SIGNIFICANCE STATEMENT

Glomerular and podocyte injuries are attributed to biochemical and genetic mechanisms, although increased capillary pressure and flow are also important. The biophysical properties of glomeruli and podocytes and the role of these factors in disease initiation and progression are not understood. In two models of podocyte injury (Tg26 mouse, protamine), the authors find that injured glomeruli and podocytes are abnormally deformable, and this is attributable to common features, including disordered podocyte cytoskeletons, responses to matrix elasticity, adhesion, and contractility. A pathologically soft environment is sufficient to cause disordered podocyte structure. These findings mean that a healthy podocyte can take on pathologic characteristics due to the mechanical environment and may partly explain why "normal" podocytes are lost after injury to neighboring cells.