

Both charge and size selectivity normally prevent virtually all plasma albumin, globulins, and other high-molecular-weight proteins from crossing the glomerular wall; however, if this barrier is disrupted, plasma proteins may leak into the urine (glomerular proteinuria; [Fig. 52-3](#)). Smaller proteins (<20 kDa) are freely filtered but are readily reabsorbed by the proximal tubule. Typically, healthy individuals excrete <150 mg/d of total protein and <30 mg/d of albumin. However, even at albuminuria levels <30 mg/d, risk for progression to overt nephropathy or subsequent cardiovascular disease is increased. The remainder of the protein in the urine is secreted by the tubules (Tamm-Horsfall, IgA, and urokinase) or represents small amounts of filtered β_2 -microglobulin, apoproteins, enzymes, and peptide hormones. Another mechanism of proteinuria entails excessive production of an abnormal protein that exceeds the capacity of the tubule for reabsorption. This situation most commonly occurs with plasma cell dyscrasias, such as multiple myeloma, amyloidosis, and lymphomas, that are associated with monoclonal production of immunoglobulin light chains.

The normal glomerular endothelial cell forms a barrier composed of pores of ~ 100 nm that retain blood cells but offer little impediment to passage of most proteins. The glomerular basement membrane traps most large proteins (>100 kDa), and the foot processes of epithelial cells (podocytes) cover the urinary side of the glomerular basement membrane and produce a series of narrow channels (slit diaphragms) to allow molecular passage of small solutes and water but not proteins. Some glomerular diseases, such as minimal change disease, cause fusion of glomerular epithelial cell foot processes, resulting in predominantly “selective” ([Fig. 52-3](#)) loss of albumin. Other glomerular diseases can present with disruption of the basement membrane and slit diaphragms (e.g., by immune complex deposition), resulting in losses of albumin and other plasma proteins. The fusion of foot processes causes increased pressure across the capillary basement membrane, resulting in areas with larger pore sizes (and more severe “nonselective” proteinuria) ([Fig. 52-3](#)).

When the total daily urinary excretion of protein is >3.5 g, hypoalbuminemia, hyperlipidemia, and edema (nephrotic syndrome;