Type – Pheno, Endo, Sub

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Current Global Initiative for Asthma (GINA) guidelines recognise the benefits of assessing airway inflammation in asthma management (Shown in Box 1) and support the identification of eosinophilic asthma and offers phenotype specific treatments such as mepolizamab, reducing eosinophilia, reducing the incidence of severe exacerbations and offering reduced requirement for oral corticosteroids (1) . Farias *et al* ask the question which sample type is best for phenotyping asthma. The answer is complex and depends on the purpose of phenotyping asthma, which may differ between the best for clinical management and treatment decision making compared with the best for understanding mechanisms.

Box 1

Sputum-guided treatment: in centers with specific expertise in inducing and analyzing sputum, adjusting treatment for severe asthma on the basis of **sputum eosinophils** may allow corticosteroid dose and/or exacerbation frequency to be reduced (1) (Evidence A).

Phenotype-guided add-on treatment: patients with severe asthma, uncontrolled on Step 4 treatment, may benefit from phenotyping ….those with severe eosinophilic asthma may benefit from mepolizumab (anti-IL5) therapy (2,3)

For those patients with eosinophilic asthma, the need for induced sputum to identify inflammatory phenotype is now diminishing. The technical nature of processing and counting inflammatory cells in induced sputum has limited its translation to primary care and alternatives have been studied for some time now. In their study, Farias *et al* studied 121 adults with moderate to severe asthma; this cohort is unusual with a high proportion of participants with neutrophilic asthma (43%) and a relatively low proportion with eosinophilic asthma, nonetheless, there were no distinguishing clinical features among the four inflammatory phenotypes. Nasal lavage offered the best concordance with induced sputum for the granulocytic dominant phenotypes (EA, NA and MGA) and a higher specificity for the identification eosinophilic asthma (94%). Blood eosinophils by comparison, had a lower specificity 72% for identifying EA and therefore a lower area under the curve following ROC analysis. The specificity of blood eosinophils reported by Farias *et al* is remarkably similar to a number of other large cohorts (4,5) and the largest study of more than 500 adults showed that blood eosinophils to be independent predictor of sputum eosinophilia (6). Sensitivity of blood eosinophils to predict sputum eosinophilia seems to vary more, with the study of Farias et al observing a much lower sensitivity around half of that reported in the other studies.

Perhaps one of the key challenges to translating inflammation monitoring into clinical practice is the technical difficulty in studying inflammation at the site. Induced sputum is a relatively safe and non-invasive technique for the examination of airway inflammation and is a key tool for studying mechanisms of inflammation. This is particularly pertinent for the non-eosinophilic inflammatory phenotypes, which make up around half of all asthma cases. The value in identifying other inflammatory phenotypes lies in the promise of understanding mechanisms that drive symptoms and exacerbations in these patients, and the hope of better therapies and management strategies. For studies of mechanisms of airway inflammation, induced sputum will remain an important tool in discovery.

Identifying the **absence** of EA, or the presence of NEA (NA, PGA) might be clinically useful to initiate a step-down of eosinophilic controlling therapies such as OCS or ICS – however further studies are required to examine the clinical implications of such strategies.

There have been very few studies of nasal wash in asthma. Reports identify that nasal wash can be used to assess the presence of inflammatory cytokines, eosinophils and eosinophil cationic protein in adults and children with asthma (7,8), which make it an alternative to induced sputum for the identification of eosinophilic asthma. Benton *et al* identified three key clusters of children with asthma, one of which was characterised by eosinophilic inflammation , poorer asthma control and allergy (9). Although not reported in the current study, it would be important to know more about the success rate for nasal wash and blood compared with induced sputum.

Conclusion

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