

Underwriting Adult Polycystic Kidney Disease (APKD)

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Polycystic kidneys are characterized by massive enlargement of these organs due to diffuse cyst formation.

In adult polycystic kidney disease (APKD), the cysts begin as tiny vesicles involving only one to two percent of the renal tubules.¹ These "renegade" nephrons enlarge slowly but progressively, compressing and virtually obliterating the normal parenchyma, ultimately inducing renal insufficiency. This deterioration in function appears to accelerate in later life. A mathematical model of spherical enlargement has been proposed wherein further increments in cyst radius impose a proportionately greater displacement of contiguous normal nephrons.²

Polycystic kidney disease occurring in adults is distinguished from the infantile form. The latter is inherited as an autosomal recessive gene; is far less common; is characterized by cysts occurring primarily in the collecting ducts, rather than all along the tubule; and is usually fatal in infancy. As such, it is of little concern for insurance purposes.

APKD is inherited instead as an autosomal dominant gene with an extraordinary high penetrance. Virtually 100% of gene carriers will manifest cystic disease by age eighty years.³ The great majority of cases have been associated with a locus on the distal third of the short arm of chromosome 16. This location is identifiable by flanking markers for the alpha-globin cluster and phosphoglycolate phosphatase.⁴ Their identification achieve a diagnostic accuracy exceeding 99%.⁵ However, in two recent reports describing families of Italian origin,^{6,7} this association was not demonstrable. This finding implies that either two different genes are linked to APKD or the culprit gene has undergone translocation to another chromosome in these families.

The availability of such DNA probes enables diagnosis very early in life, even as early as a nine-week fetus.⁸ The availability of such information, were it available, would, understandably, have a profound effect on underwriting individuals with a parental history of APKD. The possible application of this methodology to insurance evaluation is the *raison d'être* of our ACLI Genetic Testing Committee. At a frequency of 1:1000, APKD is the most common lethal hereditary disease with which we are confronted.

Whereas genetic means can exclude the diagnosis early in the life of individuals at risk, our other diagnostic techniques do not achieve reasonable certainty until the third or fourth decade of life. For those at risk, over age 19, who have normal urograms with nephrotomography and radionuclide imag-

ing, the chance of having inherited the responsible gene was claimed to be less than 5%.⁹ Although these investigators did not consider ultrasonography to be any more sensitive than these other two diagnostic techniques, most studies have concluded that the sonogram is the best screening method.¹⁰ Computed tomography, arteriography and renal biopsy are, of course, more accurate but not practical as a requirement for insurance.

In another cohort study of relatives defined at risk for APKD, ultrasound was diagnostic in 72% during the second decade and in 86% during the third decade.¹¹ Hence, a negative echo study beyond age 30 makes this diagnosis improbable or, at least, unlikely to be severe clinically. Even for those discovered to have APKD, the probability of being alive and *not* having end-stage kidney disease (ESKD) was 77% by age 50, 57% by age 58, and 52% by age 73.¹²

Although designated as kidney disease, APKD should, perhaps, be regarded as a systemic disorder in view of the frequent extrarenal manifestations variably expressed. Many other viscera may also be involved concurrently by cysts, especially so the liver in at least one-third of cases, but their organ function is not compromised significantly.

Mitral valve prolapse occurs in nearly 30% of such patients and other valve abnormalities are more common than in the general population.¹³ This has been attributed to an underlying defect in the extracellular matrix causing structural abnormalities of the heart valves, vascular tree, gastrointestinal tract and kidneys.¹⁴

Colonic diverticular disease is said to be more frequent. Association with intracranial aneurysms is well recognized, more so if there is a family history for these vascular lesions. Reported frequencies of 10 to 36% raises the question whether screening should be done routinely when there is a positive family history.^{15,16} Annuloaortic ectasia and abdominal aortic aneurysms are also more prevalent.

The course of APKD is highly variable. Of those more severely affected, clinical onset is usually in the third and fourth decades. It is characterized by flank pain and colic, hematuria, nocturia, hypertension, abdominal masses and slowly aggressive azotemia terminating in end-stage after another decade or so,¹⁷ although, uremia has been described in the mid-thirties. These overt manifestations clearly render such individuals unacceptable risks.

Although uncontrolled hypertension will accelerate cardiovascular disease, the major impact of APKD on mortality

is renal failure. At 8% of such cases, APKD is the third most common cause of ESKD.¹⁸

Nevertheless, it should be emphasized that it is not unusual for the affected individual to remain asymptomatic, unaware of his APKD, and retain a normal life span.¹⁷ With a reported incidence as low as one per 500 autopsies,³ it is evident that many die of unrelated causes. Prognosis for subjects with this hereditary disorder is much better than suggested by earlier reports.¹¹ Those reports focused on symptomatic patients referred for treatment. Thus, the incidental discovery of APKD in an older patient or a positive family history in an uninvestigated young adult should not preclude consideration for insurance coverage. Moreover, if, and when, the need arises,

the availability of chronic dialysis and renal transplantation^{19,20} can extend the uremic patient's survival for many years. Hence, a diagnosis of APKD in an asymptomatic individual or its potential inheritance no longer need carry the ominous connotations of earlier years.

Our traditional approach has been to decline all cases of APKD, whether actual or potential, symptomatic or asymptomatic. It would appear that such a stance is now outmoded. An appreciable number of applicants may indeed be insurable at relatively modest ratings, bearing in mind the additional risk of a fatal ruptured cerebral aneurysm. An estimated one-half million Americans harbor polycystic kidneys and not all should be denied insurance coverage.

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