Minimal-Change Disease

This relatively benign disorder is characterized by diffuse effacement of foot processes of visceral epithelial cells (podocytes), detectable only by electron microscopy, in glomeruli that appear virtually normal by light microscopy. It is the most frequent cause of nephrotic syndrome in children, but it is less common in adults (Table 20-7). The peak incidence is between 2 and 6 years of age. The disease sometimes follows a respiratory infection or routine prophylactic immunization.

Etiology and Pathogenesis. Although the absence of immune deposits in the glomerulus excludes classic immune complex mechanisms, several features of the disease point to an immunologic basis, including (1) the clinical association with respiratory infections and prophylactic immunization; (2) the response to corticosteroids and/or other immunosuppressive therapy; (3) the association with other atopic disorders (e.g., eczema, rhinitis); (4) the increased prevalence of certain HLA haplotypes in patients with minimal-change disease associated with atopy (suggesting a genetic predisposition); and (5) the increased incidence of minimal-change disease in patients with Hodgkin lymphoma, in whom defects in T cell-mediated immunity are well recognized.

The current leading hypothesis is that minimal-change disease involves some immune dysfunction that results in the elaboration of factors that damage visceral epithelial cells and cause proteinuria. Candidate pathogenic factors such as angiopoietin-like-4 have been identified in animal models but none have been proven to cause the human disease. The ultrastructural changes point to a primary *visceral epithelial cell injury* (podocytopathy), and studies in animal models suggest the loss of glomerular polyanions. Thus, defects in the charge barrier may contribute to the proteinuria. The actual route by which protein traverses the epithelial cell portion of the capillary wall remains an enigma. Possibilities include transcellular passage through the epithelial cells, passage through residual spaces between remaining but damaged foot processes or through abnormal spaces developing underneath the portion of the foot process that directly abuts the basement membrane, or leakage through foci in which the epithelial cells have become detached from the basement.

MORPHOLOGY

The glomeruli are normal by light microscopy (Fig. 20-13). By electron microscopy the GBM appears normal, and no electron-dense material is deposited. **The principal lesion is in the visceral epithelial cells, which show a uniform and diffuse effacement of foot processes,** these being reduced to a rim of cytoplasm with loss of recognizable intervening slit diaphragms (Fig. 20-13). This change, often incorrectly termed "fusion" of foot processes, actually represents simplification of the epithelial cell architecture with flattening, retraction, and swelling of foot processes. Foot process effacement is also present in other proteinuric states (e.g., membranous glomerulopathy, diabetic nephropathy); it is only when effacement is associated with normal glomeruli by light microscopy that the diagnosis of minimal-change disease can be made. The visceral epithelial changes are completely reversible after corticosteroid therapy, concomitant with remission of the proteinuria. The cells of the proximal tubules are often laden with lipid and protein, reflecting tubular reabsorption of lipoproteins passing through diseased glomeruli (thus, the historical name **lipoid nephrosis** for this disease). Immunofluorescence studies show no Ig or complement deposits.

Clinical Features. Despite massive proteinuria, renal function remains good, and there is commonly no hypertension or hematuria. The proteinuria usually is highly selective, most of the protein being albumin. **A characteristic feature is its usually dramatic response to corticosteroid therapy.** Most children (>90%) with minimal-change disease respond rapidly to this treatment. However, proteinuria may recur, and some patients may become

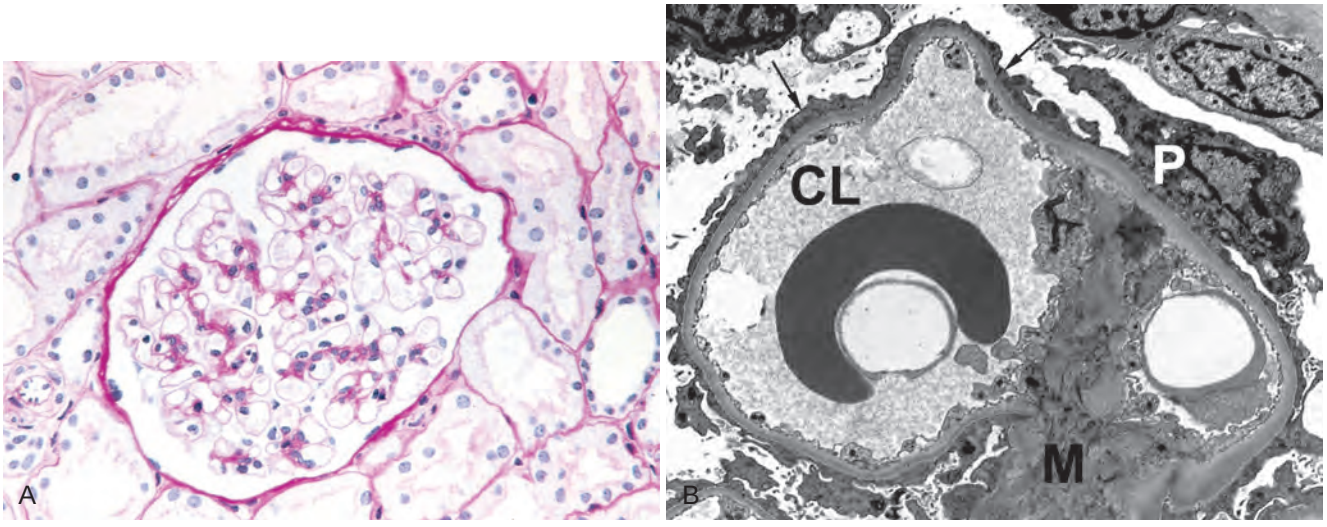

Figure 20-13 Minimal-change disease. **A,** Glomerulus stained with PAS. Note normal basement membranes and absence of proliferation. **B,** Ultrastructural characteristics of minimal-change disease include effacement of foot processes *(arrows)* and absence of deposits. *CL,* Capillary lumen; *M,* mesangium; *P,* podocyte cell body.