to environmental exposures may also produce heritable patterns of asthma. Many of the genes related to asthma have been associated with risk for atopy. However, there appear to be genetic modifications that predispose to asthma and its severity. Association studies have identified multiple candidate genes. In many cases, these genes vary from population to population. The most consistently identified include *ORMDL3/GSDMB* (in the 17q21 chromosomal region), *ADAM33, DPP-10, TSLP, IL-12, IL-33, ST2, HLA-DQB1, HLA-DQB2, TLR1*, and *IL6R*. In many cases, association studies have identified polymorphisms in noncoding regions of the genome, suggesting that the majority of the currently identified traits act as "enhancers" of biologic processes.

Genetic polymorphisms have also been associated with differential responses to asthma therapies. Variants in the β-receptor (Arg16Gly in $ADRB_2$), the glucocorticoid-induced transcript 1 gene, and genes in the leukotriene synthesis and receptor pathways have been associated with altered response to the pharmacologic agents acting at those receptors or through those pathways.

While genetic variation plays a key role in asthma susceptibility, it is important to understand that unraveling the complexities of the genetic contribution to asthma remains elusive. To wit, only 2.5% of asthma risk can be explained by the 31 single nucleotide polymorphisms that have been associated with asthma.

A significant proportion of the heritability of asthma relates to the heritability of atopy. Atopy is the genetic tendency toward specific IgE production in response to allergen exposure. Serum levels of IgE correlate closely with the development of asthma. The National Health and Nutrition Examination Survey (NHANES) III found that half of asthma in patients aged 6–59 could be attributed to atopy with evidence of allergic sensitization. The allergens most associated with risk include house dust mites, indoor fungi, cockroaches, and indoor animals.

■ EXPOSURES AND RISK FACTORS

Allergic Sensitization and Allergen Exposure Like asthma, the development of allergic sensitization involves an interplay between heritable susceptibility and allergen exposure. Allergen exposure