Sex Differences in the Progression of Systemic Lupus Erythematosus
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Systemic lupus erythematosus (SLE), an autoimmune disease that affects young women at a ratio of 9:1 over men, begins with the production of autoantibodies that contributes to sustained renal inflammation and injury. To combat aberrant inflammation, activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to the release of cortisol, but the axis is impaired in SLE. We hypothesized that 1) female SLE mice would have heightened disease compared to males early in disease progression and 2) administration of dexamethasone, a synthetic cortisol, would lower inflammation in female SLE mice. We monitored dsDNA autoantibodies, a hallmark of SLE, and albuminuria, an index of renal injury in 25-week male and female SLE (NZBWF1) mice and parental controls (NZW) for 4 weeks, and also in a separate set of 31-week female SLE and C57BL/6 mice that were administered dexamethasone (1.5mg/kg, IP, 4 weeks). At 28 weeks, female SLE mice had higher autoantibodies than female controls and male control and SLE mice (p<0.05), whereas 20% of female SLE mice developed renal injury (albuminuria ≥ 300mg/dL) and no males. At 35 weeks, SLE mice had higher autoantibodies than controls but dexamethasone did not alter disease severity in these mice (n=3-4/group). Albuminuria was higher in SLE mice administered dexamethasone (50%) compared to those administered vehicle (33%) and all controls (0%). In summary, male SLE mice are indeed protected but additional studies are needed to determine the mechanisms involved and also the efficacy of dexamethasone therapy on SLE disease progression. Funded by NIH (1K01HL139859), Lupus Research Alliance (550778).