enhancing the ability of the immune system to detect and remove malignant cells.

We therefore feel that caution is warranted when treating patients with asthma with statins; in some cases these drugs can represent more a poison than a snake oil.

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Authors' reply

Mascitelli and colleagues propose caution in the use of statins for asthma because they might provoke the development of cancer.

At present the relationship between statins and cancer is controversial. In some clinical studies statins might have been responsible for an increased rate of breast cancer[1] or prostate cancer.[2] On the other hand, statins are considered as anticancer drugs.[3] In a large-scale study, patients treated with statins were found to have a lower risk of cancer development.[3] The relationship between Tregs and cancer is also unclear. We agree that Tregs may suppress antitumour immunity. However, deficiency of Treg function might also result in oncogenesis. Furthermore, the immunosuppressive effect of statins is not only exhibited by increasing the number and function of Tregs, although there is a reciprocal developmental pathway for Th17 and Tregs. We did not examine the effect of pravastatin on the induction of Tregs in our experimental model of allergic airway inflammation, so it is not clear whether suppression of interleukin 17 (IL17) by pravastatin results in the development of Tregs.

Taken together, although we admit that careful observation is necessary, we do not think that the treatment of asthma with statins is contraindicated because of a possible risk of cancer.

In the accompanying editorial Rubin insists that statins are not necessary for the treatment of asthma because extremely effective medications are available for asthma and the safety of statins has not been fully confirmed.[4] However, there are still some patients with asthma who are resistant to current medications including systemic corticosteroids. For these patients, novel therapies are still awaited. One of the characteristic features of these patients—particularly those with more severe disease—during exacerbations and with cigarette smoking is a neutrophilic inflammation in the airway.[5] It is well established that IL17 plays an important role in the recruitment of neutrophils into the lung, and treatment with pravastatin decreased IL17 production in our study.[6] Statins might therefore be effective in some types of asthma with neutrophilic inflammation.

In summary, we consider that (1) to confirm the long-term safety of statins, further clinical studies with asthma or other disorders should be conducted; and (2) when the safety is definitely confirmed, statins could be a therapeutic candidate for some patients with severe steroid-resistant asthma.

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Effects of methacholine challenge on alveolar nitric oxide

Exhaled nitric oxide (FE_{NO}) is established as a surrogate of airway inflammation.[1] Based on the two-compartment model of nitric oxide production in the lungs, the contribution of the alveolar compartment to exhaled nitric oxide (CA_{NO}) can be calculated.[2] CA_{NO} is raised in chronic obstructive pulmonary disease and severe asthma, even when treated with inhaled corticosteroid.[2] Forced manoeuvres and bronchial challenge are known to reduce FE_{NO} measurements;[1] however, changes in CA_{NO} after challenge have not been reported.

Forty-eight patients with mild to moderate asthma performed fractionated exhaled nitric oxide before methacholine challenge and again after the methacholine concentration provoking a fall in forced expiratory volume in 1 s (FEV_1) of 20% or more (PC_{20}) or 8 mg/ml had been reached. Participants had a physician diagnosis of persistent asthma and were receiving treatment with $\leqslant$1000 μg/day beclometasone or equivalent. Spirometry was performed using a SuperSpiro spirometer (Micro Medical, Chatham, Kent, UK). Exhaled nitric oxide was performed on a NIOX chemiluminescence analyser (Aerocrine AB, Solna, Sweden) at three flow rates (50, 100 and 200 ml). A linear regression equation was applied to derive values for FE_{NO}, CA_{NO} and bronchial flux (J_{NO}).[3] Nitric oxide values were logarithmically transformed to achieve Gaussian distribution prior to analysis.

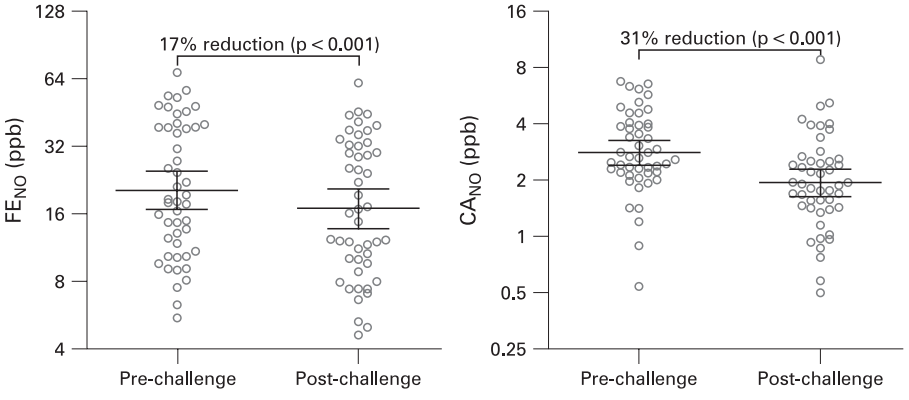

Figure 1 Scatter plots for effect of methacholine challenge on exhaled nitric oxide (FE_{NO}) and the contribution of the alveolar compartment to exhaled nitric oxide (CA_{NO}). Individual data points are shown with geometric means and 95% confidence intervals.

Mean pre- and post-challenge values were analysed with a paired *t* test. Analyses were performed using SPSS version 15.0 (Chicago, Illinois, USA).

The mean age of the patients was 38.5 years. Thirty-eight patients had a methacholine PC_{20} <8 mg/ml. The mean fall in FEV_1 was 21%. Geometric mean pre-challenge FE_{NO} was 20.4 ppb compared with 16.9 ppb post-challenge, a difference of 17% (95% CI 13% to 21%, p<0.001; fig 1). Geometric mean CA_{NO} was 2.9 ppb pre-challenge and 1.9 ppb post-challenge, a difference of 31% (95% CI 17% to 43%, p<0.001). Differences in NO at flow rates of 50, 100 and 200 ml were 15% (95% CI 10% to 19%), 11% (95% CI 6% to 16%) and 17% (95% CI 11% to 22%), respectively (p<0.001). Baseline values for FE_{NO} and CA_{NO} showed no correlation with methacholine PC_{20}, baseline FEV_1 or final percentage fall in FEV_1. The percentage change in CA_{NO} following challenge showed a positive correlation with the baseline value (r = 0.59, p<0.001).

To our knowledge, this is the first study to report the effects of methacholine challenge on CA_{NO}. We have shown that methacholine challenge significantly reduces CA_{NO}, and this effect is relatively more marked than for FE_{NO}. The effect on FE_{NO} is known, and is thought to be due to washout of nitric oxide from the airways. There was a proportionally greater suppression of FE_{NO} at 200 ml (17%) than at 50 ml (15%) and 100 ml (11%). This has a more significant effect on the slope of the regression line and hence the CA_{NO} is relatively more suppressed than FE_{NO}. This is an important consideration for planning and interpreting study visits in clinical trials.

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CORRECTION

doi:10.1136/thx.2008.102970corr1

M-C Breton, M-F Beauchesne, C Lemière, *et al*. Risk of perinatal mortality associated with asthma during pregnancy. *Thorax* 2009;**64**:101–6. The values for parity 1 and parity ≥2 in table 2 were transposed. The correct table is printed below.

Table 2 Crude and adjusted odds ratios (ORs) of perinatal mortality in women with and without asthma for the complete and final model (n = 41 142)

	Crude OR (95% CI)	Adjusted OR for all covariates (95% CI)	Adjusted OR for confounders only (95% CI)
Asthma yes/no	1.35 (1.08 to 1.67)	0.95 (0.74 to 1.22)	0.93 (0.75 to 1.17)
Age			
<18	1.19 (0.73 to 1.91)	0.91 (0.49 to 1.69)	†
18–34	Reference (–)	Reference (–)	
≥35	1.59 (1.16 to 2.18)	1.40 (0.97 to 2.01)	
Social assistance yes/no	1.32 (1.05 to 1.67)	0.80 (0.60 to 1.06)	†
Level of education			
≤11	1.25 (0.98 to 1.59)	0.95 (0.72 to 1.26)	†
≥12	Reference (–)	Reference (–)	–
Missing	4.49 (3.39 to 5.95)	2.44 (1.73 to 3.45)	
Parity			
1	Reference (–)	Reference	†
≥2	1.13 (0.89 to 1.43)	1.12 (0.86 to 1.47)	
PIH yes/no	1.24 (0.82 to 1.89)	0.53 (0.32 to 0.87)	†
Diabetes mellitus yes/no	1.97 (1.07 to 3.60)	1.58 (0.79 to 3.18)	†
Gestational diabetes yes/no	0.80 (0.51 to 1.26)	0.72 (0.43 to 1.21)	†
Placental abruption yes/no	7.33 (5.59 to 9.62)	1.75 (1.28 to 2.40)	†
Infection of amniotic cavity yes/no	3.74 (2.80 to 4.99)	1.92 (1.37 to 2.68)	†
Cord around neck yes/no	0.74 (0.55 to 1.01)	0.86 (0.61 to 1.21)	†
Birth weight ≤2500/>2500 g	34.75 (27.58 to 43.79)	10.55 (7.40 to 15.15)	9.11 (6.61 to 15.55)
Gestational age at birth <37/≥37 weeks	30.62 (24.27 to 38.63)	6.24 (4.37 to 8.90)	7.07 (5.12 to 9.77)

†Not a confounder variable.
PIH, pregnancy-induced hypertension.