

## Improving Asthma Outcomes: Strategies for the Future

Tow Keang Lim, <sup>1</sup>*MBBS, MMed (Respir), FAMS*

### Introduction

Despite accelerated research and major advances in the treatment of asthma in recent years, the disease burden remains high even in well resourced countries where up to 50% of patients may experience poor control of clinical disease. This is a global challenge which calls for a robust collective response.<sup>1,2</sup> Thus, establishing future strategies to improve asthma outcomes is an important responsibility for both physicians and policy makers.

### Primary Prevention

During early life, priming of our immune system in response to microbes and allergens in the environment appears to be pivotal in the development of allergic diseases. Changes in the profile of this microbiota is probably the main cause of the dramatic rise in asthma prevalence associated with the transition from rural to urban lifestyles. Exposure to complex traditional farm dust protects children from developing asthma.<sup>3</sup> This protective effect appears to be mediated by a negative feedback loop following the activation of innate immunity.<sup>4</sup> Thus, manipulation of microbiota and allergen compositions in the environment which prime the immune system during early life may be an effective strategy for the primary prevention of asthma in high-risk families. This prospect, however, remains in a more distant future.

### Behaviour Change

The most prevalent yet preventable barrier to better asthma outcomes is poor adherence to current guideline-based best practice by both patients and their doctors. This is best seen in the study of a tip-of-the-iceberg situation like the UK National Review of Asthma Deaths which concluded that complacency with respect to asthma care was an important potentially preventable factor in asthma deaths.<sup>5</sup> We need to design and test more effective treatment adherence

interventions based more firmly on the theory of behaviour change.<sup>6,7</sup> These will certainly need to be augmented by mobile information technology (IT) support tools.<sup>8-11</sup> IT support for behaviour change requires careful detailing in designs which encourage regular use and minimise burden to patients and physicians. They will also need to be adaptive in relation to local patient culture and practice settings. Improving basic adherence to current asthma treatment is an urgent priority and probably the most cost-effective strategy to improve overall asthma outcomes and reduce preventable asthma deaths.

### Oral Immunotherapy

Until recently immunotherapy in asthma requires regular injections, has modest effects, is inconvenient, potentially risky and not popular with either patients or physicians. However, immunotherapy with sublingual house dust mite allergens is a notable advance.<sup>12</sup> It appears to reduce asthma exacerbations safely in adults.<sup>13</sup> This is a promising development but it requires further development and evaluation.

### More Mileage for Old Strategies

The cornerstone of conventional treatment for persistent asthma is inhaled corticosteroids (ICS) followed by, in non-responding cases, adding on long-acting bronchodilators. Recent advances in this approach include potent ICS with minimal effects on the hypothalamic-pituitary axis, ultra-long active beta agonist (LABA), ultra-long acting muscarinic antagonist (LAMA) and more convenient, patient-preferred devices.<sup>14</sup> Some of these ultra-long acting bronchodilators may also possess rapid onset action and so they serve as quick relievers during asthma exacerbations.<sup>15</sup> Thus, in future, the basic maintenance inhalational therapy for asthma may consist of all 3 drugs in a single device to be taken once per day for prevention and acute flare-ups.

---

<sup>1</sup>Department of Medicine, National University Hospital Singapore, Singapore  
Address for Correspondence: Prof Lim Tow Keang, Department of Medicine, National University Hospital Singapore, NUHS Tower Block Level 10, 1E Kent Ridge Road, Singapore 119228.  
Email: mdclimtk@nus.edu.sg

## Targeted Treatment

The novel strategy of targeted or personalised treatment arose from research on asthma which is refractory to conventional treatment. The era of targeted treatment commenced with the discovery of a series of new drugs which inhibit different immunopathogenic pathways, or endotypes, in type 2 immunity (TH2).<sup>16</sup> Effective treatments which block TH2 pathways include omalizumab (anti-IgE) for severe persistent allergic IgE-mediated asthma and mepolizumab (anti-IL5) for severe eosinophilic asthma.<sup>17,18</sup> These treatment options are already recommended at step 5 of the practice guidelines promulgated by the Global Initiative for Asthma.<sup>2</sup> A large and growing number of similar drugs are currently under investigation. But all these new asthma treatments have been designed to target different aspects of TH2 inflammation. Thus, this targeted approach is not yet possible for the minority of patients with non-TH2-mediated asthma. However, other treatment options for these patients may also be effective. They include macrolides and bronchial thermoplasty.<sup>19,20</sup> Further research is needed on the most reliable diagnostic tests which will differentiate between asthma endotypes for appropriately customised treatment. We anticipate the advent of novel endotypes and new treatments in this rapidly expanding field.

## Conclusion

The future appears propitious for patients with asthma. However, before patients can enjoy real benefits, the disparate advances in many different fields ranging from molecular biology to IT, delivery devices and the social sciences need to be coordinated and translated into comprehensive treatment strategies. Areas of potential improvement include primary prevention of asthma, enhanced convention treatment and targeted customised treatment according to precisely defined asthma endotypes. Improving asthma outcomes is a priority and an eminently attainable goal.

## REFERENCES

1. Global Asthma Network. The global asthma report 2014. Available at: <http://www.globalasthmareport.org>. Accessed on 2014.
2. Global initiative for asthma. Available at: <http://ginasthma.org/>. Accessed on 2 October 2016.
3. Birzele LT, Depner M, Ege MJ, Engel M, Kublik S, Bernau C, et al. Environmental and mucosal microbiota and their role in childhood asthma. *Allergy* 2016. [Epub ahead of print]
4. Chatila TA. Innate immunity in asthma. *N Engl J Med* 2016;375:477-9.
5. Levy ML. The national review of asthma deaths: what did we learn and what needs to change? *Breathe (Sheff)* 2015;11:14-24.
6. McCullough AR, Ryan C, Macindoe C, Yii N, Bradley JM, O'Neill B, et al. Behavior change theory, content and delivery of interventions to enhance adherence in chronic respiratory disease: a systematic review. *Respir Med* 2016;116:78-84.
7. Mosavianpour M, Sarmast HH, Kisoorn N, Collet JP. Theoretical domains framework to assess barriers to change for planning health care quality interventions: a systematic literature review. *J Multidiscip Healthc* 2016;9:303-10.
8. Yasmin F, Banu B, Zakir SM, Sauerborn R, Ali L, Souares A. Positive influence of short message service and voice call interventions on adherence and health outcomes in case of chronic disease care: a systematic review. *BMC Med Inform Decis Mak* 2016;16:46.
9. Koufopoulos JT, Conner MT, Gardner PH, Kellar I. A web-based and mobile health social support intervention to promote adherence to inhaled asthma medications: randomized controlled trial. *J Med Internet Res* 2016;18:e122.
10. Kolmodin MacDonell K, Naar S, Gibson-Scipio W, Lam P, Secord E. The Detroit young adult asthma project: pilot of a technology-based medication adherence intervention for African-American emerging adults. *J Adolesc Health* 2016;59:465-71.
11. Kew KM, Cates CJ. Remote versus face-to-face check-ups for asthma. *Cochrane Database Syst Rev* 2016;4:CD011715.
12. Normansell R, Kew KM, Bridgman AL. Sublingual immunotherapy for asthma. *Cochrane Database Syst Rev* 2015;8:CD011293.
13. Virchow JC, Backer V, Kuna P, Prieto L, Nolte H, Villesen HH, et al. Efficacy of a house dust mite sublingual allergen immunotherapy tablet in adults with allergic asthma: a randomized clinical trial. *JAMA* 2016;315:1715-25.
14. Allen A, Schenkenberger I, Trivedi R, Cole J, Hicks W, Gul N, et al. Inhaled fluticasone furoate/vilanterol does not affect hypothalamic-pituitary-adrenal axis function in adolescent and adult asthma: randomised, double-blind, placebo-controlled study. *Clin Respir J* 2013;7:397-406.
15. Singh D, Ravi A, Reid F, Buck H, O'Connor G, Down G. Bronchodilator effects, pharmacokinetics and safety of PSX1002-GB, a novel glycopyrronium bromide formulation, in COPD patients; a randomised crossover study. *Pulm Pharmacol Ther* 2016;37:9-14.
16. Wenzel SE. Emergence of biomolecular pathways to define novel asthma phenotypes. Type-2 immunity and beyond. *Am J Respir Cell Mol Biol* 2016;55:1-4.
17. Normansell R, Walker S, Milan SJ, Walters EH, Nair P. Omalizumab for asthma in adults and children. *Cochrane Database Syst Rev* 2014;1:CD003559.
18. Powell C, Milan SJ, Dwan K, Bax L, Walters N. Mepolizumab versus placebo for asthma. *Cochrane Database Syst Rev* 2015;7:CD010834.
19. Brusselle GG, Vanderstichele C, Jordens P, Deman R, Slabbynck H, Ringoet V, et al. Azithromycin for prevention of exacerbations in severe asthma (AZISAST): a multicentre randomised double-blind placebo-controlled trial. *Thorax* 2013;68:322-9.
20. Zhou JP, Feng Y, Wang Q, Zhou LN, Wan HY, Li QY. Long-term efficacy and safety of bronchial thermoplasty in patients with moderate-to-severe persistent asthma: a systemic review and meta-analysis. *J Asthma* 2016;53:94-100.