



**FIGURE 40.1** Expanded polyglutamine toxicity. Expansion of the polyglutamine tract results in protein cleavage, nuclear uptake, and generation of aggregates. The cells cope with the accumulation of aberrant species, trying to increase protein folding through chaperone activity and protein degradation through the ubiquitin–proteasome system and autophagy. If this process is inefficient, the aberrant protein accumulates in the cell, affecting several cellular processes, such as transcription, axonal transport, signal transduction, and mitochondrial function. This leads to neuronal dysfunction and eventually to death.