using a separate population of people with paucigranulocytic asthma, using decision tree analysis. This study highlights that psychological dysfunction and smoking are two areas to target in paucigranulocytic asthma. Further studies are needed to explore whether stratifying patients in these clusters improves treatment outcomes.

INHIBITING NEUTROPHIL PROTEASES IN BRONCHIECTASIS: NEW TREATMENT OFFERING POTENTIAL FOR FEWER EXACERBATIONS

Neutrophil serine proteases mediate airway inflammation in bronchiectasis, and are increased during exacerbations. Dipeptidyl peptidase-1 (DPP-1) activates neutrophil serine proteases during neutrophil maturation in the bone marrow. Chalmers *et al* (*New Engl J Med* 2020;383:2127) performed a phase 2, randomised, double-blind parallel-group trial of brensocatic (DPP-1 inhibitor) in idiopathic bronchiectasis. The primary outcome was the time to the first exacerbation during the 24-week trial period. Patients were randomised 1:1:1 to placebo (n=87), brensocatic 10 mg (n=82) or 25 mg (n=87). Patients enrolled were predominantly female (63%–71%) and white (82%–93%). Compared with placebo, brensocatic increased time to the first exacerbation (brensocatic 10 mg p=0.03; brensocatic 25 mg p=0.04) and reduced the incidence rate of exacerbations (brensocatic 10 mg Incidence Rate Ratio 0.64, 95% CI 0.42 to 0.98, p=0.04; brensocatic 25 mg IRR 0.75, 95% CI 0.50 to 1.13, p=0.17). There were no serious adverse events and infection rates did not increase in the brensocatic groups, but the short duration of this trial meant that it is unclear if brensocatic is associated with a long-term risk of infection. This study highlights the potential benefits of suppressing neutrophilic inflammation in bronchiectasis, but longer studies are needed to comprehensively assess the risk of subsequent bacterial infection.

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PREVENTION OF ASTHMA: ANTIBIOTIC STEWARDSHIP IN INFANCY MAY BE IMPORTANT

Dysbiosis of the gut microflora is associated with the development of asthma, and antibiotic use is a risk factor for dysbiosis. However, it is unclear if antibiotic stewardship in young children is associated with a reduction in asthma incidence. Patrick *et al* (*Lancet Respir Med* 2020;8:1094) performed a population-based study of paediatric antibiotic prescribing and asthma incidence in British Columbia, Canada, between 2000 and 2014. Antibiotic use and asthma incidence were also assessed in 2644 children recruited to a longitudinal birth cohort from cities across Canada. The authors sequenced the gut microbiota of 917 of these children in their first year of life, to examine any relationships among microbiota diversity, asthma incidence and antibiotic use. Over the study period (2000–2014), the incidence of asthma in children aged 1–4 years old decreased by 26.0%, while antibiotic prescriptions in the first year of life decreased by 61.0%. Multivariate analysis demonstrated that a 10% increase in antibiotic prescribing was associated with a 24% increase in asthma incidence (adjusted incident rate ratio 1.24, 95% CI 1.20 to 1.28). After excluding children who received antibiotics for a respiratory cause (to reduce confounding), multivariate analysis of the birth cohort showed that antibiotic use in the first year of life was associated with asthma at age 5 years (aOR 2.15, 95% CI 1.37 to 3.39). This association demonstrated a significant dose–response effect. Structural equation modelling demonstrated that gut microbiota was a significant mediator between antibiotic use in the first year of life and development of asthma by age 5 years ($\beta=0.07$). While studies of the airway microbiota are needed, these findings suggest that antibiotic stewardship in infancy may contribute to the reduction in asthma incidence at a population level.

PHENOTYPING ASTHMA: BLOOD, BREATH, SPUTUM... AND NOW URINE

Current measures of T helper 2 (Th2) inflammation are either invasive (blood eosinophils) or infrequently used in primary care (sputum eosinophils and FeNO). Kolmert *et al* (*Am J Respir Crit Care Med* 2021;203:37) performed a cross-sectional study of urinary eicosanoid metabolites, markers of Th2

inflammation, in 497 people with asthma and 100 healthy controls. The results from the cross-sectional study were internally validated during an 18-month longitudinal study of 302 individuals with severe asthma, and externally validated using a separate population of 95 children with asthma. There was a trend towards a progressive increase of urinary eicosanoid metabolites between different asthma severities, but this only reached statistical significance for urinary leukotriene E4 (LTE₄) (4.5 vs 3.1 ng/mmol for mild-to-moderate asthma vs healthy controls, p<0.001; 6.3 vs 4.5 ng/mmol for severe asthma vs mild-to-moderate asthma, p<0.001). Elevated levels of urinary LTE₄ were associated with a Th2 inflammatory profile, and urinary combined prostaglandin D2 metabolites (c-PGD₂) was associated with most Th2 biomarkers, except FeNO and serum periostin. These findings were replicated in the longitudinal study of people with severe asthma, which also showed that >95.0% of participants had LTE₄ values within 1 SD between the start and endpoints of the study. Furthermore, the external validation study showed that urinary PDG₂ metabolites were associated with Th2 biomarkers in children with asthma. This study highlights the potential of urinary eicosanoid metabolites to assess Th2 inflammation, which may be particularly useful in patients for whom it is difficult to obtain blood or sputum samples (such as children).

PAUCIGRANULOCYTIC ASTHMA: CLINICALLY RELEVANT CLUSTERS IDENTIFIED

Paucigranulocytic asthma (defined by absent eosinophilic or neutrophilic inflammation) comprises approximately 40% of asthma, but little is known about its characteristics. Deng *et al* (*J Allergy Clin Immunol Pract* 2021; DOI: 10.1016/j.jaip.2021.01.004) stratified 145 patients with paucigranulocytic asthma into clusters, and then performed a 12-month prospective cohort study to assess the exacerbation risk of each cluster. Three clusters were identified. Cluster 1 (n=110; 76%) was characterised by non-smoking females with normal lung function; Cluster 2 (n=20; 14%) was characterised by patients with mental health conditions (100.0% of patients) and allergic diseases (80.0% of patients); Cluster 3 (n=15; 10%) was characterised by older, current smokers (100.0% of patients). In the 12-month follow-up, patients in cluster 3 had significantly more severe exacerbations than patients in cluster 1 (RR 6.43, 95% CI 1.24 to 33.33). Overall, 70.0% of patients remained in the same cluster during the follow-up period. The clusters were validated

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