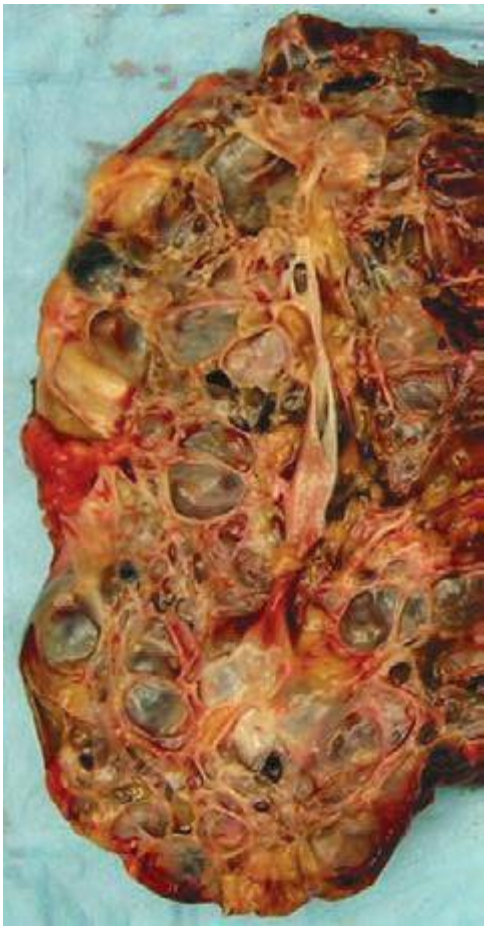

**FIGURE 339-2 Photograph showing a kidney from a patient with autosomal dominant polycystic kidney disease.** The kidney has been cut open to expose the parenchyma and internal aspects of cysts.

may coexist if the cyst that ruptures is connected with the collecting system. Proteinuria is usually a minor feature of ADPKD. Infection is the second most common cause of death for patients with ADPKD. Up to half of patients with ADPKD will have one or more episodes of renal infection during their lifetime. An infected cyst and acute pyelonephritis are the most common renal infections often due to gram-negative bacteria, which are associated with fever and flank pain, with or without bacteremia. These complications and renal insufficiency often correlate with structural abnormality of the renal parenchyma. Kidney stones occur in ~20% of patients with ADPKD. Different from the general population, more than half of the stones in patients with ADPKD are composed of uric acid, with the remainder due to calcium oxalate. Distal acidification defects, abnormal ammonium transport, low urine pH, and hypocitraturia may be important in the pathogenesis of renal stones in ADPKD. Renal cell carcinoma is a rare complication of ADPKD with no apparent increased frequency compared to the general population. However, in ADPKD, these tumors are more often bilateral at presentation, multicentric, and sarcomatoid in type. Radiologic imaging is often not helpful in distinguishing cyst infection and cyst hemorrhage because of their complexity. Computed tomography (CT) scan and magnetic resonance imaging (MRI) are often useful in distinguishing a malignancy from a complex cyst. Cardiovascular complications are the major cause of mortality in patients with ADPKD. Hypertension is common and typically occurs before any reduction in glomerular filtration rate (GFR). Hypertension is a risk factor for both cardiovascular and kidney disease progression in ADPKD. Notably, some normotensive patients with ADPKD may also have left ventricular hypertrophy. Hypertension in ADPKD may result from the increased activation of the renin-angiotensin-aldosterone system, increased sympathetic nerve activity, and impaired endothelial cilium function-dependent relaxation of small resistant blood vessels.

The progression of ADPKD has striking inter- and intrafamilial variability. The disease can present as early as in utero, but end-stage renal disease typically occurs in late middle age. Risk factors include early diagnosis of ADPKD, hypertension, gross hematuria, multiple pregnancies, and large kidney size. Liver cysts derived from the biliary epithelia are the most common extrarenal complication. Polycystic liver disease associated with ADPKD is different from autosomal dominant polycystic liver disease (ADPLD), which is caused by mutations in at least two distinct genes (*PRKCSH* and *SEC63*) and does not progress to renal failure. Massive polycystic liver disease occurs almost exclusively in women with ADPKD, particularly those with multiple pregnancies.

Intracranial aneurysm (ICA) occurs four to five times more frequently in ADPKD patients than in the general population and causes high mortality. The disease gene products PC1 and PC2 may be directly responsible for defects in arterial smooth muscle cells and myofibroblasts. The focal nature and the natural history of ICA in ADPKD remain unclear. A family history of ICA is a risk factor of aneurysm rupture in ADPKD, but whether hypertension and cigarette smoking are independent risk factors is not clear. About 20–50% of patients may experience "warning headaches" preceding the index episode of subarachnoid hemorrhage due to ruptured ICA. A CT scan is generally used as the first diagnostic test. A lumbar puncture may be used to confirm the diagnosis. The role of radiologic screening for ICA in asymptomatic patients with ADPKD remains unclear. ADPKD patients with a positive family history of ICAs may undergo presymptomatic screening of ICAs by magnetic resonance angiography. Other vascular abnormalities in ADPKD patients include diffuse arterial dolichoectasias of the anterior and posterior cerebral circulation, which can predispose to arterial dissection and stroke. Mitral valve prolapse occurs in up to 30% of patients with ADPKD, and tricuspid valve prolapse is less common. Other valvular abnormalities occurring with increased frequency in ADPKD patients include insufficiency of the mitral, aortic, and tricuspid valves. Most patients are asymptomatic, but some may progress and require valve replacement. The prevalence of colonic diverticulae and abdominal wall hernias is also increased in ADPKD patients.

**Diagnosis** Diagnosis is typically made from a positive family history consistent with autosomal dominant inheritance and multiple kidney cysts bilaterally. Renal ultrasonography is often used for presymptomatic screening of at-risk subjects and for evaluation of potential living-related kidney donors from ADPKD families. The presence of *at least two renal cysts (unilateral or bilateral)* is sufficient for diagnosis among at-risk subjects between 15 and 29 years of age with a sensitivity of 96% and specificity of 100%. The presence of *at least two cysts in each kidney* and the presence *at least four cysts in each kidney* are required for the diagnosis of at-risk subjects age 30 to 59 years and age 60 years or older, respectively, with a sensitivity of 100% and specificity of 100%. This is because there is an increased frequency of developing simple renal cysts with age. Conversely, in subjects between age 30 and 59 years, the absence of *at least two cysts in each kidney*, which is associated with a false-negative rate of 0%, can be used for disease exclusion. These criteria have a lower sensitivity for patients with a *PKD2* mutation because of a late onset of ADPKD2. CT scan and T2-weighted MRI, with and without contrast enhancement, are more sensitive than ultrasonography and can detect cysts of smaller size. However, a CT scan exposes the patient to radiation and radiocontrast, which may cause serious allergic reactions and nephrotoxicity in patients with renal insufficiency. T2-weighted MRI, with gadolinium as a contrast agent, has minimal renal toxicity and can detect cysts of only 2–3 mm in diameter. However, a large majority of cysts may still be below the detection level. Genetic testing by linkage analyses and mutational analyses is available for ambiguous cases. Because of the large size of the *PKD1* gene and the presence of multiple highly homologous pseudogenes, mutational analysis of the *PKD1* gene is difficult and costly. Application of new technologies, such as paired-end