Sepsis is a dynamic, acute, infectious disease syndrome characterized by dysregulated thrombo-inflammatory responses. Advances in the treatment of sepsis have been modest and many promising therapies have failed to demonstrate sustained clinical utility. Given the persistently high morbidity and mortality associated with sepsis, a better understanding of the dysregulated cellular biology underpinning sepsis is needed. Platelets are small, anucleate cells that have hemostatic, inflammatory, and immune mediating properties. Platelets are the second most common circulating blood cell and emerging evidence suggests that platelets serve as sentinel and effector cells that respond to invading pathogens. Platelet responses to pathogens include activation of thrombo-inflammatory cascades, signaling to other innate and adaptive immune cells, and in some cases direct engulfment of pathogens or pathogen particles. These responses may be both adaptive and maladaptive for host recovery during acute infectious illnesses. This talk will review the pathophysiology of septic syndromes and established and emerging data on how platelets mediate host responses to pathogens.