Nitric Oxide Nitric oxide is a potent vasodilator, and in vitro studies suggest that it can increase mucus production and smooth-muscle proliferation. It is produced by epithelial cells, especially in response to IL-13, and by stimulated inflammatory cells including eosinophils, mast cells, and neutrophils. Its precise role in the asthmatic diathesis is unclear. However, its production is increased in the airways in the presence of asthmatic eosinophilic inflammation, and it can be detected in exhaled breath.

Reactive Oxygen Species When allergens, pollutants, bacteria, and viruses activate inflammatory cells in the airway, they induce respiratory bursts that release reactive oxygen species that result in oxidative stress in the surrounding tissue. Increases in oxidative stress have been shown to affect smooth-muscle contraction, increase mucus secretion, produce airway hyperresponsiveness, and result in epithelial shedding.

Chemokines A variety of chemokines are secreted by the epithelium (as well as other inflammatory cells) and attract inflammatory cells into the airways. Those of particular interest include eotaxin (an eosinophil chemoattractant), TARC and MDC (which attract T_H2 cells), and RANTES (which has pluripotent pro-phlogistic effects).

ETIOLOGIC MECHANISMS, RISK FACTORS, TRIGGERS, AND COMPLICATING COMORBIDITIES

As illustrated in Fig. 287-1, the development of asthma involves an interplay between risk factors and exposures (see Table 287-1) and genetic predisposition.

■ HERITABLE PREDISPOSITION

Asthma has a strong genetic predisposition. Family and twin studies suggest a 25–80% degree of heritability. Genetic studies suggest complex polygenic inheritance complicated by interaction with environmental exposures. Further, epigenetic modifications related