Mechanisms of Proteinuria Induced by Antikidney Antibodies in Noninflammatory Experimental Glomerulonephropathy

William G. Couser, David J. Salant, and Magda M. Stilmant

1. Introduction

A number of studies carried out largely in the past 5 years have contributed to a significant increase in our understanding of the determinants which regulate the permeability of the normal glomerulus to various macromolecules (Rennke and Venkatachalam, 1977; Brenner et al., 1978). These morphologic and physiologic studies have been well summarized elsewhere in this volume (Chapters 1, 2, and 6). The topic of this chapter is renal disease mediated by antikidney antibodies. To link the material presented earlier on glomerular permeability with diseases induced by antikidney antibodies, the present discussion will review some of the recent studies of immunologic mechanisms of proteinuria carried out largely in two models of experimental nephropathy in Couser’s laboratory.

It is well established that complement–neutrophil (PMN)-mediated inflammatory glomerular injury results in structural damage to the glomerular capillary wall (Kuhn et al., 1977). This discussion will focus on proteinuria
mediated by glomerular antibody deposition in the absence of detectable inflammatory changes or structural alterations in the proximal layers of the glomerular filtration barrier. A full understanding of the mechanisms of immunologically induced proteinuria requires that a much better correlation be established between the immunologic agents and mediator systems which induce glomerular disease and the determinants of glomerular permselectivity defined by physiologic and ultrastructural studies than is possible at the present time.

2. Complement-Independent Nephrotoxic Nephritis in the Guinea Pig

Injection of outbred guinea pigs with sheep antibody to guinea pig glomerular basement membrane (GBM) induces an initial oliguric period lasting for 1–2 hr followed by a marked but transient increase in urine protein excretion which reaches a peak value of over 25 mg/hr within 5–6 hr but returns to essentially normal values within 36 hr (Fig. 1). (Couser et al., 1977). Electrophoretic studies have shown the urine protein to be composed of over 90% albumin. This dramatic change in GBM permeability is accompanied by linear deposition of both \( y_1 \) and \( y_2 \) subgroups of sheep IgG on the GBM. However, there is no detectable deposition of guinea pig C3 or C4 in vivo, and these glomerular antibody deposits do not fix guinea pig or human C3 in vitro (Couser et al., 1977).

Figure 1. Time course of proteinuria induced by administration of sheep antibody to guinea pig GBM.