Atopic eczema (AE) is one of the most common inflammatory diseases, often constituting a lifelong burden for afflicted individuals. Recent findings have provided new insights into the pathogenesis of AE, revealing contributions of genetics, skin microbiota, and both innate and adaptive immunity in disease onset and progression. We review these findings here, assembling contributing factors conceptually into four modules that can interact in various ways to ultimately lead to epidermal barrier impairment, unchecked type 2 immunity, and chronic disease. We present this modular framework as a basis for understanding the varied presentations of AE, and in this context we propose a diagnostic and therapeutic algorithm aimed at the precise stratification of AE patients and the implementation of individualized medicine in AE standard of care.