African dust exhibits strong variability on a range of time scales. Here we show that the interhemispheric contrast in Atlantic SST (ICAS) drives African dust variability on interannual, multidecadal, and millennial timescales, and a strong anthropogenic decline of African dust in the future can be expected due to the projected increase of the ICAS. During the recent past, the ICAS is found to significantly correlate with various dust observations and proxies that extend as far back as 1851. Physically, positive ICAS anomalies induce large-scale circulation changes that push the Intertropical Convergence Zone (ITCZ) northward and decrease surface wind speed over African dust source regions, which reduces dust emission and transport to the tropical Atlantic. The ICAS-ITCZ-dust relationship also finds robust support from paleo-climate observations that span the last 17,000 years. The ICAS drive of African dust variability is consistent with documented relationships between dust activity and Sahel precipitation6, the North Atlantic Oscillation7, and time series of a surface wind speed pattern over Northern Africa8, and offers a unified framework to understand them. The ICAS-dust connection implies that human activities that change ICAS through emitting greenhouse gases and pollutions have affected and will continue to affect African dust. Climate models project that anthropogenic increase of the ICAS can push the ICAS value to surpass the highest level attained during the Holocene by the end of this century and decrease African dust activity by as much as 60% off its current level, which has broad consequences for aspects of the climate in the North Atlantic region and beyond.