childhood Adenotonsillectomy Trial (CHAT), the largest RCT of AT in children with obstructive sleep apnea (OSA) to test the hypothesis that AT would result in fewer wheezing episodes.

Methods: In the CHAT study, 464 children with OSA, aged 5-9 years, were randomized to early AT (n = 226) or watchful waiting with supportive care (WWSC) (n = 227). For this post-hoc analysis, children were categorized as having "any wheezing" versus "no wheezing" at baseline and at 7 months of follow-up. A multivariate analysis was conducted to evaluate the association between "any wheezing" at follow-up and treatment group after controlling for several potential confounders.

Results: Children in the "any wheezing" group were predominantly black, had more allergic rhinitis, eczema, second-hand smoke exposure, body mass index, apnea-hypopnea index (AHI), and had lower maternal education and family income than those in the "no wheezing group." In the AT arm, the prevalence of wheezing significantly decreased from baseline to follow-up (at 7 months of the intervention) (47% vs. 21.6%, p < 0.001); while in the WWSC arms did not change (45.2% vs. 43.1%, p = 0.67). In the multivariate analysis, second-hand smoke exposure, wheezing at baseline, and belong to WWSC arm (odds ratio: 3.65 [2.16-6.19]) increase the risk of wheezing at follow-up.

Conclusion: This study demonstrated that AT decreased the risk of wheezing at 7 months of follow-up.

Keywords: adenotonsillectomy; asthma; recurrent wheezing.

- 16 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Species–agnostic polymeric formulations for inhalable messenger RNA delivery to the lung

Laura Rotolo [# 1], Daryll Vanover [# 1], Nicholas C Bruno [# 2], Hannah E Peck [1], Chiara Zurla [1], Jackelyn Murray [3], Richard K Noel [4], Laura O'Farrell [4], Mariluz Araínga [5], Nichole Orr-Burks [3], Jae Yeon Joo [1], Lorena C S Chaves [1], Younghun Jung [1], Jared Beyersdorf [1], Sanjeev Gumber [6], Ricardo Guerrero-Ferreira [7], Santiago Cornejo [8], Merrilee Thoresen [8], Alicia K Olivier [8], Katie M Kuo [2], James C Gumbart [2 9], Amelia R Woolums [8], Francois Villinger [5], Eric R Lafontaine [3], Robert J Hogan [3 10], M G Finn [2 11], Philip J Santangelo [12]

Affiliations expand

Abstract

Messenger RNA has now been used to vaccinate millions of people. However, the diversity of pulmonary pathologies, including infections, genetic disorders, asthma and others, reveals the lung as an important organ to directly target for future RNA therapeutics and preventatives. Here we report the screening of 166 polymeric nanoparticle formulations for

functional delivery to the lungs, obtained from a combinatorial synthesis approach combined with a low-dead-volume nose-only inhalation system for mice. We identify P76, a poly-β-amino-thio-ester polymer, that exhibits increased expression over formulations lacking the thiol component, delivery to different animal species with varying RNA cargos and low toxicity. P76 allows for dose sparing when delivering an mRNA-expressed Cas13a-mediated treatment in a SARS-CoV-2 challenge model, resulting in similar efficacy to a 20-fold higher dose of a neutralizing antibody. Overall, the combinatorial synthesis approach allowed for the discovery of promising polymeric formulations for future RNA pharmaceutical development for the lungs.

- [32 references]

SUPPLEMENTARY INFO

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Review

Applying Lessons from the COVID-19 Pandemic to Improve Pediatric Asthma Care

Stephanie Lovinsky-Desir [1], Anna Volerman [2]

Affiliations expand

Abstract

Asthma is the most common chronic childhood condition and is a risk factor for severe respiratory viral infections. Thus, early during the coronavirus disease 2019 (COVID-19) pandemic there was concern that children with asthma would be at risk for severe COVID-19 illness and that asthma control could worsen as a result of the pandemic. This article seeks to summarize what was learned in the early stages of the pandemic about the impact of COVID-19 on children with asthma. We review evidence from several studies that demonstrated a significant decline in asthma morbidity in the first year of the pandemic. Additionally, we describe several potential mechanisms that may explain the reduced frequency in childhood asthma exacerbations as well as review lessons learned for future management of childhood asthma. While the COVID-19 pandemic initially brought uncertainty, it soon became clear that the pandemic had several positive effects for children with asthma. Now we can apply the lessons that were learned during the pandemic to re-examine asthma care practices as well as advocate for best approaches for asthma management.

Keywords: Asthma triggers; Children; Coronavirus; Emergency department; Environmental exposures; Exacerbations; Hospitalization; Morbidity.

- 29 references

- 1 figure

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Cluster analysis of patients with chronic rhinosinusitis and asthma after endoscopic sinus surgery

Cong Li [1], Bo Zhang [2], Min Yan [2], Yueqi Li [3], Jingyuan Chen [3], Zhiying Nie [4], Yuanyuan Guo [4], Jianbo Shi [3], Fenghong Chen [5]

Affiliations expand

Abstract

Background: Patients with chronic rhinosinusitis with nasal polyps and asthma (CRSwAS) are highly heterogenous in severity and prognosis. The clinical phenotypes and inflammatory endotypes of CRSwAS and their association with outcomes of endoscopic sinus surgery (ESS) have not been fully studied yet.

Objective: We aimed to find out the clinical phenotypes of CRSwAS and explore their relationship with ESS outcomes using cluster analysis.

Methods: We recruited 103 consecutive adult patients with CRSwAS who had undergone ESS and been followed up for more than 1 year. For cluster analysis, we collected the data from 63 variables pertaining to demographic characteristics, preoperative disease status, surgical techniques, postoperative medical treatment, and outcomes. Eosinophilic CRS was defined as greater than or equal to 10 eosinophils/high-power field, and sinus computed tomography was evaluated by Lund-Mackay sinus computed tomography score (LM score).

Results: We screened 92 eligible patients and 13 preoperative variables for balanced iterative reducing and clustering using hierarchies cluster analysis. Patients with CRSwAS were divided into 4 clusters with distinct ESS outcomes: (1) cluster 1, characterized by aspirin-exacerbated respiratory disease, eosinophilic CRS, high preoperative LM score, moderate-to-severe asthma, and uncontrolled CRS after ESS; (2) cluster 2, characterized as having female dominance (66.67%), non-aspirin-exacerbated respiratory disease, eosinophilic CRS, high preoperative LM score, moderate-to-severe asthma, and uncontrolled CRS after ESS; (3) cluster 3, characterized as having female dominance (95.83%), noneosinophilic CRS, low preoperative LM score, moderate asthma, and controlled CRS after ESS; and (4) cluster 4, characterized as men-only, smoker, noneosinophilic CRS, low preoperative LM score, mild asthma, and controlled CRS after ESS.

Conclusion: CRSwAS has distinct clusters, each corresponding to unique clinical and inflammatory characteristics and ESS outcomes.

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The effect of applied force and device design on skin prick test performance

Muthita Chiaranairungroj [1], Pantipa Chatchatee [2], Werayut Srituravanich [3]

Affiliations expand

- PMID: 36436784

- DOI: 10.1016/j.anai.2022.11.014

Abstract

Background: Skin prick tests (SPTs) are difficult to standardize, and SPT performance mainly relies on the clinician's expertise. So far, the effect of various factors such as device types, shape, variety of material type, and applied force on the performance of SPT has not been extensively investigated.

Objective: To investigate the effect of various factors, including type or shape of devices, material type, and applied force, on the performance of SPT.

Methods: Four SPT devices with different shapes and materials were applied on 12 subjects under 3 different applied forces (30, 45, and 60 g). The results were compared with standard method using an ALK lancet pricked by an experienced clinician.

Results: A total of 480 pricks were conducted on 12 subjects. The wheal sizes and sensitivities of all devices increased with higher applied forces. The thinner lancets with a long sharp tip had relatively higher analytical sensitivities and provided 100% sensitivity at applied forces of 45 g and above. The pain scores of all devices at applied forces of 30 to 60 g ranged from 1.00 to 1.81 with minimal incidences of bleeding (0%-4.17%), whereas the pain score of the standard method by the ALK lancet was 2.08 with much higher incidences of bleeding at 27.08%.

Conclusion: The type/shape of the SPT device and applied force are the essential factors affecting the performance of SPT. The study result could pave the way toward higher performance and standardized SPT.

Trial registration: The Thai Clinical Trials Registry identification number: TCTR20220627004 (https://www.thaiclinicaltrials.org/show/TCTR20220627004).

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Antioxidant, anti-inflammatory and analgesic activity of Mimosa acutistipula (Mart.) Benth

Layza Fernanda Gomes Bezerra [1], Ana Paula Sant'Anna da Silva [1], Rebeca Xavier da Cunha [1], João Ricardhis Saturnino de Oliveira [1], Mateus Domingues de Barros [1], Vycttor Mateus de Melo Alves da Silva [1], Vera Lúcia de Menezes Lima [2]

Affiliations expand

- PMID: 36436717

Abstract

Ethnopharmacological relevance: Medicinal plants belonging to the genus Mimosa, such as Mimosa tenuiflora, M. caesalpinifolia, and M. verrucosa are known for their popular use for asthma, bronchitis and fever. Ethnopharmacological studies report that Mimosa acutistipula is used to treat alopecia and pharyngitis, conditions that can be related to oxidative stress, inflammatory processes and painful limitations. However, there is no studies on its efficacy and mechanism of action.

Aim of the study: To elucidate the antioxidant, anti-inflammatory, analgesic and antipyretic activity of M. acutistipula leaves.

Materials and methods: Phytochemical profile of M. acutistipula extracts was evaluated by several reaction-specific methods. Secondary metabolites such as tannins, phenols and flavonoids were quantified with colorimetric assays. In vitro antioxidant potential was evaluated using DPPH and ABTS + as free radical scavenging tests, FRAP and phosphomolybdenum as oxide-reduction assays, and anti-hemolytic for lipid peroxidation evaluation. In vivo anti-inflammatory evaluation was performed by paw edema, and peritonitis induced by carrageenan. Analgesic effect and its possible mechanisms were determined by acetic acid-induced abdominal writhing and the formalin test. Antipyretic activity was evaluated by yeast-induced fever.

Results: Cyclohexane, chloroform, ethyl acetate and methanol extracts of leaves had presence of tannins, flavonoids, phenol, alkaloids, terpenes (except methanolic extract), and saponins (only for methanolic and chloroformic extracts). In phenols, flavonoids and tannins quantification, methanolic and ethyl acetate extract had higher amounts of this phytocompounds. Ethyl acetate extract, due to its more expressive quantity of phenols and flavonoids, was chosen for carrying out the in vivo tests. Due to the relationship between oxidative stress and inflammation, antioxidant tests were performed, showing that ethyl acetate extract had a high total antioxidant activity (70.18%), moderate activity in DPPH radical scavenging, and a moderate ABTS + radical inhibition (33.61%), and FRAP assay (112.32 μg Fe^{2+}/g). M. acutistipula showed anti-inflammatory activity, with 54.43% of reduction in paw edema (50 mg/kg) when compared to the vehicle. In peritonitis test, a reduction in the concentration of NO could be seen, which is highly involved in the anti-inflammatory activity and is responsible for the increase in permeability. In the analgesic evaluation, most significant results in writhing test were seen at 100 mg/kg, with a 34.7% reduction of writhing. A dual mechanism of action was confirmed with the formalin test, both neurogenic and inflammatory pain were reduced, with a mechanism via opioid route. In the antipyretic test, results were significantly decreased at all concentrations tested.

Conclusion: M. acutistipula leaves ethyl acetate extract showed expressive concentrations of phenolic compounds and antioxidant activity. It also exhibited anti-inflammatory and

analgesic activity, besides its antipyretic effect. Thus, these results provide information regarding its popular use and might help future therapeutics involving this specimen.

Conflict of interest statement

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Review

[Metabolomics of asthma, COPD, and asthma–COPD overlap: an overview](#)

[Sanjukta Dasgupta](#) [1], [Nilanjana Ghosh](#) [1], [Parthasarathi Bhattacharyya](#) [2], [Sushmita Roy Chowdhury](#) [3], [Koel Chaudhury](#) [1]

Affiliations expand

- PMID: 36420874

- DOI: [10.1080/10408363.2022.2140329](#)

Abstract

The two common progressive lung diseases, asthma and chronic obstructive pulmonary disease (COPD), are the leading causes of morbidity and mortality worldwide. Asthma-COPD overlap, referred to as ACO, is another complex pulmonary disease that manifests itself with features of both asthma and COPD. The disease has no clear diagnostic or therapeutic guidelines, thereby making both diagnosis and treatment challenging. Though a number of studies on ACO have been documented, gaps in knowledge regarding the pathophysiologic mechanism of this disorder exist. Addressing this issue is an urgent need for improved diagnostic and therapeutic management of the disease. Metabolomics, an increasingly popular technique, reveals the pathogenesis of complex diseases and holds promise in biomarker discovery. This comprehensive narrative review, comprising 99 original research articles in the last five years (2017-2022), summarizes the scientific advances in terms of metabolic alterations in patients with asthma, COPD, and ACO. The analytical tools, nuclear magnetic resonance (NMR), gas chromatography-mass spectrometry (GC-MS), and liquid chromatography-mass spectrometry (LC-MS), commonly used to study the expression of the metabolome, are discussed. Challenges frequently encountered during metabolite identification and quality assessment are highlighted. Bridging the gap between phenotype and metabotype is envisioned in the future.

Keywords: COPD; Metabolomics; NMR; asthma; asthma-COPD overlap; mass spectrometry.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

FULL TEXT LINKS

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[Directionality of the Association Between Epilepsy and Depression: A Nationwide Register-Based Cohort Study](#)

[Eva Bølling-Ladegaard](#) [1], [Julie Werenberg Dreier](#) [2], [Lars Vedel Kessing](#) [2], [Esben Budtz-Jørgensen](#) [2], [Kasper Lolk](#) [2], [Jakob Christensen](#) [2]

Affiliations expand

- PMID: 36414426

- DOI: [10.1212/WNL.0000000000201542](#)

Abstract

Background and objectives: Epilepsy and depression share a bidirectional relationship; however, its magnitude and long-term temporal association remain to be elucidated. This study investigates the magnitude and long-term association between epilepsy and depression, comparing with the risks of the 2 disorders after another chronic medical illness (asthma).

Methods: In a nationwide register-based matched cohort study, we identified all individuals who received a first diagnosis of epilepsy, depression, and asthma from January

1, 1980, to December 31, 2016. We used a Cox regression model to estimate the risk of epilepsy after depression and vice versa and the risk of epilepsy or depression after asthma, compared with healthy references matched on age and sex, adjusting for medical comorbidity, substance abuse, and calendar time. Results were stratified by epilepsy subtype. We furthermore investigated the risk of admission with acute seizures for persons with epilepsy who became depressed.

Results: In a population of 8,741,955 individuals, we identified 139,014 persons with epilepsy (54% males, median age at diagnosis 43 years [inter quartile range (IQR) 17-65 years]), 219,990 persons with depression (37% males, median age at diagnosis 43 years [IQR 29-60 years]), and 358,821 persons with asthma (49% males, median age at diagnosis 29 years [IQR 6-56 years]). The adjusted hazard ratio (aHR) of depression after epilepsy was 1.88 (95% CI 1.82-1.95), and the aHR of epilepsy after depression was 2.35 (95% CI 2.25-2.44). The aHR of depression after asthma was 1.63 (95% CI 1.59-1.67) and that of epilepsy after asthma, 1.48 (95% CI 1.44-1.53). The risk of depression was highest in the few years preceding and after an epilepsy diagnosis, and vice versa, but remained elevated during the entire follow-up period for both directions of the association. There was no evidence of a stronger association with depression for any epilepsy subtype. Receiving a diagnosis of depression subsequent to an epilepsy diagnosis was associated with a 1.20-fold (95% CI 1.07-1.36) increased HR of acute hospital admission with seizures.

Discussion: We identified a long-term bidirectional relationship between depression and epilepsy in a large-scale cohort study. Risk estimates were higher than those of epilepsy or depression after asthma.

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Comment in

- [Epilepsy and Depression: How Are They Related?](#)
  Karceski S.Neurology. 2023 Feb 28;100(9):e995-e997. doi: 10.1212/WNL.0000000000207070.PMID: 36849454 No abstract available.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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How does one get around many of the confounding factors influencing the response to methacholine?

Allan L Coates [1] [2]

Affiliations expand

- PMID: 36411237

- DOI: 10.1111/resp.14416

Free article

No abstract available

Keywords: asthma; methacholine; oscillometry; respiratory function test; small and large airways.

- 6 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

FULL TEXT LINKS

Editorial

Environmental plastics and lung health: Increasing evidence for concern

Rajen N Naidoo [1]

Affiliations expand

- PMID: 36411227

- DOI: 10.1111/resp.14411

Free article
No abstract available

Keywords: antenatal exposure; asthma; bisphenol-A; environment; lung function trajectories; phthalate metabolites.

- 17 references

SUPPLEMENTARY INFO

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Leveraging genetic ancestry to study severe asthma exacerbations in an admixed population

Yadu Gautam [1], Tesfaye B Mersha [2]

Affiliations expand

No abstract available

Keywords: Asthma; Asthma Genetics.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

FULL TEXT LINKS

BMJ Full Text

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Review

A review of cannabis allergy in the early days of legalization

Alessandro Toscano [1], Didier G Ebo [2], Khaldon Abbas [3], Hannelore Brucker [4], Ine I Decuyper [5], David Naimi [6], Anil Nanda [7], Ajay P Nayak [8], Isabel J Skypala [9], Gordon Sussman [10], Joanna S Zeiger [11], William S Silvers [12]; International Cannabis Allergy Collaboration

Affiliations expand

- PMID: 36384984

- DOI: 10.1016/j.anai.2022.10.016

Abstract

Cannabis allergy is a burgeoning field; consequently, research is still in its infancy and allergists' knowledge surrounding this topic is limited. As cannabis legalization expands across the world, it is anticipated that there will be an increase in cannabis use. Thus, we hypothesize that a concomitant rise in the incidence of allergy to this plant can be expected. Initiatives aimed at properly educating health care professionals are therefore necessary. This review presents the most up-to-date information on a broad range of topics related to cannabis allergy. Although the clinical features of cannabis allergy are becoming more well described and recognized, the tools available to make a correct diagnosis are meager and often poorly accessible. In addition, research on cannabis allergy is still taking its first steps, and new and potentially groundbreaking findings in this field are expected to occur in the next few years. Finally, although therapeutic approaches are being developed, patient and physician education regarding cannabis allergy is certainly needed.

SUPPLEMENTARY INFO

Publication typesexpand

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Triptonide, a Diterpenoid Displayed Anti-Inflammation, Antinociceptive, and Anti-Asthmatic Efficacy in Ovalbumin-Induced Mouse Model

Zhen Li [1], Yanhong Geng [2], Qingke Wu [3], Xin Jin [3], Vidya Devanathadesikan Seshadri [4], Hao Liu [5][6]

Affiliations expand

Abstract

The present study was intended to explore the valuable effects of triptonide on inflammation, asthmatic, and nociceptive. Triptonide possesses numerous beneficial effects extensively managed in the treatment of inflammation disease condition. Initially, triptonide showed anti-inflammation properties over lipopolysaccharide-induced RAW 264.7 cells. Hence, the present study was directed to explore the protecting efficacy of triptonide in ovalbumin (OVA)-induced asthma in mice. Asthma was induced intraperitoneally administration (200μL) in female BALB/c mice with suspension which has ovalbumin (100 μg/mL) and aluminum hydroxide (10 mg/mL). Triptonide (30 mg/kg) over OVA-induced experimental animals altered lung mass, nitric oxide, myeloperoxidase, immunoglobulin E status, interleukins (4, 5, and 13) inflammatory cytokines status, and histological modifications. Animals were also managed with the standard drug dexamethasone (50 mg/kg) followed by the asthma induction, which is also efficient over OVA-induced experimental animals. The nociception was provoked in male Swiss mice by various chemicals (acetic acid, capsaicin, and glutamate). The animals were administered with triptonide (5, 10, and 15 mg/kg) and separate standard drugs like diclofenac sodium (10 mg/kg) and morphine (5 mg/kg) over chemical-induced nociceptive animals. The present outcome evidently established that the triptonide considerably reduced the various chemical-induced nociception in mice (Fig. 7A, B, and C). Ultimately, the present work explored the evident powerful anti-inflammation, antinociceptive, and anti-asthma properties of a diterpenoid, triptonide experimental animal models. And it is recommended that triptonide is an excellent compound in the management of asthma and its related diseases.

Keywords: Asthma; Inflammation; Nociceptive; Ovalbumin; Triptonide.

- 41 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

FULL TEXT LINKS

SpringerLink
FULL-TEXT ARTICLE

RHINITIS

Screening for asthma in preschool children with sickle cell disease

Kok Hoe Chan[1], James M Stark[2], Ricardo A Mosquera[2], Deborah L Brown[2], Neethu Menon[2], Trinh T Nguyen[3], Aravind Yadav[2]

Affiliations expand

- PMID: 36867136

- DOI: 10.1080/02770903.2023.2187305

Abstract

Background: Asthma in preschool children is poorly defined, proving to be a challenge for early detection. The Breathmobile Case Identification Survey (BCIS) has been shown to be a feasible screening tool in older SCD children and could be effective in younger children. We attempted to validate the BCIS as an asthma screening tool in preschool children with SCD.

Methods: This is a prospective, single-center study of 50 children aged 2-5 years with SCD. BCIS was administered to all patients and a pulmonologist blinded to the results evaluated patients for asthma. Demographic, clinical and laboratory data were obtained to assess risk factors for asthma and acute chest syndrome in this population.

Results: Asthma prevalence (n = 3/50; 6%) was lower than atopic dermatitis (20%) and allergic rhinitis (32%). Sensitivity (100%), specificity (85%), positive predictive value (30%) and negative predictive value (100%) of the BCIS were high. Clinical demographics, atopic dermatitis, allergic rhinitis, asthma, viral respiratory infection, hematology parameters, sickle hemoglobin subtype, tobacco smoke exposure and hydroxyurea were not different between patients with or without history of ACS, although eosinophil was significantly lower in the ACS group (p = 0.0093). All those with asthma had ACS, known viral respiratory infection resulting in hospitalization (3 RSV and 1 influenza), and HbSS (homozygous Hemoglobin SS) subtype.

Conclusion: The BCIS is an effective asthma screening tool in preschool children with SCD. Asthma prevalence in young children with SCD is low. Previously known ACS risk factors were not seen, possibly from the beneficial effects of early life initiation of hydroxyurea.

Keywords: Acute chest syndrome; RSV; allergic rhinitis; asthma; atopic dermatitis; eosinophils; hydroxyurea; screening; sickle cell disease.

Proceed to details

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☐ 2

Early exposure to infections increases the risk of allergic rhinitis–a systematic review and meta-analysis

JunRong Chen [# 1], Xiaohua Liu [# 1 2], Zixin Liu [1 3], Yaqian Zhou [1 4], Li Xie [1], Jialin Zhang [1], Jin Tan [1], Yide Yang [5], Mei Tian [1], Yunpeng Dong [# 6], Jian Li [# 7 8]

Abstract

Objective: The purpose of this study was to provide evidence for early life care by meta-analyzing the relationship between infection during pregnancy and up to 2 years of age and the risk of subsequent allergic rhinitis (AR).

Methods: Published studies up to April 2022 were systematically searched in PubMed, Embase, Web of Science, Cochrane Library, SinoMed, CNKI, Wanfang Database, and VIP. Literature screening, including quality assessment, was performed, and the effect values (OR, HR, RR) and 95% confidence intervals (95% CI) of infection during pregnancy and up to 2 years of age and allergic rhinitis were extracted from each qualified study.

Results: In total, 5 studies with a sample size of 82,256 reported the relationship between infection during pregnancy and offspring AR. Meta-analysis showed that maternal infection during pregnancy was associated with an increased risk of childhood AR in offspring (OR = 1.34, 95% CI: 1.08-1.67). Altogether, 13 studies with a sample size of 78,426 reported evidence of an association between infection within 2 years of age and subsequent AR in children. A pooled meta-analysis of all studies showed that early infection within 2 years of age was closely associated with childhood AR (OR = 1.25, 95% CI: 1.12-1.40), especially upper respiratory tract infection (OR = 1.32, 95% CI: 1.06-1.65) and gastrointestinal infections (OR = 1.37, 95% CI: 1.01-1.86), but ear infection showed similar results in the cohort study (OR = 1.13, 95% CI: 1.04-1.22).

Conclusion: Current evidence suggests that infection during pregnancy, early upper respiratory infection, gastrointestinal infections and ear infection within 2 years of age would increase the risk of AR in children. Therefore, the prevention of infection during pregnancy and in infancy and young children needs to be emphasized.

Keywords: Allergic rhinitis; Children; Infections; Meta-analysis.

Conflict of interest statement

The authors declare no competing interests.

- 54 references
- 5 figures

New Concepts in Barrier Dysfunction in CRSwNP and Emerging Roles of Tezepelumab and Dupilumab

Simon Chiang[1], Stella E Lee[1]

Affiliations expand

- PMID: 36848281

- DOI: 10.1177/19458924231154061

Abstract

Background: Epithelial barrier disturbances in CRSwNP patients play an important role in both the innate and adaptive immune responses, contributing to chronic inflammation, olfactory dysfunction, and impairments in quality of life.

Objective: To evaluate the role of the sinonasal epithelium in disease and health, review the pathophysiology of epithelial barrier dysfunction in CRSwNP, and the immunologic targets for treatment.

Methods: Literature review.

Results: Blockade of cytokines such as thymic stromal lymphopoietin (TSLP), IL-4, and IL-13 have shown promise in barrier restoration and IL-13, specifically may be central to olfactory dysfunction.

Conclusion: The sinonasal epithelium plays a crucial role in the health and function of the mucosa and immune response. Increased understanding of the local immunologic dysfunction has led to several therapeutics that can potentially restore epithelial barrier function and olfaction. Real world and comparative effectiveness studies are needed.

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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☐ 4

Understanding the CRSwNP Patient as Whole

Sindhura Bandi[1], Ellen Stephen[1], Keerthi Bansal[1], Mahboobeh Mahdavinia[1]

Affiliations expand

Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a distinct inflammatory disease of the upper airways with a significant impact on the health and quality of life of affected patients. Several comorbid conditions such as allergic rhinitis, asthma, sleep disorders, and gastroesophageal reflux disease are commonly reported in patients with CRSwNP.

Objective: In this article, we intended to review the UpToDate information on how these comorbidities can impact CRSwNP patients' health and well-being.

Methods: A PUBMED search was performed to review relevant recent article on the topic.

Results: While there have been significant advances in the knowledge and management options for CRSwNP in the past few years, additional studies are needed to understand the underlying pathophysiologic mechanisms of these associations. In addition, awareness of the impact of CRSwNP on mental health, quality of life, and cognition is paramount to treating this condition.

Conclusion: Recognition and addressing CRSwNP comorbidities such as allergic rhinitis, asthma, sleep disorders, gastroesophageal reflux disease, and cognitive function impairment are important to optimally understand and manage the patient with CRSwNP as a whole.

Keywords: allergic rhinitis; asthma; chronic rhinosinusitis; cognitive function; gastroesophageal reflux disease (GERD); nasal polyps; sleep disorders.

SUPPLEMENTARY INFO

MeSH termsexpand

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☐ 5

Scientific Advancements That Empower Us to Understand CRS Pathophysiology

[Hannan A Qureshi](#)[1], [Zechariah G Franks](#)[1], [Asiana Gurung](#)[1], [Murugappan Ramanathan Jr](#)[1]

Affiliations expand

Abstract

Background: Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a multifactorial inflammatory condition that remains poorly understood. Over the past decade, we have witnessed impressive scientific advancements that have allowed us to better understand the molecular and cellular mechanisms that underlie the inflammatory processes in mucosal diseases including asthma, allergic rhinitis, and CRSwNP.

Objective: The present review aims to summarize and highlight the most recent scientific advancements that have enriched our understanding of CRSwNP.

Methods: A comprehensive review of the available literature on the use of new scientific techniques in CRSwNP was performed. We evaluated the most recent evidence from studies using animal models, cell cultures, and genome sequencing techniques and their impact on our understanding of CRSwNP pathophysiology.

Results: Our understanding of CRSwNP has rapidly progressed with the development of newer scientific techniques to interrogate various pathways involved in its pathogenesis. Animal models remain powerful tools and have elucidated the mechanisms behind esinophilic inflammation in CRSwNP; however, animal models reproducing polyp formation are relatively sparse. 3D cell cultures have significant potential to better dissect the cellular interactions with the sinonasal epithelium and other cell types in CRS. Additionally, some groups are starting to utilize single-cell RNA sequencing to investigate RNA expression in individual cells with high resolution and on a genomic scale.

Conclusion: These emerging scientific technologies represent outstanding opportunities to identify and develop more targeted therapeutics for different pathways that lead to CRSwNP. An additional understanding of these mechanisms will be critical for developing future therapies for CRSwNP.

Keywords: animal models; chronic rhinosinusitis; genetic polymorphisms; nasal polyposis; organoids; single-cell sequencing.

SUPPLEMENTARY INFO

Publication types, MeSH termsexpand

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Cite

B Lineage Cells and IgE in Allergic Rhinitis and CRSwNP and the Role of Omalizumab Treatment

Junqin Bai[1], Bruce K Tan[1][2]

Affiliations expand

- PMID: 36848269

- DOI: 10.1177/19458924221147770

Abstract

Background: Allergic rhinitis (AR) and chronic rhinosinusitis (CRS) are two prevalent nasal diseases where both type 2 inflammation and immunoglobulin E (IgE) may play important roles. Although they can exist independently or comorbidly, subtle but important differences exist in immunopathogenesis.

Objective: To summarize current knowledge of pathophysiological roles of B lineage cells and IgE in AR and CRS with nasal polyps (CRSwNP).

Methods: Searched PubMed database, reviewed AR and CRSwNP-related literature, and discussed disease diagnosis, comorbidity, epidemiology, pathophysiology, and treatment. Similarities and differences in B-cell biology and IgE are compared in the 2 conditions.

Results: Both AR and CRSwNP have evidence for pathological type 2 inflammation, B-cell activation and differentiation, and IgE production. However, distinctions exist in the clinical and serological profiles at diagnosis, as well as treatments utilized. B-cell activation in AR may more frequently be regulated in the germinal center of lymphoid follicles, whereas CRSwNP may occur

via extrafollicular pathways although controversies remain in these initial activating events. Oligoclonal and antigen-specific IgE maybe predominate in AR, but polyclonal and antigen-nonspecific IgE may predominate in CRSwNP. Omalizumab has been shown efficacious in treating both AR and CRSwNP in multiple clinical trials but is the only Food and Drug Administration-approved anti-IgE biologic to treat CRSwNP or allergic asthma. *Staphylococcus aureus* frequently colonizes the nasal airway and has the ability to activate type two responses including B-cell responses although the extent to which it modulates AR and CRSwNP disease severity is being investigated.

Conclusion: This review highlights current knowledge of the roles of B cells and IgE in the pathogenesis of AR and CRSwNP and a small comparison between the 2 diseases. More systemic studies should be done to elevate the understanding of these diseases and their treatment.

Keywords: B cell; allergic rhinitis; autoantibody; chronic rhinosinusitis with nasal polyps; extrafollicular; germinal center; immunoglobulin E; omalizumab; plasma cell; type 2 inflammation.

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Publication types, MeSH terms, Substancesexpand

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☐ 7

Current advances in house dust mite allergen immunotherapy (AIT): Routes of administration, biomarkers and molecular allergen profiling

Thierry Batard [1], Walter G Canonica [2], Oliver Pfaar [3], Mohamed H Shamji [4], Robyn E O'Hehir [5], Menno C van Zelm [5], Laurent Mascarell [6]

Affiliations expand

Abstract

Allergy to house dust mites (HDM) is a perennial respiratory disease that affect more than half a billion people worldwide. Dermatophagoides pteronyssinus and D. farinae, two HDM species, are major sources of indoor allergens triggering allergic inflammation. Although symptomatic drugs are widely used to block the allergic reaction, allergen immunotherapy is the only curative treatment of IgE-mediated type I respiratory allergies. In this article, we review recent advances in various routes of allergen immunotherapy. We particularly focus on subcutaneous (SCIT) and sublingual (SLIT) immunotherapy, used as a reference therapy since they have transformed allergic treatments by improving symptoms (asthma and rhinitis) as well as the quality of life of patients. We also highlight recent data in more exploratory routes (i.e., oral, intralymphatic, epicutaneous and intradermal) and discuss respective advantages of various route, as well as their foreseen modes of action. Finally, we provide an update on biomarkers as well as on the relevance of the molecular profiling of allergic individuals related to treatment efficacy or asthma prediction.

Keywords: Administration routes; Allergen immunotherapy; Biomarkers; House dust mite; Molecular reactivity profiling.

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Recent insights into comorbidities in atopic dermatitis

Caroline Gewiss [1], Matthias Augustin [1]

Affiliations expand

- PMID: 36796057

- DOI: 10.1080/1744666X.2023.2181790

Abstract

Introduction: The relationship between atopic dermatitis and atopic diseases such as food allergies, asthma, and allergic rhinitis in terms of co-occurrence, underlying mechanisms, and therapy is well documented. There is increasing evidence that atopic dermatitis is associated with non-atopic comorbidities such as cardiac, autoimmune, and neuropsychological comorbidities, as well as cutaneous and extracutaneous infections, establishing atopic dermatitis as a systemic disease.

Areas covered: The authors reviewed evidence on atopic and non-atopic comorbidities of atopic dermatitis. A literature search was conducted in PubMed for peer-reviewed articles published until October 2022.

Expert opinion: Atopic and non-atopic diseases coexist with atopic dermatitis more often than would be expected by chance. The effect of biologics and small molecules on atopic and non-atopic comorbidities may contribute to a better understanding of the relationship between atopic dermatitis and its comorbidities. Their relationship needs to be explored further to dismantle the underlying mechanism and move toward an atopic dermatitis endotype-based therapeutic approach.

Keywords: Atopic dermatitis; autoimmune; cardio-metabolic; comorbidities; cutaneous; eczema; extracutaneous; infections; neuropsychological; non-atopic.

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Immunotherapy

Real-world study: drug reduction in children with allergic rhinitis and asthma receiving immunotherapy

Jorge Sánchez [1], Leidy Alvarez [2], Elizabeth García [3]

Affiliations expand

- PMID: 36789565

- DOI: 10.2217/imt-2022-0215

Abstract

Background: The reduction of pharmacological treatment after allergen immunotherapy (AIT) for house dust mites (HDMs) has been little studied in children. **Objective:** To evaluate the reduction of pharmacological treatment comparing children that receive HDM immunotherapy (AIT group) versus only pharmacotherapy. **Methods:** A historic cohort of children with rhinitis or asthma was assessed. The main outcome was the frequency of complete drug discontinuation. **Results:** 100% drug reduction was higher for rhinitis (4-year cumulative incidence: 30 vs 10.7%) and asthma (24.1 vs 10.5%) in the AIT group (n = 987) than in the pharmacotherapy group (n = 2012). **Conclusion:** Immunotherapy is associated with a significant reduction of pharmacotherapy in children. This is a marker of clinical control and could be associated with positive economic impact.

Keywords: allergen; allergy; asthma; immunotherapy; mites; pharmacotherapy; real-life; real-word; rhinitis.

Plain language summary

The benefits of allergen immunotherapy for house dust mites has been little studied in children. The usefulness of this treatment in asthma over the use of pharmacotherapy has also not been clearly evaluated. The use of immunotherapy allowed greater reductions in pharmacological treatment in children with rhinitis and asthma. Immunotherapy is a useful treatment for childhood rhinitis and asthma and reduces the risk of adverse effects from pharmacological treatments.

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

Trigeminal Sensitivity in Patients With Allergic Rhinitis and Chronic Rhinosinusitis

Georg Karl Ludwig Burghardt[1], Mandy Cuevas[1], Rumi Sekine[1][2], Thomas Hummel[1]

Affiliations expand

- PMID: 36504410

- DOI: 10.1002/lary.30512

Abstract

Objective: Allergic rhinitis (AR) and chronic rhinosinusitis with nasal polyps (CRSwNP) are of high importance in otorhinolaryngology. Some of their symptoms are related to changes in the nasal trigeminal sensitivity. The aim of this study was to compare nasal trigeminal sensitivity in patients with AR, CRSwNP, and healthy controls (HC).

Methods: A total of 75 individuals participated (age 19-78 years; 34 AR, 10 CRSwNP and 31 HC). Olfactory function was determined using the extended Sniffin' Sticks test battery. Trigeminal

sensitivity was assessed with CO_2 detection thresholds. Trigeminal negative mucosal potentials (NMP) and EEG-derived event-related potentials (ERP) were recorded in response to selective olfactory (phenylethyl alcohol) and trigeminal (CO_2) stimuli using high-precision air-dilution olfactometry.

Results: In comparison to HC, AR patients had lower CO_2 thresholds, also reflected in shorter peak latencies in NMP and trigeminal ERP measurements. CRSwNP patients had a decreased sensitivity for trigeminal stimuli, also reflected in prolonged trigeminal ERP latencies, and reduced olfactory function compared to HC.

Conclusion: AR patients seemed to be more sensitive to trigeminal stimuli than CRSwNP patients. Importantly, the differences could be shown on psychophysical and electrophysiological levels. The changes in trigeminal sensitivity appear to be present already at the level of the respiratory epithelium. The differences between the two groups may depend on the specific inflammatory changes accompanying each disorder, the degree of inflammatory activity, or duration of the inflammatory disorder. However, because the sample sizes are relatively small, these results need to be confirmed in the future studies with larger groups.

- 49 references

SUPPLEMENTARY INFO

MeSH terms, Substancesexpand

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Allergy

-
-
-

. 2023 Mar;78(3):731-742.

Specific IgE against the house dust mite allergens Der p 5, 20 and 21 influences the phenotype and severity of atopic diseases

Theresa Walsemann[1], Marisa Böttger[1], Stephan Traidl[2], Christian Schwager[1], Askin Gülsen[3], Sina Freimooser[2], Lennart Matthias Roesner[2][4], Thomas Werfel[2][4], Uta Jappe[1][3]

Affiliations expand

- PMID: 36239002

- DOI: 10.1111/all.15553

Abstract

Background: House dust mites (HDM) are among the most important sources for airborne allergens with high relevance for atopic diseases. Routine tests contain only 4 of 32 registered allergens of Dermatophagoides pteronyssinus. Clinical relevance and pathomechanistic properties of many allergens are not well understood.

Objective: The association of several HDM allergens with allergic rhinitis, allergic asthma, and atopic dermatitis was investigated to identify allergens with biomarker potential and to transfer them into diagnostics.

Methods: Eight out of nine D. pteronyssinus allergens (nDer p 1, rDer p 2, rDer p 5, rDer p 7, rDer p 10, rDer p 13, rDer p 20, rDer p 21, rDer p 23) were recombinantly expressed and purified. Sensitization patterns of 384 HDM-allergic individuals exhibiting different clinical phenotypes were analyzed with a serum-saving multiplex array.

Results: Sensitization to more than three mite allergens (sensitization count) was associated with allergic asthma and/or atopic dermatitis. Reactions to Der p 5 and Der p 21 were more frequent in allergic asthma compared to allergic rhinitis. Atopic dermatitis patients were more often sensitized to Der p 5, Der p 20, and Der p 21 among others. Der p 20-IgE > 80 kU/L was associated with severe atopic dermatitis in 75% of patients.

Conclusion: This study demonstrates the clinical importance of the sensitization count and of certain allergens (Der p 5, Der p 20, and Der p 21) not available for routine diagnostics yet. Implementing them as well as the sensitization count in diagnostic measures will improve diagnosis and risk assessment of HDM-allergic patients.

Keywords: allergens and epitopes; allergy diagnosis; asthma; atopic dermatitis; biomarkers.

- 84 references

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Blood eosinophil count in the diagnosis of allergic-like rhinitis with chronic rhinosinusitis

Qiqi Luo[1], Siyi Zhou[1], Bo Yuan[1], Zeli Feng[2], Guolin Tan[1], Honghui Liu[1]

Affiliations expand

- PMID: 36222453

- DOI: 10.1111/coa.13990

Abstract

Background: Allergic rhinitis (AR) and nonallergic rhinitis (NAR) often are comorbid with chronic rhinosinusitis (CRS). Finding a convenient test that distinguishes these complex conditions is helpful for effective treatment. We aimed to analyse blood parameter differences between AR and NAR patients with/without CRS.

Methods: Eight hundred thirteen patients, including AR and NAR with different conditions [CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP)] were analysed in this retrospective study. Patients with a nasal deviation alone were included as healthy controls (HC). Receiver operating characteristic analysis was used to assess the value of blood parameters for diagnosing AR or NAR with/without CRS.

Results: Compared to nonallergic-like rhinitis (HC, CRSwNP and CRSsNP), the blood eosinophil count was significantly increased in the allergic-like rhinitis groups, except for NAR-CRSsNP (AR, AR-CRSwNP, AR-CRSsNP, NAR and NAR-CRSwNP). The NAR-CRSsNP group had a higher level of eosinophils than the HC and CRSsNP groups. Among allergic-like rhinitis patients, eosinophils were higher in allergic-like rhinitis patients with CRSwNP (AR-CRSwNP and NAR-CRSwNP) than in allergic-like rhinitis patients without CRSwNP (AR, AR-CRSsNP, NAR and NAR-CRSsNP). However, no difference in blood eosinophils was observed between AR and NAR. There was also no difference among nonallergic-like rhinitis patients. Similar findings were found for the blood eosinophil proportion. Furthermore, the blood eosinophil count was a good predictor of allergic-like rhinitis, especially allergic-like rhinitis with CRSwNP.

Conclusion: The blood eosinophil count and proportion may be good diagnostic predictors of allergic-like rhinitis but cannot differentiate between AR and NAR. This indicator may be much better in predicting allergic-like rhinitis with CRSwNP.

Keywords: allergic rhinitis; blood parameters; eosinophil; nonallergic rhinitis.

- 28 references

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Clin Otolaryngol

Differentiation of eosinophilic and non‑eosinophilic chronic rhinosinusitis on preoperative computed tomography using deep learning

Hong-Li Hua[1], Song Li[2], Yu Xu[1], Shi-Ming Chen[1], Yong-Gang Kong[1], Rui Yang[1], Yu-Qin Deng[1], Ze-Zhang Tao[1][3]

Affiliations expand

Abstract

Objectives: This study aimed to develop deep learning (DL) models for differentiating between eosinophilic chronic rhinosinusitis (ECRS) and non-ECRS (NECRS) on preoperative CT.

Design: Axial spiral CT images were pre-processed and used to build the dataset. Two semantic segmentation models based on U-net and Deeplabv3 were trained to segment the sinus area on CT images. All patient images were segmented using the better-performing segmentation model and used for training and testing of the transferred efficientnet_b0, resnet50, inception_resnet_v2, and Xception neural networks. Additionally, we evaluated the performances of the models trained using each image and each patient as a unit.

Participants: A total of 878 chronic rhinosinusitis (CRS) patients undergoing nasal endoscopic surgery at Renmin Hospital of Wuhan University (Hubei, China) between October 2016 to June 2021 were included.

Main outcome measures: The precision of each model was assessed based on the receiver operating characteristic curve. Further, we analyzed the confusion matrix and accuracy of each model.

Results: The Dice coefficients of U-net and Deeplabv3 were 0.953 and 0.961, respectively. The average area under the curve and mean accuracy values of the four networks were 0.848 and 0.762

for models trained using a single image as a unit, while the corresponding values for models trained using each patient as a unit were 0.893 and 0.853, respectively.

Conclusions: Combining semantic segmentation with classification networks could effectively distinguish between patients with ECRS and those with NECRS based on preoperative sinus CT images. Furthermore, labeling each patient to build a dataset for classification may be more reliable than labeling each medical image.

Keywords: CT; deep learning; differentiation; eosinophil; rhinosinusitis.

- <u>34 references</u>

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Review

Systematic review of real-world persistence and adherence in subcutaneous allergen immunotherapy

Michelle J Park [1], Shrey Kapoor [1], Julie Yi [1], Nanki Hura [1 2], Sandra Y Lin [1 3]

Affiliations expand

- PMID: 36083799

- DOI: 10.1002/alr.23078

Abstract

Background: Given that subcutaneous immunotherapy (SCIT) adherence in the literature is often studied in closely monitored trials, few studies report real-world SCIT adherence. The purpose of this review is to assess SCIT adherence in real-world settings.

Methods: A literature search of PubMed, Embase, Cochrane Library, Web of Science, and Scopus for real-world studies examining SCIT adherence was performed. Paired investigators independently reviewed all articles. For this review, "persistence" was defined as continuing therapy and not being lost to follow-up after initiating SCIT, and "adherence" defined as persistence in accordance with prescribed SCIT dose, dosing schedule, and duration. Article quality was first assessed using a modified Newcastle-Ottawa scale and then converted to Agency for Healthcare Research and Quality standards (good, fair, and poor).

Results: The search yielded 1596 nonduplicate abstracts, from which 17 articles (n = 263,221 patients) met inclusion criteria. Fourteen (82%) studies reported persistence rates, ranging from 16.0% to 93.7%. Seven (41%) studies reported adherence rates, ranging from 15.1% to 99%. Five (29%) studies (n = 416 patients) collected original data on reasons for discontinuing SCIT, of which inconvenience was most cited. All studies were Oxford level of evidence 2b and of good (n = 10) to fair (n = 7) quality.

Conclusion: Real-world SCIT persistence and adherence rates are poor, with the majority of included studies reporting rates <80%; however, they range widely, explained in part by inter-study differences in measuring and reporting adherence-related findings. Future studies on SCIT adherence may benefit from following concordant definitions of persistence and adherence in addition to standardized reporting metrics.

Keywords: adherence; allergic rhinitis; allergy injections; compliance; persistence; subcutaneous immunotherapy.

- Cited by 1 article
- 39 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

Nasal nerve ablation, nasal swell body and inferior turbinate reduction for nasal obstruction and congestion relief

Y P Krespi [1], K A Wilson [1], V Kizhner [2]

Affiliations expand

- PMID: 35346410

- DOI: 10.1017/S0022215122000871

Abstract

Objective: Nasal obstruction and congestion can occur because of turbinate and septal variations with or without rhinitis. A combined treatment for nasal obstruction and congestion was examined retrospectively in cases where the nasal swell body was addressed with inferior turbinectomy, with or without posterior nasal nerve ablation.

Methods: A 940 nm laser was utilised for contact (nasal swell body, septum and inferior turbinate) and non-contact (posterior nasal nerve) ablation. Total Nasal Symptoms Score, visual analogue scale pain score, complications and procedure location (office *vs* operating theatre) were recorded.

Results: All 242 patients underwent nasal swell body reduction with inferior turbinate reduction, and 150 had posterior nasal nerve ablation also. No laser complications were observed. An 80 per cent reduction in medication usage was noted. Total Nasal Symptoms Score decreased by 73 per cent; rhinorrhoea and congestion scores decreased by 54 per cent and 81 per cent respectively. Crusting, epistaxis and infections were minimal, and resolved within two weeks.

Conclusion: Nasal swell body with inferior turbinate reduction, with or without posterior nasal nerve ablation, is a new method of treating nasal obstruction and congestion. Laser posterior nasal nerve ablation can be utilised as a complementary tool to deliver anatomical obstruction relief.

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Observational Study

Daratumumab infusion reaction rates pre- and post-addition of montelukast to pre-medications

Kelsey Coffman[1], Coby Carstens[1], Susan Fajardo[1]

Abstract

Daratumumab, a CD38-directed monoclonal antibody indicated for multiple myeloma treatment in adult patients, is associated with a high incidence of infusion-related reactions (IRRs). Due to CD38 receptor presence in the lungs, many reactions present similarly to asthma or allergic rhinitis. Montelukast, a leukotriene receptor antagonist, has been hypothesized to reduce daratumumab IRRs due to its efficacy in treating allergic rhinitis and asthma and the presence of leukotriene receptors in the lungs. Recently published data reported daratumumab can be safely administered via rapid rate protocol that reduces infusion time from 195 min to 90 min after completion of two doses. This retrospective, observational cohort study examined 73 patients who received daratumumab in the outpatient setting between December 2015 and April 2020. Patients were included if they were 18 years or older, had an International Classification of Disease (ICD)-10 diagnosis code for multiple myeloma, and received daratumumab intravenously. The primary outcome was a comparison of IRRs between those who did and did not receive montelukast. Secondary outcomes included IRR symptoms, rescue medications utilized for IRRs, and rapid rate administration outcomes. Montelukast use was associated with a lower rate of IRRs (44.4% vs. 65.2%, p = 0.044). Pulmonary IRR symptoms were more common in those who did not receive montelukast. Rapid rate administration of daratumumab did not lead to any IRRs. Adding montelukast as a pre-medication for daratumumab infusions led to a reduction in IRRs, and rapid rate administration was found to be safe after completion of two full doses of daratumumab.

Keywords: daratumumab; infusion-related reactions; montelukast.

- Cited by 1 article

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Publication types, MeSH terms, Substancesexpand

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Long-Term Follow-Up After Maxillary Sinus Balloon Sinuplasty and ESS

Anni Koskinen [1], Marie Lundberg [1], Markus Lilja [1], Jyri Myller [2], Matti Penttilä [3], Heini Huhtala [4], John M Lee [5], Karin Blomgren [1], Sanna Toppila-Salmi [6]

Affiliations expand

- PMID: 33601904

- DOI: 10.1177/0145561320986030

Abstract

Objectives: The aim of this controlled follow-up study was to compare the need for revision surgery, long-term efficacy, and satisfaction in chronic rhinosinusitis patients who had undergone maxillary sinus operation with either balloon sinuplasty or traditional endoscopic sinus surgery (ESS) technique.

Methods: Thirty-nine ESS patients and 36 balloon patients of our previously described cohort, who had been primarily operated in 2008 to 2010, were contacted by phone. Symptoms, satisfaction, and need for revision surgery were asked. In addition, we collected data of patients who had undergone primary maxillary sinus balloon sinuplasty in the Helsinki University Hospital during the years 2005 to 2019. As a control group, we collected data of patients who had undergone primary maxillary sinus ESS at 3 Finnish University Hospitals, and 1 Central Hospital in years 2005, 2008, and 2011.

Results: Altogether, 77 balloon patients and 82 ESS patients were included. The mean follow-up time was 5.3 years in balloon group and 9.8 years in ESS group. Revision surgery was performed on 17 balloon patients and 6 ESS patients. In the survival analysis, the balloon sinuplasty associated significantly with a higher risk of revision surgery compared to ESS. According to the phone interviews, 82% of ESS patients and 75% of balloon patients were very satisfied with the primary operation.

Conclusion: Although the patient groups expressed equal satisfaction and change in symptoms after the operations, the need for revision surgery was higher after balloon sinuplasty than after ESS. This should be emphasized when counselling patients regarding surgical options.

- Cited by 1 article

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

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CHRONIC COUGH

Critically appraised paper: In patients with chronic obstructive pulmonary disease, the addition of oscillatory positive expiratory pressure to usual care improves cough-specific and general quality of life [commentary]

Christian Osadnik [1]

No abstract available

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Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand

Anne B Chang [1] [2] [3], Scott C Bell [4] [5] [6], Catherine A Byrnes [7] [8], Paul Dawkins [9] [10], Anne E Holland [11] [12] [13], Emma Kennedy [14] [15] [16], Paul T King [17], Pamela Laird [18] [19] [20], Sarah Mooney [9] [21], Lucy Morgan [22], Marianne Parsons [23], Betty Poot [24] [25], Maree Toombs [26], Paul J Torzillo [27] [28], Keith Grimwood [29] [30]

Affiliations expand

- PMID: 36863703

- DOI: 10.1111/resp.14479

Abstract

This position statement, updated from the 2015 guidelines for managing Australian and New Zealand children/adolescents and adults with chronic suppurative lung disease (CSLD) and bronchiectasis, resulted from systematic literature searches by a multi-disciplinary team that included consumers. The main statements are: Diagnose CSLD and bronchiectasis early; this requires awareness of bronchiectasis symptoms and its co-existence with other respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease). Confirm bronchiectasis with a chest computed-tomography scan, using age-appropriate protocols and criteria in children. Undertake a baseline panel of investigations. Assess baseline severity, and health impact, and develop individualized management plans that include a multi-disciplinary approach and coordinated care between healthcare providers. Employ intensive treatment to improve symptom control, reduce exacerbation frequency, preserve lung function, optimize quality-of-life and enhance survival. In children, treatment also aims to optimize lung growth and, when possible, reverse bronchiectasis. Individualize airway clearance techniques (ACTs) taught by respiratory physiotherapists, encourage regular exercise, optimize nutrition, avoid air pollutants and administer vaccines following national schedules. Treat exacerbations with 14-day antibiotic courses based upon lower airway culture results, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients with severe exacerbations and/or not responding to outpatient therapy are hospitalized for further treatments, including intravenous antibiotics and intensive ACTs. Eradicate Pseudomonas aeruginosa when newly detected in lower airway cultures. Individualize therapy for long-term antibiotics, inhaled corticosteroids, bronchodilators and mucoactive agents. Ensure ongoing care with 6-monthly monitoring for complications and co-morbidities. Undertake optimal care of under-served peoples, and despite its challenges, delivering best-practice treatment remains the overriding aim.

Keywords: adolescents; adults; bronchiectasis; children; evidence base practice; systematic review.

- 26 references

SUPPLEMENTARY INFO

Grant supportexpand

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Exhaled biomarkers in adults with non-productive cough

Össur Ingi Emilsson [1], Spela Kokelj [2], Jörgen Östling [3], Anna-Carin Olin [2]

Affiliations expand

- PMID: 36859273

- PMCID: PMC9976497

- DOI: 10.1186/s12931-023-02341-5

Abstract

Background: Chronic cough is a common condition but disease mechanisms are not fully understood. Our aim was to study respiratory biomarkers from the small airways in individuals with non-productive cough.

Methods: A cohort of 107 participants answered detailed questionnaires, performed spirometry, exhaled NO measurement, impulse oscillometry, gave blood samples and particles in exhaled air (PEx) samples. Current smokers (N = 38) were excluded. A total of 14 participants reported non-productive cough (cases). A total of 55 participants reported no cough (control group). PEx samples, containing exhaled particles derived from small airways, were collected and analysed with the SOMAscan proteomics platform.

Results: Participants with non-productive cough had similar age, sex, BMI, and inflammation markers in blood tests, as participants without cough. The proteomics analysis found 75 proteins significantly altered among participants with chronic cough

compared to controls, after adjusting for sex and investigator performing the PExA measurement (all with p-value < 0.05 and q-value ≤ 0.13, thereof 21 proteins with a q-value < 0.05). These proteins were mostly involved in immune and inflammatory responses, complement and coagulation system, but also tight junction proteins and proteins involved in neuroinflammatory responses.

Conclusions: This exploratory study on proteomics of exhaled particles among individuals with chronic cough found alterations in relative abundance of 75 proteins. The proteins identified are implicated in both pathways known to be implicated in cough, but also potentially new pathways. Further studies are needed to explore the importance of these findings.

Keywords: Chronic cough; Exhaled biomarkers; PExA.

Conflict of interest statement

ÖE: Has received honoraria from MSD, not related to this article. SK: No conflicts of interests. JÖ: Reports personal fees from PExA AB during the conduct of the study and was employed by PExA AB while writing the manuscript, but not during the planning and completion of the study. ACO: Is a chair-holder and a board member of PExA AB.

- 39 references
- 3 figures

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substances, Grant supportexpand

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Novel capsaicin cough endpoints effectively discriminate between healthy controls and patients with refractory chronic cough

Kimberley J Holt [1], John Belcher [2], Jaclyn A Smith [3]

Affiliations expand

- PMID: 36736541

- DOI: 10.1016/j.rmed.2023.107142

Abstract

Rationale: Chronic cough is a common problem, substantially affecting quality of life. Effective treatments and diagnostic clinical tools for refractory chronic cough are lacking which remains a diagnosis of exclusion.

Objectives: To investigate capsaicin evoked cough responses in healthy volunteers and refractory chronic cough patients and assess the discriminatory ability of novel endpoints.

Methods: Dose-response capsaicin cough challenges were performed, and receiver operating characteristic curves constructed to evaluate the discriminatory value of novel endpoints; Emax (maximum number of coughs evoked by any capsaicin concentration) and ED50 (capsaicin concentration evoking at least half of Emax).

Measurements and main results: Ninety-three healthy volunteers (median age 39yrs(IQR; 29-52), 47 females) and 51 refractory chronic cough patients (59yrs(53-67), 31 females) were studied. Emax was significantly higher in the patient group compared to healthy volunteers ($p < 0.001$) and ED50 was significantly lower ($p = 0.001$). Both parameters were influenced by gender; females had a higher Emax ($p = 0.009$) and more sensitive ED50 ($p < 0.001$) but there were no correlations with other patient demographics. There was a significant relationship between Emax and cough frequency in the patient group ($p < 0.001$). Emax effectively discriminated between the groups (AUC = 0.83, 95% CI; 0.75-0.90, $p < 0.001$) independently of ED50 which was less favourable (AUC = 0.66, 95% CI; 0.57-0.76, $p = 0.002$). Emax and ED50 were shown to be repeatable, and the dose-response method well tolerated.

Conclusion: Novel capsaicin dose-response endpoints effectively discriminate between healthy controls and refractory chronic cough patients, which may better represent pathophysiological mechanisms and show promise for development as a tool to identify patients with cough hyper-excitability.

Clinical trial registration: www.isrctn.com; ISRCTN23684347.

Keywords: Cough challenge; Cough response; ED50; Emax; TRPV1.

Conflict of interest statement

SUPPLEMENTARY INFO

MeSH terms, Substances, Grant supportexpand

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☐ 5

Prevalence of abnormal spirometry in individuals with a smoking history and no known obstructive lung disease

Thuonghien V Tran [1], Gregory L Kinney [2], Alejandro Comellas [3], Karin F Hoth [4], Arianne K Baldomero [5], A James Mamary [6], Jeffrey L Curtis [7], Nicola Hanania [8], Richard Casaburi [9], Kendra A Young [2], Victor Kim [6], Barry Make [10], Emily S Wan [11], Alejandro A Diaz [12], John Hokanson [2], James D Crapo [10], Edwin K Silverman [13], Surya P Bhatt [14], Elizabeth Regan [15], Spyridon Fortis [16]; COPDGene® Investigators – Core Units; COPDGene® Investigators – Clinical Centers

Collaborators, Affiliations expand

Abstract

Introduction: Recent evidence suggests a high prevalence of undiagnosed chronic obstructive pulmonary disease (COPD). These individuals are at risk of exacerbations and delayed treatment. We analyzed an at-risk population for the prevalence of abnormal spirometry to provide clarity into who should undergo early spirometry.

Methods: We analyzed data from the COPDGene study. Participants with ≥10 pack-years of smoking were included. Individuals with self-reported or physician-diagnosed COPD, asthma, chronic bronchitis, emphysema and/or were on inhalers were excluded. Parsimonious multivariable logistic regression models identified factors associated with abnormal spirometry, defined as either airflow obstruction (AFO) or preserved ratio impaired spirometry. Variables were selected for the final model using a stepwise backward variable elimination process which minimized Akaike information criterion (AIC). Similarly, during the 5-year follow-up period, we assessed factors associated with incident diagnosis of COPD.

Results: Of 5055 individuals, 1064 (21%) had undiagnosed AFO. Age, pack-years, current smoking and a history of acute bronchitis were associated with AFO while body mass index, female sex, and Black race were inversely associated. Among 2800 participants with 5-year follow-up, 532 (19%) had an incident diagnosis of COPD. Associated risk factors included mMRC ≥2, chronic productive cough, respiratory exacerbations during the follow-up period, and abnormal spirometry. Age was inversely associated.

Conclusions: The prevalence of undiagnosed COPD is high in at-risk populations. We found multiple factors associated with undiagnosed COPD and incident diagnosis of COPD at follow up. These results can be used to identify those at risk for undiagnosed COPD to facilitate earlier diagnosis and treatment.

Keywords: Chronic obstructive pulmonary disease; Diagnosis.

Conflict of interest statement

SUPPLEMENTARY INFO

MeSH terms, Grant supportexpand

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Review

[Chronic cough]

[Article in German]

M Schellenberg [1], F J F Herth [2]

Affiliations expand

- PMID: 36703081

- DOI: 10.1007/s00108-022-01467-w

Abstract

in English, German

Coughing is an important protective reflex of the respiratory tract and primarily serves clearance of the bronchial system. It is also an exceptionally common symptom in outpatient care that can be an expression of a variety of diseases. Coughing duration of longer than 8 weeks is referred to as chronic cough. A structured, often interdisciplinary diagnostic process is essential. The aim here is to identify causal treatment options, avoiding overdiagnosis and simultaneously not overlooking severe illness. This article discusses current diagnostic procedures, important differential diagnoses and possible treatment options.

Keywords: Antitussive agents; Chronic idiopathic cough; Cough/diagnosis, differential; Cough/etiology; Interdisciplinary diagnostic process.

- 23 references

SUPPLEMENTARY INFO

Publication types, MeSH terms, Substancesexpand

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Yardstick for managing cough, part 1: In adults and adolescent patients older than 14 years of age

Richard S Irwin [1], John J Oppenheimer [2], Whitney Dunlap [3], Jay A Lieberman [4], Anne B Chang [5]

Affiliations expand

Abstract

Nationwide statistics in the United States and Australia reveal that cough of undifferentiated duration is the most common complaint for which patients of all ages seek medical care in the ambulatory setting. Management of chronic cough is one of the most common reasons for new patient visits to pulmonologists. Because symptomatic cough is such a common problem and so much has been learned about how to diagnose and treat cough of all durations but especially chronic cough, this 2-part yardstick has been written to review in a practical way the latest evidence-based guidelines most of which have been developed from recent high quality systematic reviews on how best to manage cough of all durations in adults, adolescents, and children. In this manuscript, part

1 of the 2-part series, we provide evidence-based, and expert opinion recommendations on the management of chronic cough in adult and adolescent patients (>14 years of age).

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[Reduced lung function and health-related quality of life after treatment for pulmonary tuberculosis in Gambian children: a cross-sectional comparative study](#)

[Esin Nkereuwem](#) [1][2], [Schadrac Agbla](#) [3][4], [Azeezat Sallahdeen](#) [5], [Olumuyiwa Owolabi](#) [5], [Abdou K Sillah](#) [5], [Monica Genekah](#) [5], [Abdoulie Tunkara](#) [5], [Sheriff Kandeh](#) [5], [Maryama Jawara](#) [5], [Lamin Saidy](#) [6], [Andrew Bush](#) [7][8], [Toyin Togun](#) [5][2][9], [Beate Kampmann](#) [5][2][10]

Affiliations expand

- PMID: 36109164

Abstract

Background: Post-tuberculosis (post-TB) lung disease is an under-recognised consequence of pulmonary tuberculosis (pTB). We aimed to estimate the prevalence of residual lung function impairment and reduced health-related quality of life (HRQoL) in children after pTB treatment completion.

Methods: We conducted a cross-sectional comparative study of children aged less than 15 years at TB diagnosis who had completed treatment for pTB at least 6 months previously with a comparator group of age-matched children without a history of pTB. Symptoms, spirometry and HRQoL measured with PedsQL scale were collected. Variables associated with lung function impairment were identified through logistic regression models.

Results: We enrolled 68 post-TB cases (median age 8.9 (IQR 7.2-11.2) years) and 91 children in the comparison group (11.5 (8.0-13.7) years). Spirometry from 52 (76.5%) post-TB cases and 89 (94.5%) of the comparison group met the quality criteria for acceptability and repeatability. Lung function impairment was present in 20/52 (38.5%) post-TB cases and 15/86 (17.4%) in the comparison group, p=0.009. Previous pTB and a history of chronic cough were significantly associated with the presence of lung function impairment (p=0.047 and 0.006 respectively). Forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC z-scores were significantly lower in the post-TB cases compared with the comparison group (p= <0.001, 0.014 and <0.001, respectively). The distribution of the self-reported physical health score, and parent-reported physical, emotional, psychological, social and total HRQoL scores were significantly lower in the post-TB cases compared with the comparison group.

Conclusions: Previous TB in children is associated with significantly impaired lung function and HRQoL.

Keywords: Clinical Epidemiology; Paediatric Lung Disaese; Respiratory Infection; Tuberculosis.

Conflict of interest statement

Competing interests: None declared.

SUPPLEMENTARY INFO

MeSH termsexpand

BRONCHIECTASIS

Thoracic Society of Australia and New Zealand (TSANZ) position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand

Anne B Chang [1] [2] [3], Scott C Bell [4] [5] [6], Catherine A Byrnes [7] [8], Paul Dawkins [9] [10], Anne E Holland [11] [12] [13], Emma Kennedy [14] [15] [16], Paul T King [17], Pamela Laird [18] [19] [20], Sarah Mooney [9] [21], Lucy Morgan [22], Marianne Parsons [23], Betty Poot [24] [25], Maree Toombs [26], Paul J Torzillo [27] [28], Keith Grimwood [29] [30]

Affiliations expand

- PMID: 36863703

- DOI: 10.1111/resp.14479

Abstract

This position statement, updated from the 2015 guidelines for managing Australian and New Zealand children/adolescents and adults with chronic suppurative lung disease (CSLD) and bronchiectasis, resulted from systematic literature searches by a multi-disciplinary

team that included consumers. The main statements are: Diagnose CSLD and bronchiectasis early; this requires awareness of bronchiectasis symptoms and its co-existence with other respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease). Confirm bronchiectasis with a chest computed-tomography scan, using age-appropriate protocols and criteria in children. Undertake a baseline panel of investigations. Assess baseline severity, and health impact, and develop individualized management plans that include a multi-disciplinary approach and coordinated care between healthcare providers. Employ intensive treatment to improve symptom control, reduce exacerbation frequency, preserve lung function, optimize quality-of-life and enhance survival. In children, treatment also aims to optimize lung growth and, when possible, reverse bronchiectasis. Individualize airway clearance techniques (ACTs) taught by respiratory physiotherapists, encourage regular exercise, optimize nutrition, avoid air pollutants and administer vaccines following national schedules. Treat exacerbations with 14-day antibiotic courses based upon lower airway culture results, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients with severe exacerbations and/or not responding to outpatient therapy are hospitalized for further treatments, including intravenous antibiotics and intensive ACTs. Eradicate Pseudomonas aeruginosa when newly detected in lower airway cultures. Individualize therapy for long-term antibiotics, inhaled corticosteroids, bronchodilators and mucoactive agents. Ensure ongoing care with 6-monthly monitoring for complications and co-morbidities. Undertake optimal care of under-served peoples, and despite its challenges, delivering best-practice treatment remains the overriding aim.

- 26 references

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Int J Tuberc Lung Dis

-

Post-TB bronchiectasis: from pathogenesis to rehabilitation

M A Martinez-Garcia [1], W-J Guan [2], D de-la-Rosa [3], R Athanazio [4], G Oscullo [5], M-X Shi [6], P Pujal-Montaña [3], B N Endlich [4], S Tiberi [7], R Centis [8], G B Migliori [8]

Affiliations expand

- PMID: 36855043

- DOI: 10.5588/ijtld.22.0566

Abstract

The destruction of lung parenchyma caused by TB can result in pulmonary sequelae that are classified as bronchiectasis due to traction (radiological sequelae), and bronchiectasis persisting with an inflammatory bronchial component and opportunistic bronchial infection. There is a lack of studies that comprehensively analyse whether post-TB bronchiectasis differs in clinical, prognostic or therapeutic aspects from bronchiectasis arising from other aetiologies. However, it has been noted that post-TB bronchiectasis tends to appear more frequently in the upper lung lobes. In many countries, TB is the most frequent known cause of bronchiectasis, but there is currently no targeted management of bronchiectasis due to TB as opposed to other aetiologies. It is imperative to first prevent TB, and when that fails to provide early diagnosis and adequate treatment for TB disease. In addition, efforts should be made to limit additional lung insults such as tobacco use and provide management of post TB bronchiectasis to minimise further pulmonary sequelae. The objective of this minireview was to provide an update on post-TB bronchiectasis, its definition, epidemiological data, pathophysiology, and clinical, diagnosis and therapeutic aspects.

SUPPLEMENTARY INFO

MeSH termsexpand

FULL TEXT LINKS

Review

MR imaging of the airways

Juergen Biederer [1][2][3][4]

Affiliations expand

- PMID: 36752590

- DOI: 10.1259/bjr.20220630

Abstract

The need for airway imaging is defined by the limited sensitivity of common clinical tests like spirometry, lung diffusion (DLCO) and blood gas analysis to early changes of peripheral airways and to inhomogeneous regional distribution of lung function deficits. Therefore, X-ray and computed tomography (CT) are frequently used to complement the standard tests.As an alternative, magnetic resonance imaging (MRI) offers radiation-free lung imaging, but at lower spatial resolution. Non-contrast enhanced MRI shows healthy airways down to the first subsegmental level/4th order (CT: eighth). Bronchiectasis can be identified by wall thickening and fluid accumulation. Smaller airways become visible, when altered by peribronchiolar inflammation or mucus retention (tree-in-bud sign).The strength of MRI is functional imaging. Dynamic, time-resolved MRI directly visualizes expiratory

airway collapse down to the lobar level (CT: segmental level). Obstruction of even smaller airways becomes visible as air trapping on the expiratory scans. MRI with hyperpolarized noble gases (^{3}He, ^{129}Xe) directly shows the large airways and peripheral lung ventilation. Dynamic contrast-enhanced MRI (DCE MRI) indirectly shows airway dysfunction as perfusion deficits resulting from hypoxic vasoconstriction of the dependent lung volumes. Further promising scientific approaches such as non-contrast enhanced, ventilation-/perfusion-weighted MRI from periodic signal changes of respiration and blood flow are in development.In summary, MRI of the lungs and airways excels with its unique combination of morphologic and functional imaging capacities for research (*e.g.,* in chronic obstructive lung disease or asthma) as well as for clinical imaging (*e.g.,* in cystic fibrosis).

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Review

Airway mucus in pulmonary diseases: Muco-adhesive and muco-penetrating

particles to overcome the airway mucus barriers

Rudra Pangeni [1], Tuo Meng [1], Sagun Poudel [1], Divya Sharma [2], Hallie Hutsell [1], Jonathan Ma [3], Bruce K Rubin [4], Worth Longest [5], Michael Hindle [1], Qingguo Xu [6]

Affiliations expand

Abstract

Airway mucus is a complex viscoelastic gel that provides a defensive physical barrier and shields the airway epithelium by trapping inhaled foreign pathogens and facilitating their removal via mucociliary clearance (MCC). In patients with respiratory diseases, such as chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), non-CF bronchiectasis, and asthma, an increase in crosslinking and physical entanglement of mucin polymers as well as mucus dehydration often alters and typically reduces mucus mesh network pore size, which reduces neutrophil migration, decreases pathogen capture, sustains bacterial infection, and accelerates lung function decline. Conventional aerosol particles containing hydrophobic drugs are rapidly captured and removed by MCC. Therefore, it is critical to design aerosol delivery systems with the appropriate size and surface chemistry that can improve drug retention and absorption with the goal of increased efficacy. Biodegradable muco-adhesive particles (MAPs) and muco-penetrating particles (MPPs) have been engineered to achieve effective pulmonary delivery and extend drug residence time in the lungs. MAPs can be used to target mucus as they get trapped in airway mucus by steric obstruction and/or adhesion. MPPs avoid muco-adhesion and are designed to have a particle size smaller than the mucus network, enhancing lung retention of particles as well as transport to the respiratory epithelial layer and drug absorption. In this review, we aim to provide insight into the composition of airway mucus, rheological characteristics of airway mucus in healthy and diseased subjects, the most recent techniques to study the flow dynamics and particle diffusion in airway mucus (in particular, multiple particle tracking, MPT), and the advancements in engineering MPPs that have contributed to improved airway mucus penetration, lung distribution, and retention.

Keywords: Aerosol; Cystic fibrosis; Microrheology; Mucociliary clearance; Multiple particle tracking; Pulmonary drug delivery; Rheology.

Conflict of interest statement

Declaration of Competing Interest The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The EEG aerosol technologies described in this publication have been filed as patent applications through Virginia Commonwealth University (VCU). Michael Hindle and Worth Longest are the co-inventors, which are subject to certain rules and restrictions under VCU policy. The terms of this arrangement are being managed by VCU in accordance with its conflict of interest policies.

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Editorial

Primary Ciliary Dyskinesia and Bronchiectasis: New Data and Future Challenges

[Article in English, Spanish]

Charlotte O Pioch [1], David W Connell [2], Amelia Shoemark [3]

Affiliations expand

- PMID: 36639347

- DOI: 10.1016/j.arbres.2022.12.001

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

FULL TEXT LINKS

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Archivos de Bronconeumología

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Biologics in Bronchiectasis: A Future Treatment?

[Article in English, Spanish]

Mattia Nigro [1], Edoardo Simonetta [2], Miguel Ángel Martínez-García [3], Stefano Aliberti [4]

Affiliations expand

No abstract available

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Gastrointestinal factors associated with risk of bronchiectasis in children

Daniel R Duncan [1], Alexandra Cohen [1], Clare Golden [1], Margot Lurie [1], Paul D Mitchell [2], Enju Liu [2], Tregony Simoneau [3], Rachel L Rosen [1]

Affiliations expand

Abstract

Objective: To evaluate gastrointestinal (GI) risk factors for bronchiectasis in children. We hypothesized that upper GI tract dysmotility would be associated with increased risk of bronchiectasis.

Study design: Subjects in this retrospective cohort study included those evaluated for persistent pulmonary symptoms in the Aerodigestive Center at Boston Children's Hospital who underwent chest computed tomography (CT) between 2002 and 2019. To determine gastrointestinal predictors of bronchiectasis, baseline characteristics, comorbidities, enteral tube status, medications received, gastroesophageal reflux burden, adequacy of swallow function, esophageal dysmotility, gastric dysmotility, and neutrophil count on bronchoalveolar lavage (BAL) were compared between patients with and without bronchiectasis. Proportions were compared with Fisher's exact test and binary logistic regression with stepwise selection was used for multivariate analysis. ROC analyses were utilized to compare BAL neutrophils and bronchiectasis.

Results: Of 192 subjects, 24% were found to have evidence of bronchiectasis on chest CT at age 7.9 ± 0.5 years. Enteral tubes (OR 5.77, 95% CI 2.25-14.83, p < 0.001) and increased BAL neutrophil count (OR 5.79, 95% CI 1.87-17.94, p = 0.002) were associated with increased risk while neurologic comorbidities were associated with decreased risk (OR 0.24, 95% CI 0.09-0.66, p = 0.006). Gastroesophageal reflux was not found to be a significant risk factor. Neutrophil counts >10% had 72% sensitivity and 60% specificity for identifying bronchiectasis.

Conclusions: Enteral tubes were associated with significantly increased risk of bronchiectasis but gastroesophageal reflux was not. Providers should consider obtaining chest CT to evaluate for bronchiectasis in children found to have unexplained elevated BAL neutrophil count.

Keywords: gastroesophageal reflux; gastrostomy tube; motility; oropharyngeal dysphagia.

Conflict of interest statement

SUPPLEMENTARY INFO

Publication types, MeSH terms, Grant supportexpand

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Ann Allergy Asthma Immunol

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-

. 2023 Mar;130(3):362-364.

 doi: 10.1016/j.anai.2022.11.024. Epub 2022 Dec 8.

Clinical characteristics of the asthma bronchiectasis phenotype

Rory Chan [1], Chary Duraikannu [2], Brian Lipworth [3]

Affiliations expand

- PMID: 36503068

- DOI: 10.1016/j.anai.2022.11.024

Free article

No abstract available

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☐ 9

Does Bronchiectasis Cause Irreversible Damage?

[Article in English, Spanish]

Layla Diab Cáceres[1], Rafael Morales Ruiz[2], Victoria Villena Garrido[3]

Affiliations expand

No abstract available

SUPPLEMENTARY INFO

Publication typesexpand

Review

The prevalence of comorbidity in the lung cancer screening population: A systematic review and meta-analysis

Anas Almatrafi [1][2], Owen Thomas [1], Matthew Callister [3], Rhian Gabe [4], Rebecca J Beeken [1][5], Richard Neal [1][6]

Affiliations expand

Free PMC article

Abstract

Objective: Comorbidity is associated with adverse outcomes for all lung cancer patients, but its burden is less understood in the context of screening. This review synthesises the prevalence of comorbidities among lung cancer screening (LCS) candidates and summarises the clinical recommendations for screening comorbid individuals.

Methods: We searched MEDLINE, EMBASE, EBM Reviews, and CINAHL databases from January 1990 to February 2021. We included LCS studies that reported a prevalence of comorbidity, as a prevalence of a particular condition, or as a summary score. We also summarised LCS clinical guidelines that addressed comorbidity or frailty for LCS as a secondary objective for this review. Meta-analysis was used with inverse-variance weights obtained from a random-effects model to estimate the prevalence of selected comorbidities.

Results: We included 69 studies in the review; seven reported comorbidity summary scores, two reported performance status, 48 reported individual comorbidities, and 12 were clinical guideline papers. The meta-analysis of individual comorbidities resulted in an estimated prevalence of 35.2% for hypertension, 23.5% for history of chronic obstructive pulmonary disease (COPD) (10.7% for severe COPD), 16.6% for ischaemic heart disease (IHD), 13.1% for peripheral vascular disease (PVD), 12.9% for asthma, 12.5% for diabetes, 4.5% for bronchiectasis, 2.2% for stroke, and 0.5% for pulmonary fibrosis.

Conclusions: Comorbidities were highly prevalent in LCS populations and likely to be more prevalent than in other cancer screening programmes. Further research on the burden of comorbid disease and its impact on screening uptake and outcomes is needed. Identifying individuals with frailty and comorbidities who might not benefit from screening should become a priority in LCS research.

Keywords: Lung cancer; comorbidity; frailty; low-dose computed tomography; screening.

Conflict of interest statement

- 121 references
- 1 figure

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Publication types, MeSH termsexpand

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'The likes of me running and walking? No chance': Exploring the perceptions of adult patients with bronchiectasis towards exercise

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Abstract

Objective: To explore the views and experiences of adult patients with bronchiectasis towards exercise. **Methods:** Semi-structured interviews with ten patients with

bronchiectasis were conducted to explore perceptions of exercise, potential barriers and facilitators of exercise. Inductive thematic analysis was used to identify key themes. **Findings:** Five main themes: 1. The language of exercise 2. Facilitators to exercise 3. Barriers to exercise 4. Exercise has a positive impact on health and life expectancy 5. Grief regarding loss of ability **Discussion:** Participants perceived exercise as positive, but there was variance regarding what this entailed. Findings suggest healthcare professionals should consider the language used when prescribing exercise and provide clarity for patients and reflect on their own role in advising on exercise. There were both common and differing barriers and facilitators to exercise between participants. Holistic needs and the identification of these potential barriers and facilitators to exercise could aid compliance. Further research is needed to explore generalisability and the effectiveness of behaviour change models to improve engagement with exercise.

Keywords: activity; bronchiectasis; exercise; respiratory.

Conflict of interest statement

- 39 references
- 2 figures

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