

Personalised medicine for asthma management in pregnancy

In *The Lancet*, Heather Powell and colleagues report the use of exhaled nitric oxide as an inflammometer to adjust asthma drugs in the management of asthma.¹ Exhaled nitric oxide can be regarded as a biomarker, and its use in asthma management is a step in the direction of personalised medicine. Personalised medicine is designed to get the right drug to the right person, at the right time.² The approach to management of asthma is in some ways already personalised since the physician chooses the drug, selects the dose, and identifies an appropriate delivery device for the drug on the basis of the patient's age and ability to cooperate with the technique. Additionally, national and global guidelines are available to assist physicians in adjustment of therapy on the basis of severity and disease control. Some potential patient characteristics and biomarkers could be used to select and adjust therapy; however, the role of genetics in this process has not been defined.³

A previous study by Green and colleagues⁴ showed that adjustment of inhaled corticosteroid dose on the basis of level of sputum eosinophils contributed to a reduction of asthma exacerbations by 50%. Several attempts have been made to substitute measures of exhaled nitric oxide for measurements of sputum eosinophils. So far, studies using exhaled nitric oxide have produced mixed results in reduction of asthma exacerbations.^{5,6} However, Gibson⁷ identified several weaknesses in the study designs and developed an improved algorithm for the application of exhaled nitric oxide measurements to adjust therapy in pregnancy.

Guidelines for management of asthma during pregnancy⁸ apply the step-care process of drug adjustment, as used in standard guidelines for management of all patients with asthma. The study by Powell and colleagues¹ compared the conventional method of asthma management to therapy based on adjustment of exhaled nitric oxide, in a trial that randomly assigned 220 pregnant women with asthma. The investigators reported that asthma exacerbations during pregnancy can be significantly reduced by the use of a validated treatment algorithm based on measurement of exhaled nitric oxide. First, the investigators should be complimented for undertaking a study during pregnancy for which there is very little

information available on direct outcome measures for intervention strategies. Second, the investigators deserve credit for carefully assessing the previous studies using exhaled nitric oxide and applying lessons learned to adjust the algorithms for application of exhaled nitric oxide measures in treatment decisions.

The algorithm designed for the accompanying study has two components. First, inhaled corticosteroid dose is adjusted on the basis of a measure of exhaled nitric oxide. Second, the use of supplementary therapy, longacting β -adrenergic agonist, is based on an assessment of symptoms, measured with the asthma control questionnaire.⁹ The key finding in Powell and colleagues' study is that application of the algorithm to adjust therapy resulted in an increased use of inhaled corticosteroids (68.5% of women vs 42.2%), a lower average inhaled corticosteroid dose (not statistically significant), and an increased use of longacting β -adrenergic agonist (40.5% vs 17.4%) during pregnancy compared with the conventional treatment approach. Some, but not all, experts in the specialty are concerned about the safety of longacting β -adrenergic agonist for the treatment of asthma.¹⁰ This approach resulted in benefits for the mother and the child. Specifically, the algorithm resulted in reduced exacerbations (a combination of moderate and severe) (incidence rate ratio 0.496, 95% CI 0.325–0.755, $p=0.001$), improved quality of life for the mother, and reduced neonatal admissions for the infant.

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These findings are remarkable and need a careful assessment of benefits and limitations for application to clinical practice. During pregnancy, the primary clinician for medical management is the obstetrician. Although these physicians are skilled in medical management of pregnancy, they are not as familiar with and do not regularly apply monitoring techniques such as spirometry and exhaled nitric oxide or standard questionnaires for management of asthma. Therefore, to extrapolate the benefits of this report to the clinical setting, obstetricians and primary care physicians will need to become familiar with these techniques or to communicate with asthma specialists who apply the measures. Neither of these approaches is impossible but will need some adjustments to present management. Some of the limitations recognised by researchers and asthma specialists in application of measurements of exhaled nitric oxide include the training that is necessary to do the technique reliably, assessment of the reliability of measurement, and variability in reimbursement procedures by health-care providers to support the application of exhaled nitric oxide measurements in clinical practice.

The study by Powell and colleagues¹ should prompt a reassessment of the conventional approach to management of asthma in pregnancy and a reassessment of techniques to apply exhaled nitric oxide measurements to clinical practice. The major application of exhaled nitric oxide is its potential use for adjustment of inhaled corticosteroid therapy; however,

previous studies point to its limitation in the adjustment of overall steps in asthma management that include the use of non-steroid drugs.⁶

Stanley J Szeffler

Divisions of Pediatric Clinical Pharmacology and Allergy and Immunology, Department of Pediatrics, National Jewish Health, Denver, CO 80206, USA; and University of Colorado School of Medicine, Denver, CO, USA
szefflers@njhealth.org

I have served as an ad-hoc consultant to Aerocrine, GlaxoSmithKline, Boehringer Ingelheim, Genentech, and Novartis.

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Lifetime risk of COPD: what will the future bring?

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Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality in high-income, low-income, and middle-income countries.^{1,2} Although the dominant risk factor for COPD in most high-income countries is smoking, ageing is also important, along with factors such as occupational exposures, respiratory infections early in life, and a history of asthma.^{2,3}

The risk of development of COPD in population-based cohorts is unclear. In *The Lancet* Andrea Gershon and colleagues⁴ assess the lifetime risk of developing COPD and compare it with that of other chronic diseases such as diabetes mellitus, congestive heart failure, prostate cancer (in men), breast cancer (in women), and asthma.

The investigators analysed 14 years of administrative data from Ontario, Canada, and report that by age 80 years about 25% of women and about 30% of men will be diagnosed with COPD. This result is interesting in its own right; the proportion of smokers who develop COPD was widely thought to be about 15%,^{5,6} although this estimate has been adjusted upwards to nearly 50% for smokers who live long enough.⁷ Gershon and colleagues did not examine cigarette smoking and thus their analysis includes current, former, and never smokers, which makes the magnitude of the lifetime estimate surprising. Additionally, findings from a high-income country such as Canada might differ from those from a low-income or middle-income country where