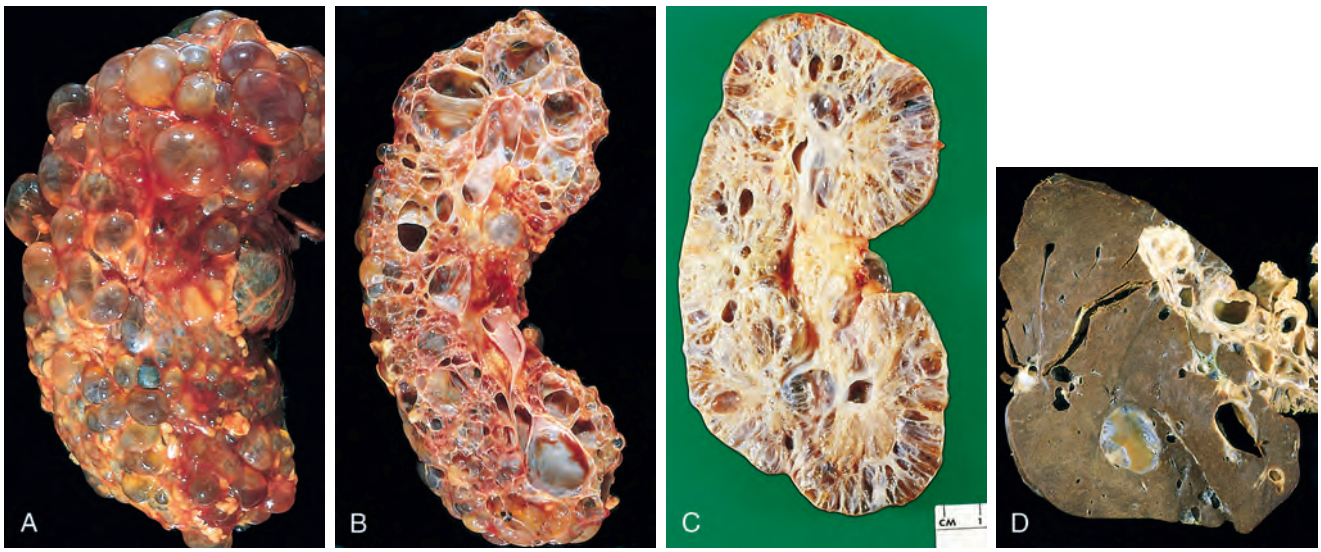

Figure 20-44 **A** and **B,** Autosomal dominant adult polycystic kidney disease (ADPKD) viewed from the external surface and bisected. The kidney is markedly enlarged and contains numerous dilated cysts. **C,** Autosomal recessive childhood PKD, showing smaller cysts and dilated channels at right angles to the cortical surface. **D,** Liver cysts in adult PKD.

MORPHOLOGY

In gross appearance, the kidneys are bilaterally enlarged and may achieve enormous sizes; weights as much as 4 kg for each kidney have been reported. The external surface appears to be composed solely of a mass of cysts, up to 3 to 4 cm in diameter, with no intervening parenchyma (Fig. 20-44*A* and *B*). However, microscopic examination reveals functioning nephrons dispersed between the cysts. The cysts may be filled with a clear, serous fluid or with turbid, red to brown, sometimes hemorrhagic fluid. As these cysts enlarge, they may encroach on the calyces and pelvis to produce pressure defects. The cysts arise from the tubules throughout the nephron and therefore have variable lining epithelia. On occasion, papillary epithelial formations and polyps project into the lumen. Bowman capsules are occasionally involved in cyst formation, and glomerular tufts may be seen within the cystic space.

Clinical Features. Many patients remain asymptomatic until renal insufficiency announces the presence of the disease. In others, hemorrhage or progressive dilation of cysts may produce pain. Excretion of blood clots causes renal colic. The enlarged kidneys, usually apparent on abdominal palpation, may induce a dragging sensation. The disease occasionally begins with the insidious onset of hematuria, followed by other features of progressive chronic kidney disease, such as proteinuria (rarely more than 2 gm/day), polyuria, and hypertension. Patients with *PKD2* mutations tend to have an older age at onset and later development of renal failure. Both genetic and environmental factors influence disease severity. Progression is accelerated in blacks (particularly in those with sickle-cell trait), in males, and in the presence of hypertension.

Individuals with polycystic kidney disease also tend to have extrarenal congenital anomalies. About 40% have one to several cysts in the liver (polycystic liver disease) that are usually asymptomatic. The cysts are derived from biliary epithelium. Cysts occur much less frequently in the spleen, pancreas, and lungs. Intracranial berry aneurysms, presumably from altered expression of polycystin in vascular smooth muscle, arise in the circle of Willis, and subarachnoid hemorrhages from these account for death in 4% to 10% of individuals. *Mitral valve prolapse* and other cardiac valvular anomalies occur in 20% to 25% of patients, but most are asymptomatic. The diagnosis is made by radiologic imaging techniques.

This form of chronic kidney disease is remarkable in that patients may survive for many years with azotemia slowly progressing to uremia. Ultimately, about 40% of adult patients die of coronary or hypertensive heart disease, 25% of infection, 15% of a ruptured berry aneurysm or hypertensive intracerebral hemorrhage, and the rest of other causes.

Autosomal Recessive (Childhood) Polycystic Kidney Disease

Autosomal recessive (childhood) polycystic kidney disease is genetically distinct from adult polycystic kidney disease. *Perinatal*, *neonatal*, *infantile*, and *juvenile* subcategories have been defined, depending on the time of presentation and presence of associated hepatic lesions. The first two are the most common; serious manifestations are usually present at birth, and the young infant might succumb rapidly to renal failure.

Genetics and Pathogenesis. In most cases, the disease is caused by mutations of the *PKHD1* gene, which maps to chromosome region 6p21-p23. The gene is highly expressed in adult and fetal kidney and also in liver and pancreas. The *PKHD1* gene encodes *fibrocystin*, a 447-kD integral membrane protein with a large extracellular region, a single transmembrane component, and a short cytoplasmic tail. The extracellular region contains multiple copies of a domain forming an Ig-like fold. Like polycystins 1 and 2, fibrocystin also has been localized to the primary cilium of tubular cells. The function of fibrocystin is unknown, but its putative conformational structure indicates it may be a