Patients become sensitized after exposure to non-self human leukocyte antigen (HLA) during pregnancy, blood transfusions, and organ transplantation. It has been estimated that 20 – 30% of patients awaiting first renal allograft are sensitized, whereas 77% of patients waiting for repeat transplant are sensitized and 30% of these are highly sensitized (patients with HLA-specific antibodies reactive with > 85% of lymphocyte panel). These patients, especially the highly sensitized, have the least chance to receive a kidney because most of the randomly performed cross-match will be positive and therefore, these patients will continue to accumulate on the waiting lists. There are three (3) main approaches that can be adopted in order to minimize the phenomenon of sensitization on one hand and maximize the chances of transplanting sensitized patients on the other hand. The first approach is preventive in nature and it concentrates on minimizing HLA mismatches in the first kidney transplant and on the use of erythropoietin or transfusion with leukocyte-depleted blood for the treatment of anemia in patients with chronic renal failure who are prepared for transplant. The second approach revolves around finding a cross-match negative kidney through national exchange programs (sharing of zero-mismatched kidneys, acceptable mismatch programs, and HLA matchmaker). The third approach attempts to remove and neutralize the donor-specific HLA antibodies from the serum of these patients before transplantation (desensitization). Desensitization protocols include the use of intravenous immunoglobulins (IVIG), plasmapheresis and IVIG, and immunoabsorption. We report our experiences in desensitizing highly sensitized patients using a variety of protocols that include: Immunoadsorption, IVIG, Rituximab, Alemtuzumab, Thymoglobulin, and Quadruple maintenance immunosuppression.