long-term and/or high-dose ICS use in young children may negatively affect BMD. The follow-up period in this study was longer than in other studies, but limitations include recall bias and failure to account for other lifestyle factors that may affect BMD. Also, the use of steroid-equivalents as the index of cumulative steroid use limits the generalizability of this study. Because the clinical implications of the decreased BMD are unclear, additional long-term studies are needed. However, this study underscores the importance of judicious use of ICS in young children.

Impact of Asthma Medication and Familial Factors on the Association Between Childhood Asthma and Attention-Deficit/Hyperactivity Disorder: A Combined Twin- and Register-Based Study

PURPOSE OF THE STUDY. Previous research has supported an association between asthma and attention-deficit/hyperactivity disorder (ADHD). The goals of this study were to assess (1) whether asthma is associated with inattentive or hyperactive/impulsive symptoms of ADHD, (2) the impact of asthma severity and asthma medications on ADHD, and (3) the contributions of shared genetic and environmental risk factors on the asthma-ADHD relationship.

STUDY POPULATION. Data were obtained from the Child and Adolescent Twin Study in Sweden (CATSS) and 3 Swedish national registers, which contained information on maternal and child diagnoses and prescribed drug dispensation. The population used in this study included all children born between 1992 and 2002 whose parents were interviewed between August 2003 and August 2011.

METHODS. Diagnoses and severity of asthma were based on responses to questions derived from the International Study of Asthma and Allergies in Childhood and codes from the National Patient Register. Similarly, data about ADHD was retrieved from parental reports, responses to the ADHD and other Comorbidities Inventory and National Patient Register codes. Statistical analyses adjusted for the child’s gender, age, birth weight, gestational age, and maternal socioeconomic variables. The classic twin design was used to assess the relative impact of genetic and environmental factors, both shared and nonshared.

RESULTS. The final study population of 20,072 was restricted to twins with complete answers to the main questions on asthma and ADHD. The overall incidences of asthma and ADHD were 14.0% and ~2%, respectively. Asthma was associated with a nearly twofold increased risk of ADHD, of both subtypes, a link that increased with asthma severity. The overlap of genetic factors was weak. Asthma medications did not affect the risk factors.

CONCLUSIONS. Children with asthma had an increased risk of ADHD, the magnitude of which increased with asthma severity.

REVIEWER’S COMMENTS. This study is unique in combining parental reports with national registers among twins in a large population. Limitations include lack of controls for comorbid mental illnesses and lack of information on school performance and ADHD impairment. Asthma and asthma severity, but not asthma medications, were associated with the diagnosis of ADHD.

Calcium-Sensing Receptor Antagonists Abrogate Airway Hyperresponsiveness and Inflammation in Allergic Asthma

PURPOSE OF THE STUDY. The symptoms of asthma are potentially controllable in most asthmatic patients using conventional therapy, but there is an unmet need for identification of novel asthma therapies that target the root cause of the disease rather than its clinical sequelae.

STUDY POPULATION. Primary human airway smooth muscle (ASM) cells were obtained from surgical lung specimens of patients undergoing lobectomy for focal noninfectious disease, including 5 each from patients with moderate asthma and patients without asthma. For animal studies, mice with calcium-sensing receptor (CaSR) targeted gene ablation within ASM cells were compared with wild-type mice without the gene ablation.

METHODS. CaSR receptor expression, calcium flux, and cell signaling pathways were assessed using molecular methods. Force measurements were conducted in intralobular bronchi using a wire myograph, and gene and protein expression of human and murine lung specimens were measured using laser capture microdissection, qRT-PCR and immunofluorescent staining. A mouse model was used to assess effects on airway resistance, inflammation, and allergen-induced responses. The CaSR antagonists NPS89636 and NPS2143 were obtained from NPS Pharmaceuticals and Tocris.
Impact of Asthma Medication and Familial Factors on the Association Between Childhood Asthma and Attention-Deficit/Hyperactivity Disorder: A Combined Twin- and Register-Based Study

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