The ability of Staphylococcus aureus to adhere to endothelial cells (EC) is a critical step in the development of metastatic infection. The importance of active complement was confirmed by experiments using serum with added EDTA or cobra venom factor, a protein that depletes C3.Log-phase S. aureus, expressing minimal capsule, was incubated with serum under various conditions, washed, and then incubated at 37?C for 30 min with cultured human umbilical vein EC (ATCC CRL-1730). Incubating S. aureus in complement-active normal human serum (NHS) decreased binding to EC by 58% compared to organisms incubated in heat-inactivated serum. This decreased by 56% in complement-active serum, suggesting that inhibition of S. aureus adherence to EC is due, in part, to complement-mediated diminished binding to fibronectin.