**Position statement of the Society for Endocrinology on the endocrine effects of inhaled corticosteroids in respiratory disease**

The use of inhaled corticosteroids (ICS, a type of steroid) is standard practice to treat bronchoconstriction and other disorders in lung disease, with ~5% of the UK population prescribed these agents (1). Whilst there is no doubting the clinical benefit that ICS can have upon some chronic lung diseases, with the development of newer, highly potent corticosteroids with prolonged half-lives such as fluticasone (e.g. S\_e\_r\_e\_t\_i\_d\_e\_), the absorption of these agents through the lung parenchyma into the circulation can become physiologically significant (2). In response to such absorbed steroids, the patient’s endogenous corticosteroid secretion by the hypothalamic-pituitary-adrenal axis (HPAA) will appropriately down-regulate, such that the overall corticosteroid exposure remains within the physiological range. At higher doses, the total corticosteroid burden may become pathological and the patient can manifest the clinical stigmata of Cushing’s syndrome (3;4). However, even sub-pathological absorption may lead to suppression of the HPAA (5) such that sudden cessation of long-term treatment can lead to adrenal crisis, as can severe trauma, sepsis and surgery (6). In addition, recovery of the HPAA following cessation of exogenous corticosterone therapy can take several years (7). Recent studies have demonstrated that greater dose and duration of treatment increases the risk of HPAA suppression (8;9), but importantly, there is a linear relationship between inhaled steroid dose and suppression of the HPAA, passing through ‘zero’, so no dose is completely without effect (10). Furthermore, HPAA suppression due to ICS may be far more prevalent than is currently appreciated - up to 50% of patients using ICS in some series (5;6;8). In addition, co-administration of common drugs may prolong the availability and augment the systemic effects of ICS (4;11), notably itraconazole and HIV protease inhibitors including ritonavir (e.g. K\_a\_l\_e\_t\_r\_a\_). Despite the potential severity of the clinical problem, it is all too easily overlooked (12), and it is therefore imperative that the community of endocrinologists and respiratory physicians are aware of such possible events. Patients with partial or full suppression of their HPAA will show very low or even undetectable levels of serum and urinary cortisol, but without evidence of Cushing’s syndrome (5). With higher absorbed doses, Cushing’s syndrome becomes obvious, with the apparent paradox of a Cushingoid habitus but suppressed cortisol levels (3;4). Even in the absence of clear clinical features, the absorbed steroids may induce osteoporosis or, at least in theory, clinical signs of the metabolic syndrome. Such problems may also occur with other forms of corticosteroid administration, such as intra-articular or topical steroids. Awareness of these possibilities should avoid the potential catastrophe of an unsuspected adrenal crisis, and should alert the clinician to the possible presence of iatrogenic Cushing’s syndrome.

This position statement has been revised and updated by Prof. Jeremy Tomlinson (University of Oxford) and Prof. Roland Stimson (University of Edinburgh) in February 2020 and is based upon the original position statement published with Prof. Ashley Grossman (University of Oxford) in July 2011. This information is provided and endorsed by the Society for Endocrinology’s Clinical Committee.

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