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## **Adrenal suppression with inhaled corticosteroids**

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## Adrenal suppression with inhaled corticosteroids : the seed and the soil

To the editor ,

Hawcutt et al report an increased susceptibility for blunting of the ACTH stimulated cortisol response with inhaled corticosteroids (ICS) in relation to the rs511198 polymorphism of the PDGFD gene locus , albeit in association with wide 95% confidence intervals <sup>1</sup> . Pointedly the low dose ACTH stimulation test has been shown to be less sensitive at detecting more subtle degrees of cortisol suppression compared to overnight or early morning urinary cortisol <sup>2</sup> . Their data does not appear to take into account other important factors which regulate cortisol suppression with ICS .

Genetic variation can only explain in part the propensity for adrenal suppression with ICS . Cortisol suppression with ICS can be thought of in terms of the seed and the soil . The seed is the particular drug and fine particle dose delivered to the lung , while the soil is the genetic susceptibility and systemic absorption from the lung .

Reduced airway calibre as FEV1 % predicted will result in lower drug absorption from the lung <sup>3</sup> . Hence patients with more severe airflow obstruction will serendipitously exhibit attenuated lung absorption when exposed to higher doses of ICS <sup>4,5</sup> . In terms of the drug the major pharmacologic factor is the degree of lipophilicity which in turn determines the degree of systemic tissue retention at steady-state , effectively resulting in prolonged drug release from a slow release reservoir . This explains why higher lipophilicity ICS such as fluticasone furoate and fluticasone propionate produce greater dose related adrenal suppression than beclometasone dipropionate or budesonide <sup>6,7</sup> . Lung deposition and fine particle dose will also alter the amount of drug available for absorption . For example inhaled fluticasone propionate via a spacer produces 5.5 fold greater cortisol suppression than a dry powder inhaler <sup>8</sup> . Thus a patient who possess the susceptible homozygous rs511198 genotype with a preserved FEV1 in the presence of prolonged exposure to fluticasone propionate via a spacer will be at high risk for developing adrenal suppression . When considering the risk of adrenal suppression in an individual patient the safest dose of ICS will be achieved by always trying to step down to lowest effective long term maintenance dose .

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