Antiphospholipid Syndrome (APS) is an autoimmune disease characterized by venous and arterial thromboembolism, adverse pregnancy outcomes, and the expression of antiphospholipid antibodies. Over the last few decades, additional manifestations have become better defined. These include seizures, cardiac valve disease, nephropathy, skin ulcers and autoimmune cytopenias. While some of these manifestations may be the result of the “final common pathway” of thrombosis in APS, others are not well explained. Traditionally, treatment of APS has anchored on anti-thrombotics. However, recent advances in the pathophysiology of the disease, plus observations in the clinical setting, have opened the door for novel treatment strategies that warrant exploration. We will review the biology of APS and its impact on treatment with the help of illustrative clinical cases.