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*Staphylococcus epidermidis* is commonly associated with foreign body infections due to its ability to form biofilms on the surface of indwelling medical devices. Understanding how the biofilms form on the top of devices and interact with the host, particularly, with human blood components, is of great interest. Here we assessed the whole transcriptome of *S. epidermidis* biofilms upon contact with human blood. Established biofilms were incubated with human blood for 2 or 4 hours. Total RNA from biofilms was extracted, complementary DNA libraries constructed using the TruSeq RNA sample preparation kit and the libraries sequenced on a MySeq system. In general, the majority of the transcripts that underwent the major changes upon contact with human blood encoded proteins involved in essential metabolic processes. A closer look at individual transcript levels revealed that genes involved in universal stress responses, programmed cell death and biofilm disassembly were also increased after 2 hours of contact with human blood, while some of the transcripts encoding factors involved in biofilm formation were found to have decreased expression. After 4 hours, the levels of transcripts for genes involved in cell death and biofilm dispersion started to decrease, some of them reaching pre-exposure levels, while transcripts of genes involved in biofilm formation were increased. These results indicate that human blood creates a stressful environment for biofilm maintenance upon first contact. However, latter on, bacteria seem to recover and strengthen the biofilm, possibly to survive in the conditions created by the presence of human blood.