Respiratory RESEARCH REVIEW™

Making Education Easy

Issue 176 – 2020

In this issue:

Abbreviations used in this issue

ACQ/ACT = Asthma Control Questionnaire/Test
FeNO = fractional exhaled nitric oxide
FEV = forced expiratory volume
GINA = Global Initiative for Asthma
ICS/OCS = inhaled/oral corticosteroid
IL = interleukin
MPR = medicines possession ratio
OR = odds ratio
RCT = randomised controlled trial
SABA = short-acting β-agonist

Welcome to issue 176 of Respiratory Research Review.

The Asthma and Respiratory Foundation New Zealand Adolescent and Adult Asthma Guidelines 2020: a quick reference guide has been published and is available on the Asthma and Respiratory Foundation NZ website, together with downloadable management plans, educational slide sets and the My Asthma App. The evidence base for these guidelines is not new for readers of Respiratory Research Review, as we reviewed them when they became available, for example in Respiratory Research Review issues 169, 163 and 157. It is important to acknowledge the leadership of Richard Beasley and his colleagues at the Research Institute of New Zealand. Much of the key research has been designed, carried out and published by this research group. We can have confidence that these new guidelines are based on the best evidence and are relevant for our unique challenges in Aotearoa. These guidelines are based on the GINA 2020 guidelines, which provide more in-depth explanations and an ample evidence base, and have been accompanied by many editorials, viewpoints and invited reviews. The most comprehensive and recent ones are probably from Christine Jenkins, Eric Bateman, Malcolm Sears and Paul O'Byrne, 'What we have learnt about asthma control from trials of budesonide/formoterol as maintenance and reliever?' (Respirology 2020), and from Richard Beasley and colleagues on the 'ICS-formoterol reliever therapy stepwise treatment algorithm for adult asthma' (Eur Respir J 2020).

Systemic OCSs became available in the 1950s and ICSs became available in the 1970s. Over the last decade, the use of OCSs has increased and despite their considerable side effects, respiratory disease is the most frequently recorded indication for OCSs, accounting for ~40% of all prescriptions. It is rather timely that the American Thoracic Society has published a state-of-the-art review on the '…systemic corticosteroid use for asthma management'. This state-of-the-art document is a systematic literature review, which is a little harder to read than the narrative review from our colleagues in Australia on 'Rational oral corticosteroid use in adults with severe asthma'. This second article is full of clinical wisdom and addresses patients' perspectives.

The new asthma guidelines allude to it; however, both The Lancet and Thorax reviewed the immunomodulation function of macrolides in detail last month. The Lancet provides an excellent overview of the role of 'Immunomodulation by macrolides: therapeutic potential for critical care' in illnesses like pneumonia, sepsis, and acute respiratory distress syndrome. It provides an excellent summary of the evidence and includes great figures explaining the possible mechanism of action. Thorax has published the 'British Thoracic Society guidelines for the use of long-term macrolides in adults with respiratory disease'. Here they review the clinical role of macrolides in the management of asthma, bronchiectasis, chronic obstructive pulmonary disease and bronchiolitis obliterans (including after lung transplantation). David Smith writes the editorial '…not quite a panacea', and reminds us of the side effects like resistance, gastrointestinal, ototoxicity and cardiac disease, and that any prescription like this is currently 'off-label'.

The last revolution in asthma care in NZ is the introduction of biological agents like omalizumab, mepolizumab, reslizumab, benralizumab and dupilumab. Our colleague Angela Moran together with Ian Pavord has summarised dupilumab, 'Anti-IL4/IL-13 for the treatment of asthma: the story so far'. The European Respiratory Society/American Thoracic Society have summarised much of the evidence in their guidelines on the management of severe asthma. Both make excellent reading, as we are becoming more familiar with the use of biological agents.

Finally, three short articles for further reading, which you may enjoy discussing. First, it is almost forgotten after COVID-19 changed the world; however, Respirology has published an invited review on the 'Health impacts of bushfire smoke exposure in Australia'. Second, hopefully we do not need this information; however, the BMJ has published a 10-minute consultation on 'assessment and management of adults with asthma during the covid-19 pandemic'. Third, and because I get asked this question from time to time, a slightly older paper on the 'combination of budesonide/formoterol on demand improves asthma control by reducing exercise-induced bronchoconstriction'.

We hope you enjoy the selection and look forward to comments/feedback.

Kind regards,

Professor Lutz Beckert
lutzbeckert@researchreview.co.nz

Six-year follow-up of a trial of antenatal vitamin D for asthma reduction

Authors: Litonjua AA et al.

Summary: These researchers reported outcomes for children at 6 years of age who had been born to women who received prenatal vitamin D in a trial that suggested that vitamin D 4400 IU/day provided better protection against the development of asthma and wheeze among offspring out to 3 years of age than vitamin D 400 IU/day. When maternal 25-hydroxyvitamin D levels were taken into account, there was no significant effect of prenatal vitamin D3 4400 vs. 400 IU/day on the incidence of asthma and recurrent wheeze, most secondary outcomes or spirometric indices among the offspring at age 6 years. Prenatal vitamin D supplementation did have a very small effect of uncertain significance on airway resistance.

Comment: The vitamin D antenatal asthma reduction trial is part of the goal of finding a way to prevent asthma. Vitamin D deficiency is correlated with the development of asthma and allergies, with supplementation potentially reducing wheeziness in children less than 3 years old. These are the 6-year data of about 800 pregnant women with asthma, atopy or allergic rhinitis, who were randomised to receive 4400 or 400 IU/day of vitamin D3 during pregnancy. At age 6 years, maternal vitamin D supplementation did not prevent the development of asthma or recurrent wheeze. **Bottom line: maternal vitamin D supplementation is not effective in the prevention of school-age asthma.**

Reference: N Engl J Med 2020;382:525–33
Abstract

Independent commentary by Professor Lutz Beckert

Professor Lutz Beckert is the Associate Dean Medical Education with the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board with particular clinical interests in interstitial lung disease, pulmonary vascular disease, respiratory physiology and COPD (chronic obstructive pulmonary disease). Lutz is happy to be contacted to discuss research ideas either as a sounding board or with the view of future collaborations.

Lung function and asthma control in school-age children managed in UK primary care

Authors: Lo DKH et al.

Summary: Abnormal spirometry and FeNO values were reported for a cohort of 612 children aged 5–16 years with asthma managed in primary care. Abnormal spirometry was evident in 23.5% of the children, 36% had FeNO values ≥35 parts per billion and 41.8% reported poor control. Abnormal spirometry and/or raised FeNO values were reported for 54% of the children with good asthma control. There was a significant decline in the mean number of unplanned healthcare attendances from 0.31 per child during the 6 months prior to review to 0.20 per child during the 6 months following review (p=0.0004), with corresponding increases in median ACT score from 20 to 22 (p=0.032) and children's ACT score from 21 to 23 (p<0.0001).

Comment: In the USA, about 200,000 people are admitted with asthma each year; 40% of these are children. The UK has a higher asthma mortality rate than other European countries. These authors identified about 600 children from ten general practices in the East Midlands and then performed spirometry, FeNO measurements and symptoms-based assessments. About a quarter of children had abnormal spirometry and about a third had raised FeNO values. The relationship to symptoms scores was weak. **Bottom line: half of the children reporting good asthma control had at least one abnormal objective measurement of asthma. This endorses the role of spirometry/ FeNO in asthma management**.

Reference: Thorax 2020;75:101–7
Abstract

For more information, please go to www.medsafe.govt.nz

Urbanisation and asthma in low-income and middle-income countries

Authors: Rodriguez A et al

Summary: This was a systematic review of 63 articles reporting differences in asthma prevalences between urban and rural areas, five comparing differences between cities and two examining intraurban variability. The prevalence of asthma was greatest in urban areas, irrespective of the asthma definition used (respective ORs for current wheeze, doctor diagnosis, ever wheeze, self-report, asthma questionnaire and exercise challenge, 1.46 [95% CI 1.22, 1.74], 1.89 [1.47, 2.41], 1.44 [1.15, 1.81], 1.77 [1.33, 2.35], 1.52 [1.06, 2.16] and 1.96 [1.32, 2.91]).

Comment: The prevalence of asthma has been increasing and so has urbanisation. According to the accompanying editorial by William Checkley, the number of people living in urban areas increased from 750 million in 1950 to 4.2 billion in 2018. Much of this increase has been in low- and middle-income countries, which has contributed to the increase in asthma prevalence, whereas in high-income countries, the asthma prevalence has reached a plateau. One take-home message from this review is that neither 'rural', 'urban' nor asthma are well defined. **Bottom line: urbanisation may cause asthma through a change in diet, reduction in infections, smaller families, less activity, passive smoking, air pollution or increased antibiotic use.**

Reference: Thorax 2019;74:1020–30
Abstract

For more information, please go to www.medsafe.govt.nz

Effect of asthma exacerbation during pregnancy in women with asthma

Authors: Abdullah K et al.

Summary: Short- and long-term intergenerational effects of asthma exacerbations during pregnancy were examined in a population-based cohort of 103,424 singleton pregnancies in women with asthma from Canada. Women who had asthma exacerbations while pregnant were more likely to experience pre-eclampsia (OR 1.30 [95% CI 1.12, 1.51]) and pregnancy-induced hypertension (1.17 [1.02, 1.33]), and their babies were more likely to have a low birthweight (1.14 [1.00, 1.31]), be born preterm (1.14 [1.01, 1.29]), have congenital malformations (1.21 [1.05, 1.39]) and develop asthma (1.23 [1.13, 1.33]) or pneumonia (1.12 [1.03, 1.22]) during their first 5 years of life.

Comment: Asthma is one of the most common chronic diseases encountered during pregnancy. Many women stop taking their asthma medications out of concerns regarding the safety of medications during pregnancy. These authors from Canada followed more than 100,000 women with asthma throughout their pregnancy. Asthma exacerbation was found in almost 5000 pregnancies. An asthma exacerbation during pregnancy increased the mother's risk of pre-eclampsia and hypertension, and it increased the baby's risk of low birthweight, preterm birth or congenital malformation. **Bottom line: improving asthma management during pregnancy may reduce pregnancy complications and improve the newborn's health.**

Reference: Eur Respir J 2020;55:1901335
Abstract

Early-life antibiotic use and risk of asthma and eczema

Authors: Slob EMA et al.

Summary: This discordant twin study explored the relationship between antibiotic use during ages 0–2 years and the development of atopic diseases during ages 3–12 years in a retrospective cohort of twins aged 3–10 years from the Netherlands Twin Register (n=35,365) and a replication cohort of twins aged 9 years from the Swedish Childhood and Adolescent Twin Study (n=7916). Unmatched analyses revealed that for both the Dutch and Swedish cohorts, early-life antibiotic use was associated with heightened risks of asthma (respective ORs 1.34 [95% CI 1.28, 1.41] and 1.45 [1.34, 1.56]) and eczema (1.08 [1.03, 1.13] and 1.07 [1.01, 1.14]); co-twin analyses of monozygotic and dizygotic twin pairs returned similar results for asthma (1.54 [1.20, 1.98] and 2.00 [1.28, 3.13]), but opposing results between the two cohorts for eczema (0.99 [0.80, 1.25] and 1.67 [1.12, 2.49]). In the Swedish cohort, antibiotics prescribed for respiratory infections were associated with an increased risk of asthma (OR 1.45 [95% CI 1.34, 1.56]), but antibiotics commonly used for urinary tract/skin infections were not (1.02 [0.88, 1.17]).

Comment: This study sheds more light on the debate between early-life antibiotic use and asthma/eczema. Early-life antibiotics are prescribed to 26–60% of all children. The relationship could be related to an unmeasured confounder, mistreatment of wheeziness with antibiotics, or causal through disturbance of the microbiome. Investigating more than 35,000 individual twins by comparing them with a general population, the dizygotic co-twin and the monozygotic twin, the authors found a strong correlation between antibiotic use and increased risk of asthma. **Bottom line: doctors should take care to prescribe antibiotics for bacterial infections only.**

Reference: Eur Respir J 2020;55:1902021
Abstract

Each month we highlight a particularly excellent paper with our butterfly symbol.

Overuse of short-acting β_2-agonists in asthma is associated with increased risk of exacerbation and mortality

Authors: Nwaru BI et al.

Summary: These authors reported a cohort study of the global SABINA (SABA use in asthma) programme in 365,324 Swedish registry patients aged 12–45 years with asthma who had collected ≥2 drugs for obstructive lung disease during the 2006–2014 period. SABA overuse (>2 canisters collected over 1 year) was seen for 30% of the patients, with 21%, 7% and 2% collecting 3–5, 6–10 and ≥11 canisters per year, respectively. Compared with collecting ≤2 SABA canisters per year, collecting 3–5, 6–10 and ≥11 canisters increased the risks of asthma exacerbations (respective hazard ratios 1.26 [95% CI 1.24, 1.28], 1.44 [1.41, 1.46] and 1.77 [1.72, 1.83]) and mortality (1.26 [1.14, 1.39], 1.67 [1.49, 1.87] and 2.35 [2.02, 2.72]).

Comment: If asthma is well controlled, one would need to use a SABA no more than twice a week or two canisters per year. The authors defined >2 canisters per year as increased SABA use in their population of more than 350,000 asthmatics. They found increased overall mortality of 25% in the cohort using 3–5 canisters per year, and a 31-fold increase of respiratory mortality in the cohort using ≥11 canisters per year. The accompanying editorial paying attention to our NZ experience gives us the **bottom line: pharmacist, patients and primary care providers should all work towards safe management options with reduced SABA use.**

Reference: Eur Respir J 2020;55:1901872
Abstract

Patient preferences for symptom-driven or regular preventer treatment in mild to moderate asthma

Authors: Baggott C et al., on behalf of the PRACTICAL study team

Summary: These researchers surveyed a subgroup of PRACTICAL trial participants who had been randomised to symptom-driven budesonide-formoterol or maintenance budesonide plus as-needed terbutaline. The survey focussed on treatment preferences, satisfaction, beliefs and experiences at the participants' final study visits; 306 out of 407 eligible participants completed the survey. The respective proportions of participants randomised to the as-needed budesonide-formoterol and maintenance budesonide arms who expressed a preference for combination preventer and reliever as-needed were 90% and 40%, and the respective proportions who indicated they preferred the twice-daily preventer inhaler with a reliever inhaler as-required were 10% and 60%. High satisfaction was reported for all study inhalers. In the as-needed budesonide-formoterol arm, 92% reported confidence in using it as a reliever inhaler at the end of the study.

Comment: We highlighted the NZ PRACTICAL study in Respiratory Research Review issue 169. This paper reports on the more than 300 participants who were asked about their preference of using separate maintenance steroids plus as-needed SABAs or symptom-driven combined therapy with budesonide-formoterol. Most patients preferred the regimen they had been randomised to; however, more people in the regular ICS group preferred combined prevention and reliever as-needed. **Bottom line: more than 90% of patients were confident using a combination inhaler regimen. Patients are likely to prefer the combination inhaler regimen if they were given the experience**.

Reference: Eur Respir J 2020;55:1902073
Abstract

Predictive value of blood eosinophils and exhaled nitric oxide in adults with mild asthma

Authors: Pavord ID et al., on behalf of the Novel START Study Team

Summary: Associations of blood eosinophil count and FeNO with outcome and response to asthma treatment were reported for participants of a 52-week, open-label trial that randomised individuals with mild asthma receiving only β-agonist reliever inhalers in a 1:1:1 ratio to receive two salbutamol 100µg inhalations as needed, maintenance inhaled budesonide 200µg twice per day plus two salbutamol 100µg inhalations as needed, or one inhalation of budesonide-formoterol 200µg/6µg as needed; 656 participants had evaluable blood eosinophil count data and 668 had evaluable FeNO measurements. The proportion of the as-needed salbutamol recipients who experienced severe exacerbations increased as blood eosinophil count increased (4%, 6% and 19% for <0.15, 0.15–<0.3 and ≥0.3×10^9/L, respectively [p=0.014]). No significant interaction was detected between blood eosinophil count or FeNO value and the effect of as-needed budesonide-formoterol versus as-needed salbutamol for exacerbations, including severe exacerbations. However, significant interactions were seen between blood eosinophil count subgroups and the effect of maintenance budesonide plus as-needed salbutamol versus as-needed salbutamol for both any exacerbations (p=0.0006) and severe exacerbations (p=0.0007). Maintenance budesonide plus as-needed salbutamol recipients with blood eosinophil counts ≥0.3×10^9/L had fewer exacerbations and severe exacerbations than their counterparts who received as-needed salbutamol (respective rate ratios 0.13 [95% CI 0.05, 0.33] and 0.11 [0.03, 0.45]); there was no significant difference for those with blood eosinophil counts <0.15×10^9/L. No consistent interaction was detected between treatment response and FeNO or the composite score based on blood eosinophil count and FeNO.

Comment: This is a slightly technical study based on the NZ-led Novel Start data exploring the role of blood eosinophilia and FeNO to predict the rate of asthma exacerbations. Patients with an eosinophil count >0.15×10^9/L were almost three times as likely to have an asthma exacerbation independent of baseline ACQ or FEV_1. Blood eosinophilia is an important component of risk assessment across the spectrum of obstructive lung diseases; FeNO didn't improve the predictive outcome. **Bottom line: the effectiveness of preventing asthma exacerbations with regular budesonide increases in parallel to the eosinophil count. As-needed budesonide-formoterol prevented exacerbations independently of a biomarker.**

Reference: Lancet Respir Med 2020;8:671–80
Abstract

Oral corticosteroid prescription patterns for asthma in France, Germany, Italy and the UK

Authors: Tran TN et al.

Summary: These researchers analysed the electronic medical records of 702,685 patients aged ≥12 years from France, Germany, Italy or the UK who had been diagnosed with asthma, and had received ≥1 non-OCS asthma medication within 6 months of diagnosis, to investigate real-world OCS use patterns in asthma management. OCS use was recorded for 14–44% of the patients, with 6–9% using ≥450mg prescribed within a 90-day window (high OCS users) at some point during follow-up. The annual prevalence of high OCS use was ~3% across the included countries. High OCS users had received a mean of 1–3 OCS prescriptions annually and an average OCS dosage of 1.3–2.2 mg/day. Among individuals who continued high OCS use, exposure remained stable at 5.5–7.5 mg/day over ≥2 years, with an associated increase in the risk of adverse effects.

Comment: Asthma exacerbations are commonly treated with OCSs, which increase the risk of adverse effects. In this study of more than 700,000 patients with asthma from several European countries, the authors defined more than 450mg prednisone every 3 months, or more than 5mg every day, as a high OCS dose. Overall, up to 44% of patients with asthma needed an OCS course and 6–9% were high OCS users. As summarised in the 'Rational oral corticosteroid use in adults with severe asthma' document, we have better strategies available. **Bottom line: the high steroid prescribing suggests suboptimal asthma management in all countries studied.**

Reference: Eur Respir J 2020;55:1902363
Abstract

Oral steroid-sparing effect of high-dose inhaled corticosteroids in asthma

Authors: Maijers I et al.

Summary: This was a systematic review and meta-analysis of 11 RCTs (n=1283) reporting the OCS-sparing effects of high-dose ICSs in patients with OCS-dependent asthma. There was a 2.1–4.9mg decrease in prednisone dose for every 1000µg increase in ICS dose, which varied according to ICS type. The respective ratios for the prednisone-sparing effect due to the systemic effects of every 1000µg of fluticasone propionate and budesonide were 1.02 (95% CI 0.68, 2.08) and 0.93 (0.63, 1.89).

Comment: ICSs are the cornerstone of asthma management, however, their dose-response curve is flat with 80–90% of the effect being achieved with daily doses of 100–200µg of fluticasone propionate, and a maximal effect can be achieved with 500µg of fluticasone propionate. Higher doses of ICSs are frequently prescribed. The ICS is absorbed via the lungs and has systemic effects like adrenal suppression. These Wellington-based researchers performed a systematic literature review estimating the dose equivalent effects of ICSs to oral prednisone. **Bottom line: >60% of the effect of high-dose ICSs is due to systemic absorption.**

Reference: Eur Respir J 2020;55:1901147
Abstract

Mepolizumab effectiveness and identification of super-responders in severe asthma

Authors: Harvey ES et al.

Summary: Findings from the Australian Mepolizumab Registry were reported for 309 patients with severe eosinophilic asthma treated with mepolizumab. The registrants had poor symptom control (median ACQ-5 score 3.4) and frequent exacerbations with a median three courses of OCSs in the prior 12 months and 47% requiring OCSs daily. Their median baseline peripheral blood eosinophil count was 590 cells/µL and comorbidities were common. When compared with the year prior to mepolizumab treatment, there were reductions in exacerbations requiring OCS treatment (annualised rate ratio 0.34 [95% CI 0.29, 0.41]) and hospitalisations (0.46 [0.33, 0.63]), a decline in median ACQ-5 score of 2.0 points at 6 months and improvements in quality of life and lung function after starting the agent. Factors significantly associated with a better ACQ-5 response to mepolizumab were a higher blood eosinophil count and later age of asthma onset, whereas factors significantly associated with a poorer response were male sex and body mass index ≥30 kg/m^2. 'Super-responders' (upper 25% of ACQ-5 responders) had a greater T2 disease burden and fewer comorbidities at baseline.

Comment: Just as NZ went into lockdown, the humanised IgG anti-IL5 monoclonal antibody mepolizumab was funded for severe eosinophilic asthma not responding to standard therapy. This article from our colleagues in Australia reports on just over 300 cases from the Australian Mepolizumab Registry. Overall, mepolizumab was very well tolerated and 86% responded to the treatment, which is higher than in the RCT, probably because the funder stipulated a higher eosinophil count. Women with a short disease history, few comorbidities and greater eosinophilia were super-responders. **Bottom line: mepolizumab was effective in treating patients with severe uncontrolled eosinophilic asthma.**

Reference: Eur Respir J 2020;55:1902420
Abstract

Effect of fixed-dose subcutaneous reslizumab on asthma exacerbations in patients with severe uncontrolled asthma and corticosteroid sparing in patients with oral corticosteroid-dependent asthma

Authors: Bernstein JA et al.

Summary: The results of two phase 3 RCTs of subcutaneous reslizumab 110mg (n=324) versus placebo (n=321) once every 4 weeks for 52 weeks (study 1) or 24 weeks (study 2) in patients with severe asthma were reported. Study 1 found no significant difference between reslizumab and placebo recipients for the exacerbation rate in an intent-to-treat analysis (rate ratio 0.79 [95% CI 0.56, 1.12]), but there was a lower exacerbation rate among reslizumab recipients in participants with blood eosinophil counts ≥400 cells/μL (0.64 [0.43, 0.95]). Participants with higher trough serum reslizumab concentrations had a significantly greater reduction in annual exacerbation risk and a significantly longer time to first exacerbation. In study 2, there was no significant difference between reslizumab and placebo recipients for reductions in daily OCS dose (p=0.47). Adverse event and serious adverse event rates were similar between reslizumab and placebo recipients in both studies.

Comment: The accompanying editorial by Richard Beasley, James Harper and Matthew Masoli assists in interpreting this negative study. Reslizumab did not reduce the exacerbations in asthmatic patients with an eosinophil count of more than 300 cells/μL; however, it worked in the subgroup with more than 400 eosinophils/μL. Reslizumab halved the need for oral steroids in about a third of the patients; however, this was no different to the placebo group. This is a stark reminder of the psychological needs and treatable traits of patients with asthma. **Bottom line: fixed-dose reslizumab in the chosen trial setting was not effective to reduce exacerbations or steroid use.**

Reference: Lancet Respir Med 2020;8:461–74
Abstract

Adherence to inhaled corticosteroids and clinical outcomes in mepolizumab therapy for severe asthma

Authors: d'Ancona G et al.

Summary: ICS adherence and clinical outcomes were reported for 91 patients with OCS-dependent severe eosinophilic asthma who received 1 year of treatment with mepolizumab. ICS adherence was good (MPR >0.75) for 68% of the patients and poor (MPR <0.5) for 18% during mepolizumab treatment, with little change seen in ICS MPR before and during mepolizumab treatment (0.81 and 0.82, respectively [p=0.78]). Compared with patients with poor adherence, those with good adherence had greater reductions in median OCS dose (100% vs. 60% [p=0.031]) and annualised exacerbation rate change (–2.1 vs. 0.3 [p=0.011]). Good ICS adherence was a predictor of stopping maintenance OCS treatment (adjusted OR 3.19 [95% CI 1.02, 9.94]).

Comment: Adherence to ICS therapy is always challenging. Researchers from London describe their experience with 100 patients on mepolizumab for whom they had data on ICS use 1 year before and after mepolizumab therapy. Nonadherence to ICS therapy and ongoing smoking were the strongest predictors of suboptimal adherence to ICS after mepolizumab treatment. The 32% of patients with suboptimal ICS adherence had a lesser reduction in OCS requirement and a lesser reduction of asthma exacerbations. **Bottom line: patients on mepolizumab should continue ICSs to achieve less airway eosinophilia, a reduction of OCS use and a reduction of asthma exacerbations.**

Reference: Eur Respir J 2020;55:1902259
Abstract

Is computed tomography airway count related to asthma severity and airway structure and function?

Authors: Eddy RL et al.

Summary: These researchers measured total airway count using CT in 70 patients with asthma, and evaluated its relationships with asthma severity, airway morphology, pulmonary function and MRI ventilation. Compared with GINA steps 1–3 patients, GINA-4 and GINA-5 patients had significantly lower total airway counts. Two GINA-4 and three GINA-5 patients had terminal airway intraluminal occlusion. All but one patient had invisible or missing sub-subsegmental airways on CT. The most common number of missing sub-subsegments was 10, and patients with more missing subsegments had a significantly lower airway wall area percentage, lumen area and ventilation defect percentage. Total airway count was a significant independent predictor of FEV_1 (R^2=0.27 [p=0.003]), and total airway count was a significant independent predictor of airway wall area percentage (R^2=0.32 [p=0.0001]).

Comment: Asthma is an illness of the airways with the hallmarks of smooth muscle abnormalities, inflammation and mucus hypersecretion, which affect the whole tracheobronchial tree from large to small airways. The small airways remain difficult to investigate, and this group from Ontario used CT scanning and MRI scanning with hyperpolarised ^{3}He to estimate the total airway count and missing subsegments in 70 patients with severe asthma. MRI ventilation heterogeneity is uniquely explained by asthma control and can predict the transition of asthma to fixed obstruction. **Bottom line: a truncated tracheobronchial tree and a reduction in the number of terminal airways correlate with severe asthma.**

Reference: Am J Respir Crit Care Med 2020;201:923–33
Abstract

CLICK HERE to read previous issues of Respiratory Research Review

New Zealand Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our **CPD page**.

This Research Review has been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and has been approved for up to 1 CME credit for the General Practice Educational Programme (GPEP) and Continuing Professional Development (CPD) purposes. You can record your CME credits in your **RNZCGP Dashboard**

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please **CLICK HERE**.