and have a histologic picture of MPGN. Fifty percent of patients with leishmaniasis will have mild to moderate proteinuria and microscopic hematuria, but renal insufficiency is rare. Acute DPGN, MGN, and mesangioproliferative glomerulonephritis have all been observed on biopsy. Filariasis and trichinosis are caused by nematodes and are sometimes associated with glomerular injury presenting with proteinuria, hematuria, and a variety of histologic lesions that typically resolve with eradication of the infection.

339 Polycystic Kidney Disease and Other Inherited Disorders of Tubule Growth and Development

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The polycystic kidney diseases are a group of genetically heterogeneous disorders and a leading cause of kidney failure. The autosomal dominant form of polycystic kidney disease (ADPKD) is the most common life-threatening monogenic disease, affecting 12 million people worldwide. The autosomal recessive form of polycystic kidney disease (ARPKD) is rarer but affects the pediatric population. Kidney cysts are often seen in a wide range of syndromic diseases. Recent studies have shown that defects in the structure or function of the primary cilia may underlie this group of genetic diseases collectively termed *ciliopathies* (Table 339-1).

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Etiology and Pathogenesis (Fig. 339-1) ADPKD is characterized by progressive formation of epithelial-lined cysts in the kidney. Although cysts only occur in 5% of the tubules in the kidney, the enormous growth of these cysts ultimately leads to the loss of normal surrounding tissues and loss of renal function. The cellular defects in ADPKD that have been known for a long time are increased cell proliferation and fluid secretion, decreased cell differentiation, and abnormal extracellular matrix. ADPKD is caused by mutations in *PKD1* and *PKD2*, which, respectively, code for polycystin-1 (PC1) and polycystin-2 (PC2). PC1 is a large 11-transmembrane protein that functions like a G protein–coupled receptor. PC2 is a calcium-permeable six-transmembrane protein that structurally belongs to the transient receptor potential (TRP) cation channel family. PC1 and PC2 are widely expressed in almost all tissues and organs. PC1 expression is high in development and low in the adult, whereas PC2 expression is relatively constant. PC1 and PC2 are found on the primary cilium, a hair-like structure present on the apical membrane of a cell, in addition to the cell membranes and cell-cell junctions of tubular epithelial cells. Defects in the primary cilia are linked to a wide spectrum of human diseases, collectively termed ciliopathies. The most common phenotype shared by many ciliopathies is kidney cysts. PC1 and PC2 bind to each other via their respective C-terminal tails to form a receptor-channel complex and regulate each other's function. The PC1/2 protein complex serves as a mechanosensor or chemical sensor and regulates calcium and G-protein signaling. The PC1/2 protein complex may also directly regulate a number of cellular functions including the cell cycle, the actin cytoskeleton, planar cell polarity (PCP), and cell migration. This protein complex has also been implicated in regulating a number of signaling pathways, including Wnt, mammalian target of rapamycin (mTOR), STAT3, cMET, phosphoinositide 3-kinase (PI3K)/AKT, G protein–coupled receptor (GPCR), and epidermal growth factor receptor (EGFR), as well as in the localization and activity of cystic fibrosis transmembrane conductance (CFTR). One hypothesis is

TABLE 339-1 INHERITED DISEASES COMMONLY ASSOCIATED WITH A CYSTIC PHENOTYPE

Disease	Mode of Inheritance	Renal Abnormalities	Other Clinical Features	Genes
Autosomal dominant polycystic kidney disease	AD	Cortical and medullary cysts	Liver, pancreatic cysts, hypertension, subarachnoid hemorrhage	*PKD1, PKD2*
Autosomal recessive polycystic kidney disease	AR	Distal and collecting duct cysts	Oligohydramnios if severe, hypertension, ascending cholangitis, liver fibrosis	*PKHD1*
Medullary cystic kidney	AD	Small fibrotic kidneys; medullary cysts	In adults, gout	*MCKD1, MCKD2/UMOD*
Nephronophthisis	AR	Small fibrotic kidneys; medullary cysts	Growth retardation, anemia (visual loss, liver fibrosis, cerebellar ataxia if associated with another syndrome)	*NPHP1-4, IQCB1, CEP290, GLIS2, RPGRIP1L, NEK8, SDCCAG8, TMEM67, TTC21B*
Senior-Løken syndrome	AR	Renal cysts	Juvenile nephronophthisis, Leber's amaurosis	*NPHP1-6, SDCCAG8*
Leber's congenital amaurosis	AR	Renal cysts	Visual impairment in first year of life, pigmentary retinopathy	*GUCY2D, RPE65, LCA3-14* (including *LCA10, CEP290*)
Meckel-Gruber syndrome	AR	Cortical and medullary cysts	CNS anomalies, polydactyly, congenital heart defects	*MKS1, TMEM216, TMEM67, CEP290, RPGRIP1L, CC2D2A, TCTN2, B9D1, B9D2, NPHP3*
Bardet-Biedl syndrome	AR	Renal cysts	Obesity, polydactyly, retinitis pigmentosa, anosmia, congenital heart defects, mental retardation	*BBS1, 2, ARL6, BBS4,5, MKKS, BBS7, TTC8, BBS9, 10, TRIM32, BBS12, MKS1, CEP290, C2ORF86;* modifiers *MKS1, MKS3, CCDC28B*
Oral-facial-digital syndrome type I	AR	Renal cysts	Oral cavity, face, and digit anomalies; CNS abnormalities; cystic kidney disease; X-linked with male lethality, primary ciliary dyskinesia	*OFD1*
Cranioectodermal dysplasia (Sensenbrenner's syndrome)	AR	Renal cysts	Skeletal dysplasia, thoracic deformities, polydactyly, renal cysts, retinitis pigmentosa	*IFT80*
Tuberous sclerosis	AD	Renal cysts	Angiomyolipomas, renal cell carcinoma, facial angiofibromas, CNS hamartomas	*TSC1, TSC2*
Von Hippel-Lindau disease	AD	Renal cysts	Renal cell carcinoma, retinal angiomas, CNS hemangioblastomas, pheochromocytomas	*VHL*

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; CNS, central nervous system.