

Clinical Preview

Identification of remission in adult-onset asthma



Our understanding of the clinical and underlying inflammatory features of adult-onset asthma is relatively poor compared with that of childhood-onset atopic asthma. Previous cross-sectional studies suggest that adult-onset asthma is more likely to be severe, less responsive to inhaled corticosteroids, and present with a greater decline in lung function than childhood-onset asthma. Additionally, less is known about the clinical predictors of persistence or remission of adult-onset asthma than child-onset asthma. Two prospective studies have been previously reported but did not have sufficient patient numbers to assess the predictors of remission by multivariable analysis. A better comprehension of this asthma phenotype is needed, not only to educate patients about their disease, but also to identify potential modifiable risk factors that could alter disease persistence or induce remission. Understanding of these risk factors (clinical and inflammatory) of adult-onset asthma also provides insights into the underlying pathology of this understudied group of patients.

In the January issue of *The Journal of Allergy and Clinical Immunology*, Guus A Westerhof and colleagues reported a subgroup analysis (examining predictors of asthma persistence vs remission) from their prospective Adult-Onset Asthma and Inflammatory Subphenotypes (ADONIS) study. Adult-onset asthma was defined as onset at older than 18 years of age, based on symptoms, and a reversible FEV₁ greater than 12% of predicted value or a positive methacholine challenge test (PC₂₀ <8 mg/mL), or both. Patients were excluded if they had reported any history of asthma, chronic respiratory diseases, frequent episodes of dyspnoea, or use of bronchodilators or other asthma medications during their childhood. Patients with an existing and ex-smoking history were included but those who smoked more than ten packs of cigarettes per year were included only if they had airway reversibility with a normal diffusion capacity. Asthma remission was defined as an absence of asthma symptoms or medication use for 1 year or more. At baseline evaluation, medical history and questionnaires to assess asthma quality of life, asthma control, and Sino-Nasal Outcome Test 22 were done, lung function was tested, upper airway was assessed for presence of nasal polyps (nasal endoscopy or sinus CT), and inflammatory markers (fractional exhaled nitric oxide, complete blood cell count, IgE, and sputum induction) were collected. This study reports the outcome of 170 patients (85% of initial cohort) who were available after a 5-year follow-up. In these patients, follow-up data was collected at the study site (64%), by phone (16%), or by the primary asthma provider (21%). Clinical remission of asthma occurred in about 16% of the patients after a median duration of 45 months. Baseline risk factors associated with asthma persistence (vs remission)

included nasal polyps (about 25% of patients), more severe bronchial hyper-responsiveness, older onset (50 [SD 14] years vs 44 [15] years), lower asthma control, requirement for higher inhaled corticosteroid doses, and higher blood neutrophils. Smoking history, atopy, body-mass index, or sex did not predict future clinical remission when patients were examined as a group overall. However, when stratified into groups of patients with and without nasal polyps, female sex and obesity were predictors of asthma persistence in those without nasal polyps. Baseline sputum inflammatory cell differentials (ie, neutrophilic or eosinophilic) and fractional exhaled nitric oxide inflammatory markers did not predict future remission. However, patients with persistent asthma at 5 years were significantly more likely to have developed increased sputum neutrophils (compared with baseline), compared with patients whose asthma remitted.

Westerhof and colleagues' study suggests a slightly higher remission rate of adult-onset asthma (ie, 3.2% per year) than suggested in other studies, which have reported rates of 0.6–3% per year. Potential reasons for this difference, addressed by the authors, include alternative definitions of asthma and asthma remission, and absence of exclusion of patients with childhood-onset asthma. The study is important because it provides prospective data on a group of understudied patients (ie, patients with adult-onset asthma) and shows that the asthma of some individuals might remit. A key message is that two factors, nasal polyposis and increased bronchial hyper-responsiveness at baseline, were identified to predict asthma persistence. Previous studies have shown an important link between the upper and lower airways; however, this study is the first to report the importance of nasal polyposis in persistence of adult-onset asthma. In this cohort, early surgical treatment of nasal polyps did not appear to prevent asthma development, suggesting that this risk

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factor might not be modifiable. Whether the nasal polyposis is part of the same underlying pathophysiology as the airway is not clear, but seems probable. Similar to childhood asthma, in which asthma persistence is more likely to be associated with increased bronchial hyper-responsiveness, the association between asthma persistence and bronchial hyper-responsiveness was significant; however, in this study it was six times weaker than that for nasal polyposis. Expectedly, the atopic sensitisation in childhood-onset asthma appears to have a more important role in asthma persistence than in this study of adult-onset asthma.

The results of this study have important clinical implications. This study highlights the importance of addressing the upper airways in patients with asthma, in particular those with late-onset disease. Patients should at minimum be questioned about upper airway symptoms and considered for nasal endoscopy. Patients with identified polyps can then receive closer follow-up of adult-onset asthma. In this study, all patients who have nasal polyposis showed asthma persistence. Airway hyper-responsiveness testing should also be considered for prognostic reasons.

Furthermore, more than 70% of patients with persistent asthma and nasal polyps were smokers and ex-smokers, suggesting yet another reason for smoking cessation.

This study is also important because it identifies an important phenotype that should be studied further. By doing more mechanistic studies in this population, we can learn more about underlying disease mechanisms and potentially offer new treatments for patients whose asthma fails to remit. We might even be able to induce remission in a greater proportion of our patients.

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Film Out of Breath



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Out of Breath

Hein Seok

South Korea, 2018, 63 min
<https://www.journeyman.tv/film/7289/out-of-breath>

North Koreans know the period from 1994 to 1998 as the arduous march. It was one of the most devastating famines in history. Some estimates put the death toll at 3 million, out of a total population of 23 million. Horrific tales of deprivation emerged from the country: entire families subsisting on tree bark and rice roots. And as malnutrition took hold, so did a tuberculosis epidemic that required a response beyond the capacity of the struggling socialist republic.

Food shortages are still a fact of life in North Korea, leaving the enervated population susceptible to disease. In 2016, the nation reported around 120 000 cases of tuberculosis. Notifications for multidrug-resistant tuberculosis hover at around 4600 cases per year, although it would not come as a surprise if the actual burden was nearer 10 000. The Global Fund to Fight AIDS, Tuberculosis and Malaria recently announced its intention to withdraw from North Korea. The national tuberculosis programme is heavily reliant on the fund. The decision has raised fears that the country will see sharp rises in multidrug-resistant tuberculosis.

Meanwhile, western foreign policy focuses exclusively on persuading North Korea to give up its nuclear programme. A wide range of tough economic sanctions have been applied and tightened. The US administration is determined to exert as much pressure as possible on the North Korean regime. The well-padded Supreme Leader

Kim Jong-un inherited the dictatorship from Kim Jong-il (1941–2011), whose catastrophic policies were responsible for the 1990s' famine. He shares his father's distrust for outsiders and obsession with nuclear weaponry.

All of this means that foreign aid agencies and non-governmental organisations are absent from North Korea. But there is one notable exception. For the past decade or so, the Eugene Bell Foundation has been providing treatment for multidrug-resistant tuberculosis. The US–South Korean partnership operates a dozen centres in North Korea, treating around 1000 patients every year. Cure rates exceed 70%, compared with a global average of roughly 50%. *Out of Breath*, which is scheduled to screen on UK and Australian television later this year, outlines the foundation's activities.

It is a fascinating insight into the intricacies of operating in the mysterious and misunderstood nation. "I would not do this project. I would not have done this project, and if I was asked to do this project now, I would refuse. It is impossible", opines KJ Seung, medical director at Eugene Bell. And yet they manage. Despite the difficulties associated with raising funds for a state widely considered to be an international pariah. Despite the interminable journey from South Korea to Pyongyang, which necessitates travelling via China. Despite the sanctions and export strictures: at one point, the team in South Korea have to remove an X-ray machine from