Although the development and progression of heart failure have traditionally been viewed as hemodynamic disorders, there is now an increasing awareness that the syndrome of heart failure cannot be simply and/or precisely defined solely in hemodynamic terms. The inability of the so-called hemodynamic hypothesis to explain the progression of heart failure has given rise to the notion that heart failure may progress as a result of the overexpression of an ensemble of biologically active molecules referred to generically as neurohormones. More recently, it has become apparent that in addition to neurohormones, another portfolio of biologically active molecules, termed cytokines, are also expressed in the setting of heart failure. This article reviews recent clinical and experimental material that suggests that the cytokines, much like the neurohormones, may represent another class of biologically active molecules that are responsible for the development and progression of heart failure.