Polycystic Kidney Disease:
Diagnosis and Treatment

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A Manuscript submitted in partial fulfillment of the requirement for the degree
Master Of Nursing
Washington State University
Intercollegiate College of Nursing
Spokane, Washington
December 2002
To the faculty of Washington State University:

The members of the committee appointed to examine the Intercollegiate College of Nursing research requirements and manuscript of JENNIFER RACHEL FROST find it satisfactory and recommend that it can be accepted.

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Acknowledgements

I would like to thank everyone who has supported me in one way or another in completing this manuscript and fulfilling my goals in pursuit of my chosen profession. My gratitude goes out to those who graciously served on my committee for this clinical project.

Dr. Margaret Bruya, committee member, who, at the beginning, served as my advisor and guided me through the difficult time of going back to school after eleven years. Having gone to nursing school outside the United States, I was unaware of what to expect and the challenges that I would have to face. Margaret made it easy to venture back into the academic portion of the program.

Dr. Lorna Schumann, committee member and mentor. Lorna has always been available to help with any questions I may have. She has been a great example of what an exemptional Nurse Practitioner and educator should be.

Dr. Curtis Wickre who has been a wonderful resource and mentor. Knowing how occupied he is with the many responsibilities that come with his profession, he has given his time and energy with a considerable amount of regard and attention to educate and guide me through this process.

Finally, I would like to thank my husband, Richard, and daughter, China who have been understanding and supportive throughout this educational experience. They were there to share my frustrations, fears as well as my triumphs and accomplishments. I could not have done it without their reassurances and encouragement.
Abstract
Polycystic Kidney Disease
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Washington State University, December 2002

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Cystic kidney disease describes several conditions in which fluid-filled cysts form in the kidneys. Polycystic Kidney Disease or PKD is the most common, life-threatening genetic disease (Breuning & Peters, 2001). These cysts can grow so large and numerous rendering the kidneys unable to function normally.

Screening individuals at risk is important especially with regards to reproduction. There is no cure for PKD. Treatment options include medications or surgery for pain control, management of hypertension and treatment of infection. Dialysis is usually necessary at end-stage renal disease. Kidney transplantation is also an option for persons with advanced PKD. It is important that health care providers recognize the implications of this disease. Referral to a nephrologist should be done in a timely manner.
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Introduction

The renal cystic disorders include a relatively large group of diseases typified by the formation of one or more fluid filled cavities within the kidneys. These cavities, or cysts, may arise in all parts of the kidney. In their formative stage, they may be slightly larger than a single nephron structure, which is a few microns in diameter, or they may be so large as to compress the abdominal viscera (Fick & Gabow, 1994). Renal cysts may be idiopathic; they may compromise renal function and cause renal failure, may be associated with non-renal disorders, may be acquired, and may be precursors of malignancy. Confusion has arisen because the terminology used to describe this large group of diseases is imprecise at times and multiple cysts do not necessarily denote a heritable condition or a specific syndrome.

Polycystic kidney disease (PKD) is one of the most common hereditary disorders, affecting 12 to 15 million people worldwide, a number greater than the combined number of those with cystic fibrosis, sickle cell anemia, muscular dystrophy, hemophilia and Down’s syndrome (Gardner & Grantham, 1985). Medical care costs for diagnosis and treatment exceeds $200 million a year (Gabow, 1993). The cysts are presumed to be what directly or indirectly cause the symptoms that are characteristic of the disease. Though they start out microscopic in size, averaging 3-5 mm. in diameter, some of these cysts can become quite large, up to 10 cm. and contain several hundred cc’s of fluid (Bayrak-Toydemir & Pergament, 2001).

PKD affects all ages, races and sexes. More than 600,000 Americans are affected by the disease [(See Figure 1) (Bhandari, Brownjohn, Eardley, Dedi & Turney, 2001)]. It is the fourth leading cause of kidney failure (See Figure 2). Significant proportions of persons who carry the gene for PKD are not aware of it nor do they have suggestive symptoms. Therefore, persons may have PKD for years before it is diagnosed (Gardner & Grantham, 1985, Gabow, 1993).
There are two genetically different types of PKD namely, Autosomal Recessive PKD (ARPKD or sometimes called “Infantile PKD”) and Autosomal Dominant PKD (ADPKD often called “Adult Onset PKD”). Autosomal recessive PKD requires a defective gene from both parents, and is thus, much more uncommon. The autosomal recessive PKD gene has been identified on chromosome 6 (Bayrak-Toydemir & Pergament, 2001). Although only an estimated one in every 10,000 to 20,000 children is born with the disorder, the odds of developing it are one in four when both parents carry the gene (De Bruyn & Gordon, 2000). A child born with autosomal recessive PKD usually dies within the first one or two months of life. The children who survive need a transplant by grade school. Sometimes, the condition may not present until adult life, and even then, the hepatic component of the disease may be the most prominent feature.

Cysts usually occur at a later age in autosomal dominant PKD, yet it has been noted to occur in younger subjects at risk, thus, making “autosomal dominant PKD” a more appropriate designation than “adult onset PKD” (Gardner & Grantham, 1985). Children of families affected with autosomal dominant PKD have a 50% chance of inheriting the disease. In children, the most helpful information in differentiating autosomal recessive PKD from autosomal dominant PKD is the presence of bilateral renal cysts in one parent (Gabow, 1993). There is a correlation between symptom severity, age of symptom onset, and the gene location involved (see Table 1). There are at least three, and maybe more genes that can cause autosomal dominant PKD. The first gene called PKD1 has been found on chromosome 16 and accounts for about 85 to 90% of known autosomal dominant PKD patients. The mean age of onset of end-stage renal disease (ESRD) is 53.0 years in PDK1.
The second gene known as PKD2 has been linked to chromosome 4, and accounts for 5 to 15% of known autosomal dominant PKD cases. Patients with PKD2 are free of symptoms 75% of the time and only 7.5% progress to ESRD. PKD2 is said to be clinically milder, with symptoms presenting later in life, and is associated with living longer and having a lower risk of progressing to renal failure and complications. The mean age for ESRD is 69.1 years in PKD2 (Arnaout, 2001, Hateboer, Dijk, Bogdanova et al., 1999).

In approximately 25 to 40% of cases, PKD occurs in people without a family history of the disease. This can represent a new mutation, or more often, particularly in non-PKD1 families, result from such slow progression that affected family members die from other causes before there are any manifestations of PKD (http://www.utdol.com).

The third gene is called PKD3, but no genomic locus has been found. The difference in gene defect location does not completely account for the variability seen in autosomal dominant PKD since a variation in severity is also seen within the same family, where presumably one would expect similar disease outcomes. Health care providers should advise their patients about the availability of prenatal screening and the importance of screening asymptomatic relatives for the purpose of identifying individuals at risk and aid in making informed medical decisions concerning long-term prognosis (Berner & Nates, 2001).

**Definition and Pathophysiology**

PKD is an abnormal condition in which the kidneys are enlarged and contain many cysts, which are sacs of fluid. It is a systemic disorder characterized by cyst formation in ductal organs, and by gastrointestinal, cardiovascular and musculoskeletal abnormalities (Gabow, 1993). Autosomal recessive PKD typically presents in infancy, although there are childhood and adolescent forms that are generally less severe (See Figure 3). The disease is usually discovered
neonatally or perinatally. Documentation of fetal renal cysts during pregnancy will not predict the clinical course (Gabow, 1993). About 60% of affected children die within the first month of life, and in those that live past one month, the mean survival is approximately six years (Berner & Nates, 2001). Hypertension, edema, impaired liver and kidney function, and frequent urinary tract infections are prevalent in autosomal recessive PKD. Affected children are at risk for hepatic fibrotic disease and are treated with dialysis and renal transplantation when ESRD occurs (Berner & Nates, 2001). Death is usually secondary to renal failure (Levine et al., 1997).

Autosomal dominant PKD is hard to overlook (See Figure 4 and 5). In the fully developed state, the kidneys are massively enlarged. Autosomal dominant PKD is usually recognized clinically after the childbearing period, and the defective gene relish nearly complete penetrance, thus ensuring a steady number of affected patients. These patients suffer in several respects. The disease causes renal failure in about 50% of affected patients, an awareness that is causing unending stress in young patients at risk (Gardner & Grantham, 1985). Cerebral aneurysms are found in a significant proportion of patients with autosomal dominant PKD, and their rupture can lead to sudden death in an otherwise asymptomatic vigorous person (Bayrak-Toydemir & Pergament, 2001).

Damage to the kidneys is caused by structural deformities caused by the enlarging cysts, as well as by elevations in blood pressure. Cysts can also form in other organs such as the liver and pancreas (Levine et al., 1997). At one point, it was thought that as the cysts grew, they simply crowded out the healthy kidney cells. However, researchers are looking at other interactions between cystic cells and their neighboring normal kidney cells to suggest a definitive basis for renal failure (Gardner & Grantham, 1985).
Pathogenetic theories of cyst formation and growth

The genetic locus of autosomal dominant PKD (PKD1) is located on the short arm of chromosome 16 which encodes a large protein, polycystin, the exact function of which is not yet known (Arnaout, 2001). It is thought that this resulted in mislocation of the Na+/K+ - ATPase pump to the apical surface, where epidermal-growth-factor receptors are located, instead of the basolateral cell surface of the kidney, such that fluid is secreted only into the cyst contributing to its growth (Gabow, 1993, Arnaout, 2001). The genetic locus of autosomal dominant PKD2 (PKD2) is located on long arm of chromosome 4, which also encodes a protein homologous to polycystin (Arnaout, 2001).

Tubular lumen destruction theory

Several theories have been suggested that contribute to cyst formation. Autosomal dominant PKD cysts are heterogeneous in size, and lined by a single layer of epithelium. Arnaout (2001) stated that cysts begin as focal ballooning of tubules with a majority losing tubular connection altogether. In this theory, obstructions of tubular lumen arise from early focal tubular dilation producing a retrograde increase in intraluminal pressure from either epithelial proliferation or an abnormally compliant basement membrane (Gabow, 1993, Woo, 1995, Arnaout, 2001, Calvet & Grantham, 2001). In many respects, the cyst’s epithelium also behaves as a benign neoplastic tissue. Endogenous growth factors, hormones, and cytokines may influence the growth of these cysts, as well as a decreased response to inhibitors of proliferation (Gabow, 1993, Arnaout, 2001, Calvet & Grantham, 2001).

Basement membrane theory

A second theory is that abnormally compliant basement membranes are thought to be present on a genetic basis, since there are some biochemical and functional differences from normal
nephrons. The basement membrane changes also precede tubular cell proliferation (Woo, 1995, Arnaout, 2001).

Extracellular matrix theory

Another theory is that the extracellular matrix is altered early in the course of renal cystogenesis, but it has not yet been possible to determine whether the cell proliferation or the matrix abnormality is the primary event coded by the mutated gene (Calvet & Grantham, 2001). The matrix abnormality ultimately leads to interstitial inflammation and fibrosis and it is these factors that may decide whether or not renal function is irreversibly compromised (Gardner & Grantham, 1985, Gabow, 1993, Woo, 1995). In addition, the systemic abnormalities associated with PKD are compatible with a defect in the composition of the extracellular matrix (Gabow, 1993).

“Double-hit” theory

Yet another theory suggests a “double-hit” mechanism for PKD cyst formation. The “first hit” is the mutation of the PKD gene inherited from a parent who has PKD. The “second hit” occurs in individual epithelial cells of the kidney. Each cyst forms as a result of a newly acquired mutation in a single clone from a kidney epithelial cell (Calvet & Grantham, 2001, Arnaout, 2001). The high rate at which “second hits” must occur to account for the large number of cysts observed suggests that unique structural features of PKD genes may be responsible for its mutability. A portion of the PKD gene is believed to cause the formation of a triple helix structure. Triple helix structures have been shown in other studies to cause increased mutations (Germino, 1997). The “double-hit” process may explain the wide variation in PKD severity seen within families, where affected individuals have the same mutation and might otherwise be expected to exhibit similar severity of this disease (Calvet & Grantham, Germino).
Still, independent variables such as increased levels of cyclic AMP, increased levels of angiotensin II, increased Na+/K+ - ATPase activity, and potassium depletion, are thought to stimulate cellular proliferation. Therefore, modification of these potential stimulants by certain therapeutic maneuvers may delay cellular proliferation (Gardner & Grantham, 1985, Torres, Young, Offord & Hattery, 1990, Calvet & Grantham, 2001).

Since only about 10% of all nephrons have cysts and since only 15-30% of cysts have a connection with their parent nephron, these cysts must grow by means other than filtration. Fluid is said to accumulate in cysts via two mechanisms. In a morphologic study of an individual cyst, it was noted that as the cyst grew, it detached from its tubular connection allowing it to be isolated from the glomerulus (Calvet & Grantham, 2001). The cyst then fills with glomerular filtrate that escapes reabsorption by tubule segments afferent to the cyst (Gabow, 1993). However, in most cysts, fluid accumulates due to the active transport of sodium chloride (NaCl) resulting from the abnormal location of the Na+/K+ - ATPase pump in cystic epithelium (Gabow, 1993). This secretion is apparently modulated by signal transduction processes, one of which involves stimulation of the intracellular production of cyclic AMP (Gardner & Grantham, 1985, Ye & Grantham, 1993, Calvet & Grantham, 2001). Thus, fluid is moved into the cyst cavity, rather than out of it by osmosis (Gabow, 1993).

Cysts were also observed to not only absorb fluid, but secrete them as well (Arnaout 2001). Ye and Grantham (1993), as well as Grantham et al. (1989) concluded in their studies that cysts from patients with PKD can secrete fluid from within, and can be increased in size by unidentified secretagogues in the cyst fluid, suggesting cyst enlargement susceptibility to pharmacologic intervention. This fluid secretion was apparently coupled to the active transport
of solutes, which is consistent with the hypothesis that cAMP is an important intermediary promoting increased transport of fluid (Calvet & Grantham, 2001).

Progression to Renal Failure

Several possibilities have been suggested to explain the progressive deterioration of renal function in PKD patients. Factors related to progression are gender, history and hypertension. Progressive arteriolar lesions and pressure from enlarging cysts may lead to atrophy of surrounding tissue and interstitial fibrosis (Ritz, Geberth, Zeier & Waldherr, 1993). Secondary environmental factors may trigger cell growth and more cyst formation. Infection and associated endotoxin might enhance cyst growth in genetically susceptible animal host. Apoptosis or programmed cell death may be enhanced in cystic and non-cystic parts of autosomal dominant PKD kidneys (Woo, 1995, Amaout, 2001, Calvet & Grantham, 2001). Uncompensated apoptosis and the inability to regenerate new nephrons would then result in progressive loss of renal tissue.

Clinical Features

In the early stages of PKD, many people with the disease show no symptoms. As PKD progresses, symptoms may gradually start to develop such as hypertension, fatigue, frequent urination, headaches, or urinary tract infections and low back or flank pain. On the average, patients begin to notice these symptoms, somewhere between ages 20 and 40 (Breuning & Peters, 2001). Somehow, females have a slower rate of decline in glomerular filtration rate (GFR) in early renal insufficiency, compared to males. However, once GFR fell below 25 mL/min per 1.73 m², the rate of decline of GFR was equivalent in males and females (National Institute of Diabetes, Digestive and Kidney Diseases, National Institute of Health [NIDDKD, NIH], 1995). This finding was supported by Choukroun et al. (1995), who also stated in their
report that the age at ESRD in male patients was lower when the disease was transmitted by mother than by father, while no significant effect of the gender of the affected parent was apparent in female patients.

Abdominal or flank pain is the most common symptom of autosomal dominant PKD. Pain may be caused by cyst hemorrhage, a renal calculi usually resulting from cyst hemorrhage or urinary stasis, and rarely, pain is caused by a renal tumor. Non-renal causes of pain such as diverticular disease, or ruptured abdominal aortic aneurysm must be considered to minimize the risk of further renal damage during therapeutic measures. The pain from polycystic kidneys is often described as dull, nagging or aching; however, it can be colicky. Differentiation among these complications is important for management purposes (Gardner & Grantham, 1985).

When the disease becomes more advanced, it begins to noticeably affect several internal organs. In patients with diffuse bilateral cysts of the kidney, the presence of liver cysts is virtually pathognomonic of autosomal dominant PKD. Cysts develop in the liver in about 60% of PKD patients, but the liver itself almost never fails because of them (Levine et al., 1997). In a few patients, renal enlargement can cause chronic pain due to the size and location of the cysts. The pancreas develops cysts in about 10% of PKD patients, but almost never causes problems. Incidence of ovarian cysts related to autosomal dominant PKD is unknown (Gabow & Fick, 1994).

Non-cystic manifestations involve several organ systems as well. The heart’s mitral valves weaken resulting into prolapse in about 26% of PKD patients. An enlarged heart is common in older individuals possibly from prolonged hypertension. Moreover, angiotensin, which is a major mediator of hypertension, may affect the growth of cysts, which will eventuate in the compression of surrounding renal parenchyma by the cysts (Gabow, 1993). Intracranial
aneurysms, one of the most devastating extrarenal manifestation of PKD, occur anywhere from 0 to 41% of PKD patients (Bayrak-Toydemir & Pergament, 2001, Ferri, 2003 Gabow, 1993) supporting the theory of having an abnormal extracellular matrix or perhaps an altered cerebral vascular reactivity in PKD (Gabow, 1993). The principal non-cystic gastrointestinal manifestation is colonic diverticula, the pathogenesis of which includes a component of abnormal extracellular matrix, which again, further supports a role for such an abnormality in PKD (Gabow, 1993).

In the final stages of PKD, the major symptom is loss of kidney function. By this time, numerous cysts have formed throughout both kidneys and have grown to a point where they are crowding out, or causing destruction of normal or non-cystic kidney tissue (De Bruyn & Gordon, 2000). As this occurs, the kidneys lose their ability to filter blood. ESRD is characterized by symptoms that result from the inability of the body to filter out waste products from the blood, leading to uremia (Bayrak-Toydemir & Pergament, 2001).

The degree and time of onset of symptoms of PKD can vary greatly from one family to the next and can also vary within families. This makes it difficult to determine beforehand what an individual's PKD course will be like (Breuning & Peters, 2001).

The younger a patient is diagnosed with polycystic kidney disease, the earlier end-stage renal disease is likely to develop (http://www.utdol.com). Because of the high variability of PKD, it is difficult to identify when someone will reach ESRD. Some people reach this stage very early in their lives and others may never lose all of their kidney function, even if and when they reach the age of 80 or more. ESRD is treatable through dialysis or transplantation. Unfortunately, neither of these treatment options cures the disease (Gardner & Grantham, 1985).
Diagnosis

Cystic renal disease is a wide spectrum of conditions and imaging forms a crucial aspect in the evaluation of the client. The ultimate diagnosis of cystic kidneys requires clinical, genetic, radiological and pathological information. A precise diagnosis is important for prognosis, treatment and genetic counseling, although this may not be possible at presentation (Bayrak-Toydemir & Pergament, 2001).

Affected patients typically present with a positive family history, flank pain or renal insufficiency, and large kidneys with multiple bilateral cysts on ultrasonography or CT scanning [(see Figures 6, 7 and 8) (Higgins & Fitzgerald, 2001)]. There are three ways to diagnose PKD: ultrasound, computed tomography, or magnetic resonance imaging (Levine et al., 1997). Ultrasound is valuable in many circumstances. There are situations where physicians cannot get information in any other way, such as with pregnant women and there are no side effects to ultrasound (Bayrak-Toydemir & Pergament, 2001). Ultrasound is the most reliable, inexpensive and non-invasive way to diagnose PKD (Gabow, Ikle & Holmes 1984, Bayrak-Toydemir & Pergament). However, other conditions require integration of many imaging modalities, when certain conditions are being considered, such as distinguishing between autosomal dominant PKD versus tuberous sclerosis in a young child. Similar imaging features may be seen in more than one condition and appearances may change with time stressing the need for a comprehensive imaging work-up at presentation and at follow-up (De Bruyn & Gordon, 2000).

Occasionally, a CT scan may detect smaller cysts that cannot be found on ultrasound (Basaria & Mehta, 2000, Bayrak-Toydemir & Pergament 2001). In some institutions, the abdominal CT scan has become the screening test for severe abdominal pain when renal stones, appendicitis, or diverticulitis is suspected. Delayed reactions are exceedingly rare. For urgent studies, the results
should be known in a relatively short period of time (Higgins & Fitzgerald, 2001). Computed
tomography has been reported to be more sensitive than ultrasonography, particularly for
complications of PKD. It is advisable to use CT in persons in whom ultrasound findings are
suspicious, but do not yield a conclusive diagnosis (Gabow, Ikle & Holmes, 1984, Levine, et al.,
1997).

In 1986, a radiologist named Bosniak proposed a classification system (see Table 2) to serve
as a point of reference in the diagnosis, classification, and characterization of cystic lesions
(Leder, 1999). The classification system is a 4-part categorization for cystic renal masses, based
on CT findings. The Bosniak classification appears to be the best system currently available for
the noninvasive classification of cystic renal masses (Leder, 1999).

For the routine evaluation of renal masses, MRI currently carries no significant advantage
over CT scan (Leder, 1999). In certain situations, however, such as a patient with contrast
material allergy, an elevated serum creatinine level or a hyperdense renal cyst, MRI is either
safer or more accurate than CT scan. Additionally, MRI can assess venous involvement in renal
cell carcinoma (Wolf, 1998).

At present, PKD cannot be diagnosed by a single blood test. However, in some situations
where it is important to have a diagnosis, as in potential living related kidney donor evaluation,
and ultrasound and CT scans are normal, gene linkage analysis can be done to determine a
definitive diagnosis in the at-risk individual. It is done by flanking DNA probes that are adjacent
and tightly linked to the PKD1 gene locus on chromosome 16. This technique, which is
available in certain molecular diagnostic and genetics laboratory, has greater than 99% accuracy
for PKD1 and can be performed prior to radiologically evident cysts. The DNA test will also
allow effective prenatal testing for those of procreative age who carry the diseased gene and
might wish to have genetic counseling in order to make decisions about reproduction (De Bruyn & Gordon, 2000, Bayrak-Toydemir & Pergament, 2001). With this comes a need to assess the psychological impact on patients’ families. The early testing of individuals at-risk can establish a diagnosis years before symptoms appear. These linkage studies will not detect non-PKD1 disease. Identification of the PKD1 gene may be replaced in the future by direct analysis of the gene (http://www.utdol.com).

The CRISP study (Consortium for Radiologic Imaging Studies in Polycystic Kidney Disease) is now underway involving three centers; the Mayo Clinic, Emory University Medical Center and the University of Kansas Medical Center. New imaging techniques involving magnetic resonance imaging (MRI) have been developed that will be able to detect small changes in renal size, as well as cyst growth, and to detect cysts smaller than have been detectable by conventional ultrasound techniques. This would allow for therapeutic interventions such as new pharmacologic therapies to be tested in individuals over a much shorter period of time than previously anticipated (http://www.pkdcure.org).

**Differential Diagnosis**

It is necessary to differentiate PKD from a simple cyst or renal carcinoma. Simple renal cysts are the most common cystic abnormality encountered in human kidneys (See Figure 9). Simple cysts are a frequent random observation on ultrasound or with CT scanning. They may be solitary or multiple. A single layer of flat epithelium lines the wall of simple cysts and the cyst fluid is chemically similar to an ultrafiltrate of plasma. Autopsy studies indicate that one or more cysts may be present in one-half of persons greater than 50 years of age. The prevalence of simple cysts increases with age, especially in males (Ravine, Gibson, Donlan & Sheffield, 1993). These cysts are rarely infected and are not associated with decreasing renal function. Hematuria
is a rare complication of simple renal cysts, and, if observed, should prompt the suspicion of renal cell carcinoma (Levine et al., 1997). Sonographic diagnosis of possible autosomal dominant PKD in those known to be at 50% risk due to a positive family history varies with age (see Table 3). Concurrent complicating renal cell carcinoma is uncommon (Arnaout, 2001)

Sensitivity and specificity

DNA analysis is the gold standard for the diagnosis of autosomal dominant PKD, especially in people less than 20 years of age. Onset of clinical disease is relatively uncommon in young children, and screening is most often performed in subjects over the age of 20 (http://www.utdol.com). Ultrasound and computed tomography are accurate methods for diagnosis of PKD; however, the ability to diagnose quickly and noninvasively both renal and associated extrarenal involvement makes ultrasound the procedure of choice for diagnosis, screening, and follow-up (Lawson, McClennan & Shirkhoda, 1978). Cysts, as small as one to one and a half centimeter in diameter can be detected by ultrasonography and half a centimeter by CT scanning.

Standard guidelines for diagnosing in patients with a family history of autosomal dominant PKD require bilateral involvement with a total of at least three to five cysts. This criterion may be too stringent for young children and too lax in older patients who may have multiple simple cysts. A study in which ultrasonography was correlated with DNA linkage for the PKD1 gene suggested that the criteria used should be modified for age to minimize both false negative and false positive results (http://www.utdol.com).

Ultrasound diagnosis is highly dependent on age. Under the age of 30, ultrasound imaging method is not recommended as a routine diagnostic procedure because ultrasound may not depict cysts smaller than one centimeter. Although ultrasound has a reported sensitivity of 93% for
individuals younger than 30 years old suspected of having PKD type 1, if there is clinical suspicion of PKD type 2 in individuals younger than 30 years, further studies such as gene linkage analysis should be considered (Nicolau et al., 1999). Ultrasound becomes 100% reliable in excluding PKD2 in family members at 50% risk over the age of 30, with an overall specificity of 100% (Demetriou et al., 2000, Nascimento et al., 2001).

With the PKD type 1 abnormality, the probability of a positive ultrasonogram in the 50% of children who have the disease is estimated to be 8%, below the age of 10, and increases to almost 100%, by the age of 30. Thus, a negative ultrasound cannot definitely exclude the disease until the patient is older than 30 to 35, although the false negative rate at age 20 is only about 4%. Sensitivity is higher with CT scanning, because of its ability to detect smaller cysts; thus the age at which a negative CT test virtually excludes the presence of PKD is about 20 to 25 (http://www.utdol.com).

The above statistics do not apply to patients with non-PKD1 defect, who form cysts at a later age. However, missing the diagnosis is less important in this setting, since the incidence and rate of progressive disease is much less. Thus, a negative ultrasound, above the age of 30 may not exclude the eventual development of polycystic kidney disease, but it is associated with a very low risk for late renal failure (http://www.utdol.com). The likelihood that a patient has autosomal dominant PKD is diminished, if by the age of 60, they have not yet developed multiple kidney cysts.

Cost Effectiveness

Ultrasound is generally agreed upon to be the best screening method, because it is the easiest and most cost-effective (Bayrak-Toydemir & Pergament, 2001). A CT scan uses radiation and often requires dye, and thus is not warranted until ultrasound has been attempted. However, both
of these methods are unable to detect very small cysts, and are more accurate when the disease has progressed somewhat (Ferri, 2003). CT usually costs less than MRI and is generally better tolerated by patients (Higgins & Fitzgerald, 2001).

A person with a family history of PKD should acquire a gene linkage study. This study is expensive, over $2,200 per family and requires that family members give blood samples. The test is highly accurate, and effectively creates a genetic map of the family showing whether or not the person in question has the gene for PKD (Gardner & Grantham, 1985). Families will then be able to make health care decisions based on this knowledge and participate earlier in reducing and treating complications associated with PKD.

Treatment Plan

A treatment or cure for PKD is not yet available, although research is being done. Many supportive treatments can be done to help prevent or slow down loss of kidney function. Medicines are used to treat hypertension, but there is no consensus about the type of antihypertensive therapy that is most appropriate for patients with autosomal dominant PKD. A PKD patient with hypertension exhibits a faster progression to ESRD and is the most important, potentially treatable variable in the disease (Ecder, Edeiletein, Fick-Brosnahan & Johnson, 2001). The disease is characterized by high renin activity as a result of activation of the renin-angiotensin-aldosterone system. Chapman, Johnson, Gabow & Schrier (1990) studied the plasma renin activity and aldosterone concentrations in hypertensive patients with PKD and compared those levels to patients with essential hypertension alone. The researchers found that the renin-angiotensin-aldosterone system is stimulated more in PKD patients, perhaps due to renal ischemia caused by cyst expansion, and is then an important factor in the initiation of hypertension in PKD. Angiotensin-converting enzyme inhibitors, as well as angiotensin II
receptor blockers may therefore be highly effective for blood pressure control (NIDDKD, NIH, 1995). Careful renal function monitoring must be continually carried out (Ferri, 2003).

Lower tract infection occurs at any one time in 30-50% of patients with autosomal dominant PKD. Such infections herald upper tract disease, which, in turn, may accelerate cyst formation and decline in renal function. Cyst infection is difficult to treat, and only a few antibiotics penetrate the cysts, such as Trimethoprim / Sulfamethoxazole (Septra, Bactrim), Ciprofloxacin (Cipro), Gentamycin (Garamycin) and Chloramphenicol because of their lipid solubility and high pKa [(The pKa is that pH at which the concentrations of the ionized and un-ionized forms are equal) (Breuning & Peters, 2001, Ferri, 2002, Gabow, 1993)]. Prompt treatment is essential, since infection may progress rapidly. Nephrectomy is necessary in advanced cases. Prolonged therapy may also be necessary with drugs that are filtered and secreted to assure cyst fluid and renal parenchyma (Gardner & Grantham, 1985).

Various medications are available to help with the pain of PKD. These medications must be taken as recommended by a health care professional, due to the possibility of damaging the kidneys and the potentially addictive effect of these scheduled drugs (Gardner & Grantham, 1985). Flank pain and hematuria, which are often recurrent, severe and disabling, may result from cyst hemorrhage, occurring randomly as part of the natural history of the disease or resulting from minor trauma to the enlarged kidney (Levine et al., 1997). Cyst hemorrhage may be severe enough to require blood transfusion, renal artery embolization or nephrectomy. Pain can usually be controlled also by restriction of activity. Surgery is sometimes used to “unroof” cysts, either by an open abdominal or laparoscopic procedure (Gabow, 1993). The criteria for surgical intervention is failure of conservative management, as defined by chronic pain that interferes with activities-of-daily living or decreases the quality of life, disability, and/or narcotic
dependence (Berner & Nates, 2001, Gabow, 1993). Cyst decompression by needle aspiration initially reduces pain, but the effect is short-lived, lasting only three to six months. This temporary effect is believed to be due to the re-accumulation of fluid in needle aspirated cysts. According to Elzinga et al. (1991), the probability of being painfree was 80% at one year and 62% at two years following cyst decompression. The preoperative and one-to-three month postoperative serum creatinine and renal function measured by GFR were not significantly different following the procedure. Cyst decompression surgery does not have a deleterious effect on renal function, but it also does not slow the progression of autosomal dominant PKD associated renal failure (Bennett, Elzinga, Golper & Barry, 1986, http://www.utdol.com, Gabow, 1993). The probability of being pain free from renal pain at 18 months was 33 ± 17% for cyst aspiration and 81 ± 12% for surgical intervention, both with an added benefit of hypertension control (Bennett, Elzinga, Golper & Barry, 1986). Nephrectomy is not indicated solely for the relief of pain in autosomal dominant PKD, since it is imperative to preserve as much functioning renal tissue, as possible.

Patients experiencing kidney failure must undergo dialysis. Cysts decrease in size with dialysis. Sixty percent of the patients with PKD will need either dialysis or a kidney transplant to survive. Kidney transplant organs are usually cadaveric and there is no recurrence of disease in the allograft (Bayrak-Toydemir & Pergament, 2001). Although routine removal of native kidneys is not recommended particularly in terms of erythropoiesis and residual renal function, most transplant programs have adopted the selective approach to bilateral nephrectomy prior to renal transplantation when it is warranted, as in patients with active or recent infections. The elective post-transplant removal of polycystic kidneys is not recommended because of the theoretical hazard of operating on an immunosuppressed host. Dialysis and transplantation can
prolong life for up to 14 years. Although current patient survival rates with dialysis are equivalent to those obtained with transplantation, renal transplantation offers more complete patient rehabilitation and is also more cost-effective (Gardner & Grantham, 1985).

Exercises such as swimming, walking and biking are well tolerated. However, activities that are potentially harmful to the kidney, such as contact sports, must be avoided. Patients need to consult their health care provider before engaging in an exercise regimen. It is also important not to become too dehydrated during any physical activity. Patients with PKD should drink plenty of water, but avoid caffeine, as it is thought to increase cyclic AMP production (Gardner & Grantham, 1985).

Most women with PKD, approximately 8%, have successful and uneventful pregnancies (Gabow, 1993). But there are some women with PKD who have an increased risk of complications for themselves and their unborn fetuses. This includes women who also have hypertension and decreased kidney function prior to pregnancy (Bayrak-Toydemir & Pergament, 2001). Women who have PKD with hypertension develop life-threatening pre-eclampsia in 40% of pregnancies and are worthy of increased surveillance. It is essential to provide genetic counseling to women with autosomal dominant PKD who are considering pregnancy or who are pregnant (Gabow, 1993).

Many studies suggest that some treatments slow the rate of kidney disease in PKD, such as protein intake modification, but further research is needed before these treatments can be widely implemented (Breuning & Peters, 2001). However, this does not mean that it is wise to eat excessive amounts of protein. According to the Modification of Diet in Renal Disease Study Group, a diet that includes a moderate amount of protein is recommended for patients with PKD, and was found to be marginally associated with a slower progression of renal disease (NIDDKD,
At present though, no specific diet is known to prevent cysts from developing in patients with PKD. Reducing sodium intake helps control hypertension. Low fat and moderate caloric intake are always recommended to avoid becoming overweight (Breuning & Peters, 2001).

Cardiovascular pathology and infections account for 90% of deaths of autosomal dominant PKD patients treated with dialysis and after renal transplantation. The prevalence of intracranial aneurysm in autosomal dominant PKD patients along with the increased mortality risk suggests early identification and intervention. The definitive diagnosis of intracranial aneurysm has been by MR angiography (Levine et al., 1997). Analysis done by Levey, Pauker & Kassirer (1983) showed that arteriography should not be carried out routinely to screen for intracranial aneurysm in PKD patients. They also state that arteriography’s benefit only exceeds one year, if the prevalence of aneurysm exceeds 30%, if the surgical complication rate is 1% or less, and if the patient is under 25 years of age. Given this marginal advantage, most patients would probably opt to avoid an invasive, uncomfortable, and expensive test.

Finally, regular health care maintenance is important. This includes prompt treatment of a bladder or kidney infection, bed rest when hematuria is first noted, and a healthy lifestyle with regard to not smoking, exercise, weight control and salt intake (Gardner & Grantham, 1985). It is also important to have other health problems taken care of as well, such as cardiovascular and pulmonary symptoms. Nurse practitioners in particular, should be able to recognize the clinical features of PKD and know when to refer to a specialist. Regular appointments with the nephrologist can help keep track of the problems caused by PKD.
Conclusion

PKD is a common disease that has improved medical services and diagnostic techniques to make earlier detection possible. It is appropriate to no longer speak of adult and childhood PKD since existence of autosomal dominant PKD in children and autosomal recessive PKD among adults have been acknowledged. The terms autosomal dominant and autosomal recessive PKD are preferred.

Survival of patients has improved in recent years. Several factors are responsible, among them the advent of dialysis and renal transplantation. Increasing attention is being paid to the extrarenal abnormalities associated with autosomal dominant PKD because improved patient survival is likely to result in less frequent morbidity and mortality from these associations (Levey, Pauker & Kassirer, 1983). Study and awareness of these associated disorders is important not only to the clinician, but also to researchers since they provide a valuable insight into future productive areas of therapy. If newer, noninvasive tests are available and proven to be reliable to screen for extrarenal manifestations such as cerebral aneurysm, these tests will then be warranted in patients with PKD.

The findings that cysts absorb and secrete fluid implies that the rate of cyst enlargement may be inhibited by pharmacologic intervention, as well as strategies to promote absorption of liquid from cysts by eliminating the effect of endogenous secretagogues (Ye & Grantham, 1993). Modification of potential stimulants, such as hypokalemia, by certain hormonal or therapeutic maneuvers, may also delay cellular proliferation. Chronic hypokalemia is known to cause tubular hypertrophy and dilation in some species and may contribute to cystogenesis (Torres, Young, Offord & Hattery, 1990). Understanding the roles of the PKD gene products and their
cellular events will enable researchers to design small molecules that can be used therapeutically to interrupt cyst formation and growth (Calvet & Grantham, 2001).

Another area for future research would be to look into the relative absence of autosomal dominant PKD, as a cause of ESRD in the black population. This is particularly intriguing, since blacks have a much higher incidence of ESRD secondary to other renal diseases such as diabetes mellitus, glomerulonephritis, and hypertension.

Effective genetic counseling could have a significant impact on the future incidence of the disease. Of course, to be truly effective, all affected individuals at-risk need to be identified. This implies family screening by genetic linkage analysis which is very expensive and is not covered under any insurance plan. While on the surface this concept could be cited with enthusiasm, some caveats are in order. First of all, identification of an individual as being affected effectively stigmatizes him or her from the point-of-view of medical and life insurance, job placement, and even attracting a mate (Gabow, 1993). The possible personal issues of feelings of depression or unworthiness or alternatively an inappropriate devil-may-care attitude must be considered.

The area of practice in nephrology for nurse practitioners must be limited to areas of expertise based on education and training, with the degree of independent practice also based on education and training. Nurse practitioners provide a large amount of care for ESRD patients in a relatively independent fashion under the supervision and interaction with nephrologists. Nurse practitioners who specialize in nephrology have a significant impact on extending the quality and quantity of patient care provided by the nephrologist equivalent to the education, experience, capabilities and productivity. A holistic patient-friendly approach is facilitated and nurse practitioners are considered an integral part of the collaborative model. The use of nurse
practitioners provides the potential for augmenting patient care, satisfaction, and access to care especially as the ESRD population continues to increase by 9% per year (Bolton, 1998). It provides an avenue for potential cost reduction in nephrology, while maintaining quality of care. Advanced practice nurses can be instrumental in assuring that quality patient care is delivered across the ESRD continuum through several different roles: clinician, educator, consultant, researcher, administrator, and case manager.

PKD has been with us for a long time. It will likely remain a significant cause of renal failure for some time. Family support groups have become popular to help individuals deal with grief, through proper support from those who suffer from the same ailment. Recognition and early referral to a nephrologist is key in preventing complications and assuring prompt care to those who are afflicted.
Table 1. Types of PKD

<table>
<thead>
<tr>
<th>PKD type</th>
<th>When disease presents</th>
<th>Genetic data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autosomal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dominant PKD</strong></td>
<td>After the childbearing period between the ages of 20-30, but occasionally in infancy.</td>
<td>Chromosome 16 (16p 13.3) which encodes a protein called polycystin</td>
</tr>
<tr>
<td>PKD1</td>
<td></td>
<td>Chromosome 4 (4q 21-23) which encodes a protein homologous to polycystin</td>
</tr>
<tr>
<td>PKD2</td>
<td></td>
<td>No locus identified</td>
</tr>
<tr>
<td>PKD3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Autosomal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Recessive PKD</strong></td>
<td>Typically presents in infancy, although there are childhood and adolescent forms that are generally less severe.</td>
<td>Chromosome 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Autosomal recessive means that a mutated gene has to be passed to the child from each parent.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If both parents are carriers of the abnormal gene, then there is a 25% chance that a child will develop the disease.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infantile PKD is therefore uncommon.</td>
</tr>
</tbody>
</table>

**Table 2.** Bosniak classification system

<table>
<thead>
<tr>
<th>Category</th>
<th>Type of mass</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category 1 lesion</strong></td>
<td>benign simple cysts</td>
<td>do not require further evaluation unless signs or symptoms develop</td>
</tr>
<tr>
<td><strong>Category 2 lesions</strong></td>
<td>minimally complicated cysts</td>
<td>followed radiographically in all but the least complicated cases because a few may subsequently reveal cancer</td>
</tr>
<tr>
<td><strong>Category 3 lesions</strong></td>
<td>truly indeterminate lesions</td>
<td>approximately 50% are malignant and surgical exploration is recommended in healthy patients</td>
</tr>
<tr>
<td><strong>Category 4 lesions</strong></td>
<td>any solid renal mass that enhances with intravenous contrast material</td>
<td>presumed malignant unless criteria for a &quot;definable benign solid mass&quot; are met or unless determined otherwise by an invasive procedure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age of Subject</th>
<th>Requirements for PKD Diagnosis</th>
</tr>
</thead>
</table>
| 30 years and younger   | - at least two cysts (unilateral or bilateral).  
|                        |  - simple renal cysts are uncommon in these patients and are rarely multiple or bilateral.  
|                        |  - previous requirement of bilateral involvement will miss approximately 11% of cases of autosomal dominant PKD in this age group |
| 30-59 years of age     | - at least two cysts in each kidney.  
|                        |  - requirement for bilateral involvement helps distinguish autosomal dominant PKD from the less common localized cystic disease of the kidney |
| 60 years and older     | - four or more cysts in each kidney to minimize false positive results due to multiple simple cysts which are relatively common in these patients.  
|                        |  - presence of extrarenal manifestations and/or enlarged kidneys can help establish the diagnosis of autosomal dominant PKD in problem cases |

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Special Instructions</th>
<th>Check-In</th>
<th>PREP</th>
<th>Exam Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal ultrasound</td>
<td>NPO after MN, drink two 10 oz. glasses of water 1 hour prior to exam. For peds (kidney only), ultrasound followed by *VCUG-NO prep</td>
<td>15 minutes</td>
<td>Drink two 10 oz. glasses of water 1 hour prior. For pediatric patients, drink one 10 oz. glass of water. DO NOT void.</td>
<td>15-20 minutes</td>
</tr>
<tr>
<td>Abdomen ultrasound</td>
<td>May take meds. with a small amount of water.</td>
<td>15 minutes</td>
<td>NPO after MN. If test is in a PM slot-- clear liquid breakfast, no dairy products, then NPO.</td>
<td>About 30 minutes</td>
</tr>
<tr>
<td>Abdomen/Pelvic ultrasound</td>
<td>May take meds. with a small amount of water.</td>
<td>15 minutes</td>
<td>Do both abdomen and pelvic prep: drink clear liquids but don't eat and DO NOT void.</td>
<td>30 min-1 hour</td>
</tr>
<tr>
<td>Abdomen CT (Diaphragm to Iliac crest)</td>
<td>Scheduled in am (preferably). If pt. is ≥60 y.o. they MUST have a serum creatinine w/in 30 days. Make sure pt. has not had a UGI or BE w/in the last 7 days. If pt. is taking &quot;Glucophage&quot;, they can't take it for 4 hours prior to scan and 48 hours after.</td>
<td>30 minutes</td>
<td>NPO after MN. If test is in a PM slot: clear liquid breakfast between 8-9 am then NPO after breakfast. If there is oral dye, and especially if it's barium, patients are instructed to drink plenty of liquids. The oral dyes used for CT are much less dense than those used in the upper GI series, and the potential of impaction is much less. Those who have had the IV dye should have no postprocedural problems.</td>
<td>30 minutes</td>
</tr>
<tr>
<td>Renal MRI</td>
<td>N/A</td>
<td>30 minutes</td>
<td>NPO 4 hours prior</td>
<td>1 1/2 hours</td>
</tr>
</tbody>
</table>

* VCUG - Vesicourethrogram - checks for reflux
Table 5. Differential Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple simple cyst disease</td>
<td>The majority of simple idiopathic cysts are found coincidentally while the patient is undergoing radiographic imaging for a different problem. These cysts are generally asymptomatic, are usually located on the outer portion of the kidney cortex, and contain clear fluid that has the composition of plasma ultrafiltrate. In most instances ultrasonography and CT are used once a cyst has been discovered to differentiate between benign and malignant renal masses (Wolf, 1998).</td>
</tr>
<tr>
<td>Calyceal cysts</td>
<td>The most common type is composed of calcium oxalate (most are opaque; 73%), calcium phosphate (8%), and magnesium ammonium phosphate or &quot;struvite&quot;. The uncommon type consists of diammonium calcium phosphate or magnesium phosphate. There are rare cysts made up of cystine (faintly opaque; 1%) or urate (lucent; 7%) and xanthine (Ferri, 2003).</td>
</tr>
<tr>
<td>Wilm's tumor or nephroblastoma</td>
<td>This arises from embryonal renal tissue (nephroblastomatosis). It is characterized as large and only 10% are calcified. Four to ten percent of tumors can be bilateral. It metastasizes to the lungs and par-aortic nodes (Ferri, 2003).</td>
</tr>
<tr>
<td>Tuberous Sclerosis or Bourneville disease</td>
<td>An autosomal dominant disease presenting with the classic triad of seizures, retardation and adenoma sebaceum. It is characterized by calcified subependymal hamartomas* and uncalcified tubers in cerebral cortex of the kidneys. The enhancing lesion transforms into a malignant giant cell astrocytoma. It is associated with skin lesions, angiomyolipoma and an increased risk of renal cell carcinoma (Ferri, 2003).</td>
</tr>
<tr>
<td>Von Hippel - Lindau Syndrome or retinocerebellar angiomatosis</td>
<td>An autosomal dominant disease with variable penetrance. The most frequent cause of death is hemangioblastoma, cerebellar being the most common and also medullary and spinal. It is characterized by cortical renal cysts (75%), cysts in virtually any organ, and renal/liver hemangioma/adenoma (Wolf, 1998). Mean age of onset is 26. Up to 70% of patients who live to 60 will develop renal cell carcinoma. Therefore, after age 20, yearly screening with ultrasound and/or CT every 3 years in patients with cysts is appropriate.</td>
</tr>
<tr>
<td>Multiple cystic dysplasia (MCD)</td>
<td>MCD is the most severe form of renal dysplasia. It is the most common cause of palpable abdominal mass in infants. It is unilateral (90%; fatal if bilateral). The ureter/renal artery is absent or hypoplastic. It is not associated with other cysts or with periportal fibrosis (De Bruyn &amp; Gordon, 2000).</td>
</tr>
</tbody>
</table>

* hamartoma – a tumor resulting from new growth of normal tissues. The cells grow spontaneously, reach maturity, and then do not reproduce. Thus, the growth is self-limiting and benign.
Table 6. Sensitivity and specificity of diagnostic exams for PKD

<table>
<thead>
<tr>
<th>Criteria: Bilateral cysts w/ at least 2 cysts in one kidney</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Ultrasound</td>
<td>93% at age 15-29 years 100% at age ≥ 30</td>
<td>100′%</td>
</tr>
<tr>
<td>Renal CT scan</td>
<td>No data available</td>
<td>No data available</td>
</tr>
<tr>
<td>Genetic linkage analysis</td>
<td>&gt; 99%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 7. Charges for diagnostic exams for PKD based on national average

<table>
<thead>
<tr>
<th>Examination</th>
<th>Technical Charge</th>
<th>Professional Fee</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Abdominal ultrasound</em></td>
<td>323</td>
<td>75</td>
<td>398</td>
</tr>
<tr>
<td><em>Dedicated renal CT</em></td>
<td>804</td>
<td>165</td>
<td>969</td>
</tr>
<tr>
<td><em>Abdominal MR with gadolinium</em></td>
<td>1,173</td>
<td>311</td>
<td>1,484</td>
</tr>
<tr>
<td><em>Genetic linkage analysis</em></td>
<td></td>
<td></td>
<td>2,200</td>
</tr>
</tbody>
</table>

Values are in United States dollars

### Table 8. Simple cyst vs. renal carcinoma vs. PKD

<table>
<thead>
<tr>
<th>Radiographic method</th>
<th>Simple cysts</th>
<th>Renal carcinoma</th>
<th>PKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVP tomograms</td>
<td>Smooth contour</td>
<td>Irregular contour</td>
<td>Calcium within mass Isodense</td>
</tr>
<tr>
<td></td>
<td>No calcium</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypodense</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Smooth wall</td>
<td>Irregular wall</td>
<td>Irregular walls</td>
</tr>
<tr>
<td></td>
<td>Echolucent</td>
<td>echogenic</td>
<td>Bilateral enlarged, lobulated kidneys</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>with multiple cysts of varying sizes</td>
</tr>
<tr>
<td>CT</td>
<td>Smooth wall</td>
<td>Irregular wall, infiltrative</td>
<td>Can reveal hyperdense cysts</td>
</tr>
<tr>
<td></td>
<td>Water density</td>
<td>Solid density</td>
<td></td>
</tr>
<tr>
<td>Cyst fluid</td>
<td>Straw colored, clear</td>
<td>Bloody or dark colored</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytology negative</td>
<td>Cytology positive</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1.

PKD patients w/ ESRD in the US

No. of patients

<table>
<thead>
<tr>
<th>Modality</th>
<th>Female Black</th>
<th>Male Black</th>
<th>Female White</th>
<th>Male White</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>604</td>
<td>518</td>
<td>2,232</td>
<td>2,342</td>
</tr>
<tr>
<td>PD</td>
<td>84</td>
<td>42</td>
<td>480</td>
<td>376</td>
</tr>
<tr>
<td>TX</td>
<td>279</td>
<td>272</td>
<td>3141</td>
<td>3839</td>
</tr>
<tr>
<td>UNK</td>
<td>13</td>
<td>11</td>
<td>79</td>
<td>94</td>
</tr>
</tbody>
</table>

Figure 2.

Incident counts of reported ESRD patients: by Primary Diagnosis from 1996-1999

**Figure 3.** The cut surface of kidneys with recessive polycystic kidney disease (RPKD) is shown here.

Source: Copied with permission from Edward C. Klatt, MD. Professor and Academic Administrator, Florida State University, College of Medicine. The Internet Pathology Laboratory for Medical Education. Pathology of Renal Cystic Diseases. http://medlib.med.utah.edu/WebPath/TUTORIAL/RENCYST/RENCYST.html#5
**Figure 4.** These markedly enlarged kidneys are seen in the retroperitoneum of an adult with dominant polycystic kidney disease (DPKD).

Source: Copied with permission from Edward C. Klatt, MD. Professor and Academic Administrator, Florida State University, College of Medicine. The Internet Pathology Laboratory for Medical Education. Pathology of Renal Cystic Diseases. http://medlib.med.utah.edu/WebPath/TUTORIAL/RENCYST/RENCYST.html#5
**Figure 5.** The cut surface of a markedly enlarged kidney from an adult with dominant polycystic kidney disease (DPKD) shows very large cysts that can be filled with clear fluid or filled with recent or organizing hemorrhage.

Source: Copied with permission from Edward C. Klatt, MD. Professor and Academic Administrator, Florida State University, College of Medicine. The Internet Pathology Laboratory for Medical Education. Pathology of Renal Cystic Diseases. 
http://medlib.med.utah.edu/WebPath/TUTORIAL/RENCYST/RENCYST.html#5
Figure 6. Polycystic kidney disease involving one kidney.

Source: Copied with permission from Eileen M. Bailey, Program Manager, International Center for Postgraduate Medical Education. The Radiology Information Network. (http://www.radinfonet.com/cme/krinsky2/images)
**Figures 7 and 8.** Gadolinium-enhanced scans performed to look for enhancement. These images reveal slightly enhanced cortical tissue; the remainder of the kidney is completely replaced by simple cysts. The scans confirm that the left kidney is completely normal.

Source: Copied with permission from Eileen M. Bailey, Program Manager. International Center for Postgraduate Medical Education. The Radiology Information Network. (http://www.radinfonet.com/cme/krinsky2/images)
**Figure 9.** Very common in adult kidneys seen at autopsy are one or several simple renal cysts. These cause no problems.

Source: Copied with permission from Edward C. Klatt, MD. Professor and Academic Administrator, Florida State University, College of Medicine. The Internet Pathology Laboratory for Medical Education. Pathology of Renal Cystic Diseases. http://medlib.med.utah.edu/WebPath/TUTORIAL/RENCYST/RENCYST.html#5
Figure 10. Normal fetal kidneys.

Source: Copied with permission from Edward C. Klatt, MD. Professor and Academic Administrator, Florida State University, College of Medicine. The Internet Pathology Laboratory for Medical Education. Pathology of Renal Cystic Diseases. http://medlib.med.utah.edu/WebPath/TUTORIAL/RENCYST/RENCYST.html#5
Figure 11.

PKD patients w/ ESRD in Washington state

Subjective data: Hematuria, flank pain, dysuria, suprapubic discomfort, and positive family history.

Objective data: Mass palpated in peritoneal area, (+) hematuria on dipstick, hypertension, (+) UTI on urine microscopy, patient w/ an affected family member has an incidental finding of multiple renal and/or hepatic cysts during abdominal imaging.

Medical history, Family history, Physical exam, urinalysis

Urine dipstick results

RBC casts or dysmorphic RBCs present

Renal parenchymal disease

Do Imaging techniques
Ultrasound (less expensive) and no contrast or radiation exposure
≤ 30 YO must have 2 cysts or > in 1 or both kidneys
30-59 YO must have at least two cysts in each kidney
60 YO and over must have at least 4 cysts in each kidney.

Offer genetic linkage analysis
Type 1 & Type 2 chromosomal location of genetic mutation.

Refer for renal evaluation; send renal laboratory tests/films.

Normal RBCs with no casts

No pyuria

Refer for urologic evaluation

Pyuria

Check urine chemistry; treat for UTI

Follow hematuria to resolution
REFERENCES


