

## Correspondence

**Safety of small-particle inhaled corticosteroids in infants**

To the Editor:

Amirav et al<sup>1</sup> provided an excellent review of the delivery of inhaled corticosteroids (ICSs) in infants and young children. They provided some compelling arguments for considering the use of devices that generate small particles, such as hydrofluoroalkane (HFA)–propelled beclomethasone dipropionate (BDP) and ciclesonide metered-dose inhalers (MDIs) with a spacer and appropriate facemasks. However, the potential for risks from this increased delivery of ICSs to infants was given short shrift, primarily because there are few data on which to draw. It would be a mistake not to take this into greater consideration because studies of larger-particle MDIs and nebulized ICSs have clearly demonstrated efficacy and safety in children 1 to 4 years of age.<sup>2-4</sup> The authors cited 2 studies on growth in older children as suggesting that small-particle MDIs were safe in this group.<sup>5,6</sup> However, neither of these studies demonstrate improved safety.

Pedersen et al<sup>5</sup> reported similar growth over a year in an open-label randomized comparison of chlorofluorocarbon-propelled BDP and HFA-BDP at one half the dose. The doses of chlorofluorocarbon-propelled BDP (200-400 µg/d) used in the study have previously been demonstrated to produce growth retardation.<sup>7</sup> Thus this study only demonstrated that the systemic effects were no worse in the HFA-BDP group.

The second trial was a 1-year comparison of ciclesonide HFA-MDI, 40 and 160 µg once daily, with placebo.<sup>6</sup> Although it demonstrated no effect of ciclesonide on linear growth, the 2 pivotal trials submitted to the US Food and Drug Administration using these same doses failed to unequivocally demonstrate efficacy and neither did the efficacy end points for this study.<sup>8</sup> Thus it is unclear that these data actually demonstrate improved safety. If in the future ciclesonide does unequivocally demonstrate greater safety at therapeutic doses in children, it is more likely to be attributed to its very low oral bioavailability and increased

systemic clearance (2-fold or greater than the other ICSs).<sup>9</sup> Clearly, the issues of both efficacy and safety need to be more thoroughly addressed before suggesting that small particle–generating devices are preferred in infants.

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