Positive streamflow trends in the Upper Mississippi River Basin (UMRB) during the 20th century are well documented. During this period, the UMRB experienced significant increases in precipitation as well as decreases in the diurnal temperature range during the growing season. Concurrently, the basin’s land cover changed through a net extensification of croplands. Previous studies have used statistical models to relate increases in annual row crop extent to increases of runoff; however, do not fully consider the influences of the observed changes in climate. To examine the influences of both climate and changing land surface vegetation patterns, simulations using the Variable Infiltration Capacity (VIC) hydrology model are conducted for different scenarios of static and dynamic representations of historical land cover, separating the influences of land use and climate on the regional hydrology of the basin. Model results suggest that climate is the dominant signal influencing the positive trends in streamflow at the outlet of the basin. The influences of land use are only significant at the local scale, increasing (decreasing) annual runoff 6% (8.5%) depending on the initial vegetation prior to conversion.