PKD PATIENT HANDBOOK

Understanding and living with autosomal dominant polycystic kidney disease

PKD FOUNDATION
Polycystic Kidney Disease

PKD FOUNDATION
Polycystic Kidney Disease

pkdcure.org
1.800.PKD.CURE

Originally Created by: Irene Duley, RN ANP and Patricia Gabow, MD
University of Colorado Health Sciences Center and Denver Hospital

Revised and updated 2015:
York Pei, M.D.
Director, Hereditary Kidney Disease Clinic
University Health Network
Toronto, Canada

Terry Watnick, M.D.
Baltimore PKD Research and Clinical Core Center
Associate Professor, Division of Nephrology
University of Maryland School of Medicine
Baltimore, Maryland

John Bissler, M.D.
Director, Division of Nephrology at St. Jude Children's Research Hospital and LeBonheur Children's Hospital
Professor of Pediatrics
Director, Tuberous Sclerosis Center of Excellence

This handbook made possible by an education grant from Otsuka America Pharmaceutical, Inc.

TABLE OF CONTENTS

Introduction

The purpose of this handbook is to provide information about autosomal dominant polycystic kidney disease (ADPKD). It will be useful to those who have the disease, those who are at risk due to an affected parent as well as invested family members and friends. It is not intended for those affected by autosomal recessive polycystic kidney disease (ARPKD). From here forward, ADPKD will be referred to simply as PKD.

WHAT IS PKD?

PKD is a genetic disease (passed from an affected parent to their child) causing uncontrolled growth of cysts in the kidney. A normal kidney is the size of a human fist and weighs about a third of a pound. PKD kidneys can be much larger and weigh many pounds each. The number of cysts can range from just a few to many. The size of the cysts can range from a pinhead to as large as a grapefruit.

Although the primary sign of PKD is cysts in the kidneys, there are other symptoms that can occur in various areas of the body. See Table 1 on next page for a list of common signs and symptoms of PKD.

Approximately 10 percent of people diagnosed with PKD have no family history. This means PKD has developed due to a spontaneous (new) mutation. Once a person has PKD, even through a spontaneous mutation, they have a 50 percent chance of passing it on to each of their children. See the genetics section on pg. 46 for more information.

How common is PKD?

PKD occurs in approximately 1 in 500 to 1 in 2000 live births affecting more than 600,000 Americans and 14.2 million people worldwide. It affects all racial and ethnic groups equally.

How will I feel if I have PKD?

Early in the disease, there are generally no symptoms at all. In fact, many people are never diagnosed with PKD because they have few or no symptoms. Often the first sign of PKD is high blood pressure, blood in the urine or a feeling of heaviness or pain in the back or abdomen. Sometimes the first sign may be a urinary tract infection or kidney stones.

How do I find out if I have PKD?

A physician is alerted to the possibility of PKD in three different settings:

- Family history of PKD
- Signs and symptoms that commonly occur in PKD
- Renal cysts are found in imaging tests

A positive family history is known in about 75 percent of patients with PKD. This is helpful to identify other at-risk family members. In general, the signs and symptoms of PKD are not specific enough to for your doctor to make the diagnosis. For example: PKD symptoms like back pain and/or high blood pressure are common in patients both with and without PKD and so are not enough for a definitive diagnosis.

Table 1

Common symptoms of PKD may include the following:

SYMPTOMS

- **Kidney cysts**
- **Enlarged kidney(s)**
- **Liver cysts**
- **Hypertension (high blood pressure)**
- **Back and/or side (flank) pain**
- **Blood in the urine**
- **Frequent urinary tract infection**
- **Kidney stones**
- **Kidney failure**

NON-KIDNEY RELATED COMPLICATIONS

Cardiovascular

- Mitral valve prolapse (floppy valve)
- Brain aneurysms: local bulging of the wall of blood vessels in the brain
- Aortic aneurysm: local bulging of the wall of the aorta
- Left ventricular hypertrophy: thickening of the heart muscle

Gastrointestinal

- Liver cysts with severe liver enlargement in a minority of patients (mostly female)
- Pancreatic cysts
- Diverticula (outpouchings or weakened areas) in the colon
- Diverticulitis (infection of the outpouchings) of the colon

Other

- Cysts in other organs such as seminal vesicles or epididymis (occurs in about 40% of males, can cause infertility in rare cases)
- Hernias of the abdomen
- Splenic cysts

Currently, there are three main tests that are used to screen for PKD:

1. **ultrasound**
2. **computed tomography (CT)**
3. **magnetic resonance imaging (MRI)**

Ultrasound is the most common and least costly screening method for PKD. There are accepted standards for ultrasound testing to determine if you have PKD. These standards include the number of cysts visible, age, and family history.

CT and **MRI** scans are considered to be more sensitive than ultrasound. CT scans, however, involve radiation or may also require iodinated contrast dye which, can be toxic to the kidneys. CT scans or MRIs may be used to look at complications like bleeding into a cyst or a suspected kidney stone. They may also be used detect small cysts as needed.

DNA Testing

DNA testing is available for PKD. There are two types of DNA tests: **Gene linkage testing** and **direct mutation analysis/DNA sequencing**. Gene linkage can determine if you have PKD with a 99 percent probability in those with family history. Linkage testing is not a direct analysis of the DNA sequence of the *PKD1* and *PKD2* genes (more information on PKD genes starting on page 48). Instead, it relies on the identification of certain "markers" in the DNA of several members of a family in which PKD has been diagnosed. For linkage analysis, blood samples must be obtained from the person being tested as well as several (typically three or more) family members including those affected and unaffected by PKD. A detailed family history is also required. The results are typically reported to all family members that provided blood samples for the analysis.

In contrast, direct **DNA sequencing requires** only a single sample from you (the person being tested). This method is a direct analysis of the DNA sequences of the *PKD1* and *PKD2* genes. It is private, and the results are only reported to you and your doctor.

Using very specialized scientific equipment, each of the nearly 17,000 "bases" of DNA are analyzed and the entire sequence is thus determined.

Should I be tested?

It is an important and impactful decision. Things to consider before being tested include:

- What will I do with the information once I have it?
- Will it prevent me from obtaining medical or life insurance?
- Am I better off knowing or not knowing?
- Can I financially afford the test?

Some people choose to remain undiagnosed but live a healthy lifestyle, eating well and monitoring their own blood pressure. They see the doctor often to monitor kidney function. If or when they have symptoms, they can revisit the decision to be tested. Our understanding of PKD is progressing every year. Early diagnosis may benefit from early therapies and could also mean you are eligible to participate in clinical studies.

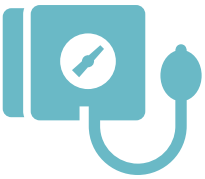
All these factors and more must be considered before making a decision.

This method is capable of identifying those changes in the sequence that cause PKD. It may be your only option if family members are unavailable or unwilling to participate in a linkage study. Each of these methods could be costly and should not be done without consideration of the pros and cons.

Health, life and disability insurance coverage vary between countries and may influence your decision to have genetic testing. In the United States, the Affordable Care Act has guaranteed health insurance for all regardless of any preexisting conditions. This does not guarantee life or disability coverage.

In the absence of an effective treatment or cure, a diagnosis of PKD should be carefully considered and discussed with your doctor.

WHAT ARE THE SIGNS AND SYMPTOMS OF PKD?

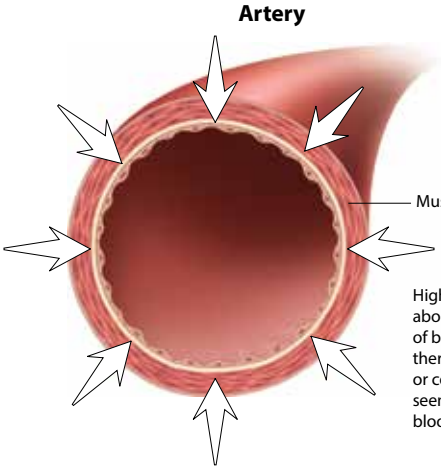


1. High blood pressure (Hypertension)

Blood pressure is a measurement of the force of the blood as it flows through the body. The pressure depends on the amount of blood and fluid in the body, the amount of blood the heart pumps each second (cardiac output) and the degree in which blood vessels are constricted or enlarged. This is similar to the force it takes to get water through a garden hose. The pressure depends on how much water is going through the faucet and how narrow the hose is (Fig. 1).

Blood pressure measurements have two parts, recorded as millimeters of mercury (mm Hg) – for example: 120/80 mm/Hg (read as 120-over-80). The top/first number is the **systolic blood pressure**, which measures the pressure when the heart is pumping. The bottom/second number is the **diastolic pressure**, which is the measurement of the pressure when the heart is relaxing between beats.

Figure 1



High blood pressure, or **hypertension**, affects about 60-70% of people with ADPKD. Control of blood pressure is complex, but in general there is either an increase in cardiac output or constriction of blood vessels. In ADPKD, it seems more likely that constricting of the blood vessels is responsible.

High blood pressure, or **hypertension**, affects about 60 – 70 percent of PKD patients and begins early in the course of the disease. Half of PKD patients who have normal kidney function have hypertension. It is more common in men than in women. Twenty to 30 percent of children with PKD also have hypertension. Many times, the increase in blood pressure is the first sign of PKD. Patients with high blood pressure generally have larger cystic kidneys than those with normal blood pressure.

High blood pressure needs to be treated aggressively. If not treated, hypertension causes further damage to the kidneys, enlarges and thickens the heart muscle, and increases the risk for strokes and other cardiovascular events.

Much has been learned to understand how hypertension occurs. In general, there is either an increase in cardiac output or constriction of the blood vessels. In PKD, enlarging cysts may press on blood vessels in the kidney which increases activity of the **renin-angiotensin-aldosterone system**.

HALT-PKD Study

In fall of 2014, a team of researchers announced the results of a national study on PKD and hypertension. The results concluded that:

- **Rigorous blood pressure control, early in the disease, could slow cyst growth in ADPKD**
- **Only one type of medication, is necessary to prevent hypertension**

Renin is an enzyme produced in the kidneys. It acts on **angiotensinogen**, a substance in the blood that forms a hormone called angiotensin. **Angiotensin** is a powerful constrictor of blood vessels; it also stimulates the production of **aldosterone**, which causes the body to retain salt and lose potassium.

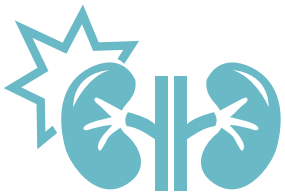
In ordinary circumstances, the kidneys make renin when blood pressure is low and the kidneys sense they need more blood flow. This is considered a protective mechanism. In PKD, cysts can press on blood vessels in the kidney, resulting in decreased blood flow to some parts of the kidney. Sensors in the nephron react as though the blood pressure in the kidney was low, triggering the secretion of renin, which in turn generates angiotensin, constricting the blood vessels, and causing high blood pressure.

There is a relationship between poor blood pressure control and progressive loss of kidney function in PKD. Even if you do not have hypertension, you should have your own blood pressure cuff to monitor and log your blood pressure regularly. This will give your doctor a better picture of your blood pressure over time.

Hypertension in PKD is often treated by a group of drugs called angiotensin converting enzyme inhibitors (**ACE inhibitors**) or angiotensin receptor blockers (**ARBs**). These two classes of drugs are usually the first drugs of choice because of the role of angiotensin in high blood pressure in PKD. In general, both types of drugs are safe and effective, however, in some patients with decreased kidney function, these drugs can make kidney function worse and can raise potassium levels.

Regardless of what kind of blood pressure medication is used, the most important thing is to have your blood pressure at or near the normal range of about 110/70 to 130/80. There are many choices of very good medications to treat high blood pressure so you should work with your doctor to find the right one(s) for you. **Remember, a blood pressure medicine only works if you take it, so you need to have a regular, perscribed time to take your medicine every day so you don't forget.**

Although medication is important in treating blood pressure, in some individuals, non-drug methods can also help to lower blood pressure. **Living a healthy life-style including weight loss, exercise, and a low-salt diet are all an important part of staying as healthy as possible.**



2. Kidney pain

Abdominal, side (flank) or back pain in patients with PKD can be severe, signaling a sudden problem like bleeding into a cyst, cyst infection or passage of a kidney stone. Intense pain in this setting can also be due to non-kidney related causes such as vertebral disc herniation, ruptured liver cyst, passage of gall stones, or diverticulitis.

Chronic pain is one of the most common problems for patients with PKD. The pain is usually in the back or the side and occasionally in the stomach. It can be intermittent and mild requiring only occasional pain medicine such as acetaminophen (Tylenol). However, in a small number of patients with severe PKD, the pain can be constant and quite severe. For these patients, surgery may be needed.

If you have a few very big cysts causing the pain, they can be **aspirated** and **sclerosed** with chemicals that are injected into cysts. Sclerosis is done using an ultrasound or CAT scan to guide your doctor to insert a needle into the cyst(s), drain the fluid, and then coat the cyst wall with a sclerosing substance to remove the cyst's lining cells. If you have severe pain due to a greatly enlarged polycystic kidney, surgical approaches may also be considered. For example, **laproscopic cyst decortication** or **surgical nephrectomy** may be possible, especially if you are already on dialysis/end stage renal disease.

Pain is a very subjective feeling. Only the person feeling the pain can measure how bad it is. It is important to remember that pain frequency and tolerance vary greatly among individuals. Pain tolerance appears to be influenced by a person's cultural background, expectations, behaviors, physical and emotional health. For this reason, **pain clinics** that utilize biofeedback and support groups can be very helpful in managing your pain. Pain clinics are sometimes a division of the anesthesiology department of a surgical hospital. To find a pain clinic, talk with your doctor or nephrologist to be directed to one that can help you with your specific PKD pain needs.

3. Blood in the urine

More than half of patients with PKD will have blood in their urine (**hematuria**) at some point. The urine may look pink, red or brown. Passing small amounts of red blood cells in the urine that can only be seen under a microscope may also occur. This is called **microscopic hematuria**.

Hematuria is more common in an individual with large kidneys and high blood pressure. It is thought that the rupture of cysts or of the small blood vessels around cysts is the cause. Other causes could include kidney or bladder infection and kidney stones.

Blood in the urine can last for less than a day or may go on for days. Notify your doctor as soon as possible if you see blood in the urine. Bed rest, increased fluid intake, and acetaminophen (if there is pain) are the usual treatments. Avoid taking **non-steroidal anti-inflammatory drugs (NSAIDs)** like aspirin or ibuprofen as they may prolong the bleeding and could damage your kidneys. If the blood is going directly into a cyst, you may not have blood in the urine but pain could be severe.

Avoid taking non-steroidal anti-inflammatory drugs (NSAIDs), like aspirin or ibuprofen.

Key Terms

Chronic pain
constant;
long duration

Aspirated
draw fluid by suction

Sclerosed
hardened

Arterial embolism
interruption of blood flow due to a clot

Nephrectomy
removal of kidney by surgery

4. Urinary tract infection

A **urinary tract infection**, commonly called a UTI, is an infection caused by bacteria in the bladder, kidneys or cysts. Other names used for UTIs are **cystitis** for bladder infection and **pyelonephritis** when the infection is in the kidney.

The infection usually starts in the **bladder** but, if not treated, can progress up the **ureters** (the tubes from the kidneys to the bladder) and into the kidneys. Although both men and women can have UTIs, they are far more common in women because they have a shorter **urethra** (the tube that goes from the bladder to the outside).

UTIs are quite common in the general population but may be more frequent in those with PKD. There is an association between frequent UTIs and worsening kidney function. Both males and females with PKD are more likely to have an infection after a Foley catheter is placed in the bladder.

The most common symptom of a UTI, particularly if the infection is in the bladder, is pain or burning with urination and/or an urgent need to urinate even though only a small amount of urine is passed. When the infection is in the kidney or in a cyst, there may be fever, chills, back or flank pain.

You should notify your doctor if any of these symptoms occur so treatment can be started. Usually a **urinalysis** is done. This includes providing a urine sample to be screened to determine the type of bacteria that is causing the infection so the appropriate antibiotic can be prescribed.

Women who have frequent bladder infections may decrease or eliminate the rate of recurrence by:

- Wiping from front to back after urinating or a bowel movement. This prevents dragging bacteria from the anus and vagina to the urethral opening.
- Avoid taking baths.
- Drinking fluid prior to intercourse and urinating afterward. This can help flush out any bacteria that may have entered the urethra.
- For those who have frequent UTIs, antibiotics may be prescribed on a daily basis to prevent recurring infections.

5. Kidney stones

Kidney stones occur in about 20 to 30 percent of patients with PKD as compared to one to two percent in the general population. One reason kidney stones are more common may be due to cysts blocking the **tubules** (filtering part of the kidney; see page 25), preventing normal drainage. When the urine stays in one area longer than it should, crystals can form and cause kidney stones. **Uric acid** and **calcium oxalate** are the two most common types of crystals that lead to stones. Stones may also form in some PKD patients because of a decrease in **urine citrate**, a substance that prevents formation of kidney stones.

The symptoms of kidney stones include severe pain in the back, side or into the groin. Kidney stones are treated the same way in PKD patients as in non-PKD patients. Smaller stones can be passed with the urine; often there is blood in the urine during the passing process. In the case of bigger stones that cannot be passed, treatment with a machine using ultrasound waves, called a **lithotripter**, may be required to break the stones into smaller pieces for easier passage. If you have recurring stones, your doctor may order a 24-hour urine collection to analyze the composition of your urine.

WHAT DIAGNOSTIC TESTS ARE FREQUENTLY PERFORMED IN PATIENTS WITH PKD?

1. Blood tests

Creatinine is a waste product of muscle metabolism (the work the muscles do). The level of creatinine in your blood is a measure of kidney function. After creatinine leaves the muscles, it enters into the blood, then is filtered by the kidneys and ends up in the urine. There is always some creatinine in your blood and urine. When you lose kidney function, your kidneys do not clear creatinine from the blood as efficiently. This causes an increase of creatinine in the blood, which can be measured by a simple blood test. Creatinine level is the preferred measure of kidney function. There are a number of equations that can be used to estimate kidney function or glomerular filtration rate from serum creatinine (called estimated GFR or eGFR).

Normal blood creatinine is generally 0.6 to 1.4 mg/dl. When a person's blood creatinine goes up to 2.0 mg/dl, they have lost approximately half of their kidney function.

Blood urea nitrogen (BUN) is another measure of kidney function. Urea nitrogen is the waste product of dietary protein. If your kidney function is decreased, the urea nitrogen builds up in the blood. A number of factors including diet, protein intake, heart function and fluid status can affect your BUN, making it less preferred than creatinine.

The normal range for BUN is 6 to 15 mg/dl.

Liver function tests are also considered blood tests. Liver function is almost always normal even if there are cysts in the liver. If at some time your liver function tests are not in the normal range, your physician should look for a cause other than PKD.

2. Urine tests

White blood cells (WBC) in urine are normally present only in small numbers; some PKD patients do pass a few more. However, large numbers of WBCs in the urine suggest a **urinary tract infection**. If this happens, your doctor will culture your urine to determine if and what types of bacteria are present and from those results plan a course of action.

Red blood cells (RBC) in the urine is also called **hematuria**. Only a few RBCs are normally found in the urine, called microscopic hematuria. Sometimes with an episode of bleeding, there are so many RBCs that they color the urine pink, red or brown. About 50 percent of PKD patients will experience this at some point.

Protein in the urine, is also called **proteinuria**. Protein is normally found in the urine only in small amounts. About one-third of those with PKD pass protein into the urine, but it is usually less than a gram in 24 hours. If protein loss is greater than one gram in 24 hours, there may be another problem occurring in the kidney along with PKD.

24-hour urine collection. This test is done in combination with the blood creatinine test to determine kidney function, called **creatinine clearance** which is an approximation of the **glomerular filtration rate (GFR)**.

3. Imaging tests

Imaging Studies are those used to see the details of organs or blood vessels in the body.

Ultrasound is a test done with sound waves and does not require the use of radiation or contrast dye to be injected. Because it is safe and accurate, ultrasound is the most common imaging test done to screen for PKD and can be done safely in pregnant women.

Echocardiogram is an ultrasound of the heart. One of the uses of an echocardiogram is to image the valves of the heart. Your physician may order this test if he or she suspects you have **mitral valve prolapse (MVP)** (see page 16 for more information on MVP).

Computed Tomography (CT Scan) is a sophisticated form of x-ray. CT scans use radiation and may use contrast dye to visualize the organ or blood vessels being studied. Contrast dye can cause allergic reaction and also kidney damage in patients with moderate to advanced kidney failure. This imaging technique is very helpful to evaluate the complications of PKD, such as bleeding into a cyst or kidneys stones.
High-resolution CT scans may be under certain circumstances used to visualize the blood vessels in the brain. We no longer use this method to routinely screen for aneurysms.

Magnetic Resonance Imaging (MRI) takes pictures of the body using a magnet that puts a certain spin on atoms that exist in a person's body. It does not require radiation. A special dye called **gadolinium** may be used in some instances to improve visualization. This dye is retained in the body with moderate to advanced kidney failure and can cause a rare but serious complication called **nephrogenic systemic fibrosis (NSF)**. If you have kidney failure and are asked to undergo an MRI with gadolinium, make sure you discuss this concern with your doctor. Cysts are easily visualized with MRI and appear in better detail than ultrasound in following the course of PKD.

Magnetic Resonance Angiography (MRA) is a type of MRI that is used to visualize the blood vessels in the brain to screen for aneurysms. This is similar to an MRI scan, but does not use contrast dyes or radiation. MRA will be used if you are allergic to contrast dyes and/or iodine, or if you have lost kidney function. MRA is the recommended method for aneurysm screening.

Angiograms are procedures that utilize contrast dye injected into the blood vessels in order to clearly visualize them. An angiogram is usually recommended when an aneurysm is suspected when it is suspected that there is an aneurysm in a blood vessel in the brain. Angiograms may also be performed to look for blockages in heart vessels.

WHAT OTHER PROBLEMS ARE ASSOCIATED WITH PKD?

PKD can affect organs other than the kidneys (table 1 on page 7). The following list of potential problems may look long and overwhelming, but it is important to remember that most people do not have all of these problems. If you have PKD, you and your family should be aware of the following possibilities so you can play an active role in understanding and managing your own healthcare.

1. Liver cysts

More than eighty percent of patients with PKD develop liver cysts during their lifetime. Liver cysts can occur in those under the age of 30, but are usually small and detectable only by MRI scanning. The liver can remain normal in size with a few cysts or can become enlarged. Even with increased liver size from PKD, the amount of functional liver tissue remains more than adequate. This means it is highly unlikely that patients with severe **polycystic liver disease (PLD)** would develop liver failure.

Although not common, severe PLD can present with symptoms due to a "mass effect" (i.e. abdominal fullness, pain, early **satiety** (feeling full), ankle swelling and fluid accumulation within the abdomen). In the severe and symptomatic cases, cyst decompression may be needed. When a few very large cysts are present, additional surgical intervention may be recommended to take care of these cysts. Partial liver resection may be considered in selected cases. This should only be performed at specialized centers with experienced surgeons.

Liver cysts occur more often in women than men. Women develop liver cysts at a younger age and have more and larger cysts than men. Women with previous pregnancies have more numerous and larger liver cysts than women without any pregnancies. This observation suggests that female hormones may influence the development of liver cysts. Because estrogen may be a factor in liver cyst growth, the benefits of estrogen replacement therapy (ERT) and the risk of PLD must be carefully weighed. A Nurses' Health study has disproved any benefit of estrogen to prevent cardiovascular disease, however, estrogen replacement therapy is protective against osteoporosis and decreases vasomotor instability – a cause of hot flashes in post-menopausal women. Thus, the risk of estrogen for aggravating PLD against its potential benefits on post-menopausal symptoms and osteoporosis needs to be weighed. Work with all of your doctors (nephrologist, Ob/Gyn, and general practitioner) to determine what would be the best course for you.

Women with PKD who use estrogen after menopause should have a baseline ultrasound of their liver before they start ERT and every two years thereafter. This will help your doctor evaluate if liver cysts are increasing in number and/or size. It is unclear at this time if it is better to take ERT in pill form or by skin patch. Theoretically, the patch would be a better choice since oral therapy provides high concentrations of estrogen directly to the liver. Finally, there is no data looking at the effect of low-dose oral contraceptives on women with ADPKD. If you have significant PLD, you should discuss the use of these with your doctor.

One complication of PLD is liver cyst infection. Symptoms range from fever to pain in the upper right side of the abdomen. These symptoms need to be reported to your doctor as soon as possible. Treatments of an infected liver cyst usually require antibiotic therapy and occasionally needle drainage.

2. Mitral valve prolapse (MVP)

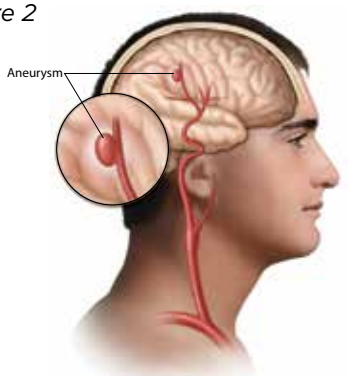
Mitral valve prolapse (MVP) is a condition where the valve separating the top and the bottom of the left side of the heart does not close properly. Sometimes this causes blood to leak back to the top part of the heart. This is called **regurgitation** and can be heard during an examination of the heart as a heart murmur. Symptoms that can be associated with MVP are palpitations, a feeling that the heart is running away or that there are extra beats in the heart and chest pain that is not associated with exercise or exertion. MVP occurs with increased frequency in patients with PKD as compared to the general population but rarely causes any significant clinical problems.

MVP is usually confirmed with an ultrasound of the heart valves called an echocardiogram. If MVP is present and causes palpitations that are bothersome, they can be treated with medications. Restricting the use of caffeine, alcohol, and cigarettes may be enough to decrease or stop the palpitations in many cases.

Rarely, an infection of a heart valve can occur as a complication of MVP. Although not a common occurrence, it can lead to destruction of the heart valve. Therefore, if you have MVP and a heart murmur, inform all doctors who care for you.

3. Aneurysm

Figure 2



An **aneurysm** is an outpouching in a blood vessel, which can leak or rupture.

Intracranial (brain) aneurysms occur in the blood vessels of the brain (Fig. 2). Symptoms can include sudden severe headache, pain in moving your neck, nausea/vomiting, difficulties with speech or movement and/or loss of consciousness. A ruptured aneurysm can be fatal. If you know you have an aneurysm (or have a family history of aneurysms) and you are experiencing any of these symptoms, you should call emergency services immediately.

Recent studies done in the United States have shown that PKD patients have about a 5 – 10 percent risk of developing intracranial aneurysms. This is about five times the risk of the general population. They also seem to cluster in certain families – that is, if a member of your family has an aneurysm or has ruptured an aneurysm, you may be at a higher risk of having an aneurysm yourself.

Because the risk for aneurysm is small, not everyone with PKD needs to be tested. However, people who have PKD and a family history of aneurysm should be tested, along with those whose job or hobbies would put them or others at risk if they lost consciousness (such as those who fly airplanes or drive buses). It is important to inform your doctor if you have a family history of intracranial aneurysms and/or if you have a high-risk occupation or hobby.

Aneurysms in other vessels such as the aorta have also been reported.

Magnetic resonance angiography (MRA) is the preferred test to screen for an aneurysm.

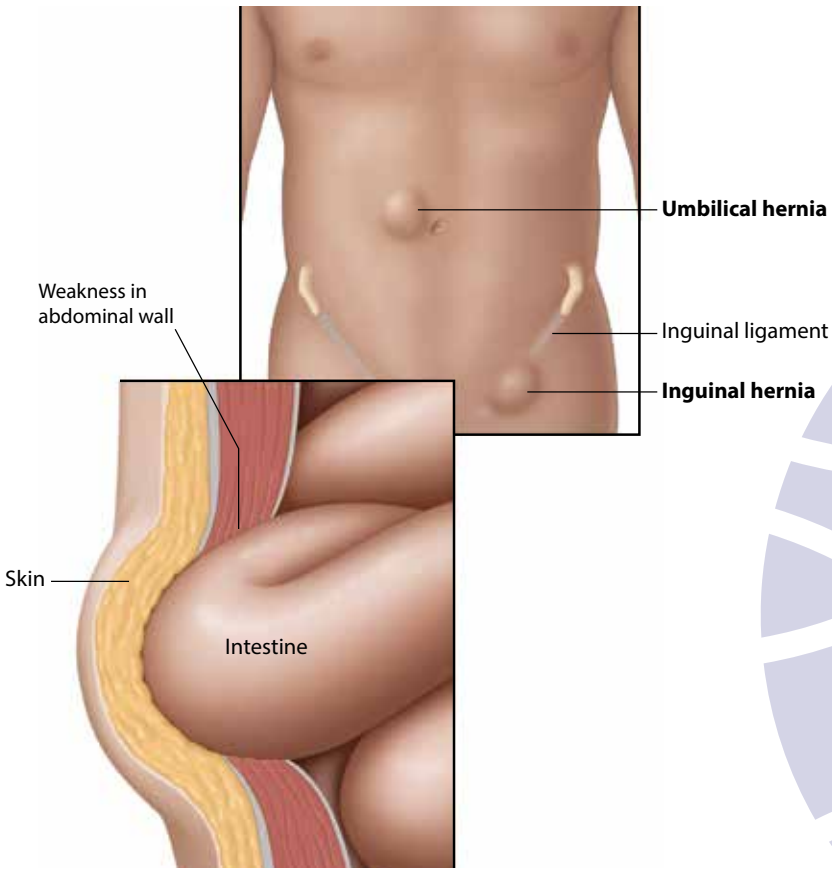
When an aneurysm is detected on an MRA, an arteriogram is usually performed. This test is more invasive and is done by putting dye directly into the blood vessels which will more clearly show if there is an aneurysm and how large it is.

If an aneurysm is found, surgical repair or a **therapeutic coil** (a device placed in the aneurysm by a **neuroradiologist**) may be recommended. If and when surgery is performed depends on the size and location of the aneurysm. Often an aneurysm can be repaired surgically before it leaks or ruptures. If you have had one aneurysm, you may develop others over time and need periodic follow-up. Recent studies suggest that patients with a positive family history of ICA should be screened with MRA every 5-10 years.

4. Hernias

Both inguinal and umbilical hernias are more common in those with PKD. Inguinal hernias are outpouchings in the area of the groin. Umbilical hernias are outpouchings at or near the navel. These should be surgically repaired if they are large or are causing problems, just as they would be in someone who does not have PKD (Fig. 3).

Figure 3



5. Diverticulosis

Diverticula are outpouchings on the large intestine (colon). It appears that patients with PKD who are on dialysis or have had a transplant have diverticula more often and also have more complications from diverticula, including infection, than patients with other kidney diseases.

Diverticulitis can occur when diverticuli rupture or become infected, requiring treatment with antibiotics. This is a rare occurrence.

WHAT SHOULD I DO TO TAKE BETTER CARE OF MYSELF?

Diet

Currently no specific diet has been proven to make your polycystic kidneys better or keep them from getting worse. It is, however, ideal to eat a balanced and healthy diet to maintain optimal body conditions. A healthy body is able to fight infection better, and bounce back faster. Accumulation of waste products filtered by your kidneys will build up in your blood as kidney function declines. At the more advanced stages of kidney failure (i.e. GFR <30-40 percent), significant accumulation of these waste products in your blood can cause symptoms of kidney failure.

Should I stop eating protein?

The major source of these waste products is the food you eat, especially protein. Therefore, when you have lost a significant amount of kidney function, a lower protein diet may be ordered by your doctor.

Studies from both animals and humans with chronic kidney failure have shown that eating large amounts of protein may accelerate the progressive decline of kidney function. However, the Modification in Diet in Renal Disease (MDRD) study done by the **National Institutes of Health (NIH)** looked at protein intake and kidney function. The results did not show any benefit of lowering protein intake in individuals with PKD. At this time, there is no convincing evidence to suggest protein restriction as beneficial unless you are in kidney failure. Despite all of this, many consider it unwise to consume a very high protein diet. If you have moderate to advanced kidney failure, however, a modest restriction may be appropriate. For more information, you should consult your doctor and a dietitian experienced with kidney disease and ideally knowledge of PKD (also known as a **renal dietician**).

Should I stop eating salt?

High blood pressure in PKD does not seem to be caused by salt intake. Regardless, excessive amounts of salt should be avoided and lowering dietarty salt may help in blood pressure control. This becomes important when people are on certain types of blood pressure medicine and when they have kidney failure.

Can I drink alcohol?

Light and/or occasional use of alcohol has not been shown to damage the kidneys or the liver. However, drinking three or more ounces of alcohol a day for many years has been associated with increases in blood pressure and can damage the liver.

Can I use tobacco?

Smoking increases the risk of heart disease and stroke and when paired with hypertension, the risks are even greater. Smoking also increases the risk of cancer.

Should I take extra vitamins to make sure I'm getting all the nutrients I need?

If you are maintaining a balanced and healthy diet, you typically will not need extra vitamins. Unlike food, vitamins are needed only in tiny amounts. Excess amounts of vitamin A, D and E can accumulate in your body and cause medical problems. Generally, if you feel you need extra vitamins, a one-a-day generic brand of vitamin is sufficient. Consult your doctor before taking extra vitamins of any kind. Because there is an increased incidence of calcium kidney stones in individuals with PKD, women with PKD should discuss with their doctor the proper amount of calcium needed. Limiting calcium in the diet will not prevent kidney stones in non-PKD patients and the beneficial effects of dairy product intake on skeletal and cardiovascular systems are well established.

How much fluid should I drink each day?

A chemical called cyclic AMP (cAMP) has been shown to promote growth of polycystic kidneys. In your kidney, cAMP is produced in response to a hormone, vasopressin, which is produced by the brain in response to not having enough water. Thus avoiding dehydration is thought to be prudent. In addition, generous water intake has the potential to suppress vasopressin production and decrease cAMP production in the kidney. Though there is no good data regarding this in humans with PKD, if kidney function is not impaired, water intake is typically safe. Therefore it seems reasonable to suggest intake of water with a goal of 2-3 quarts of urine output daily. Your urine should generally be pale in color. This will tend to suppress vasopressin production by the brain and cAMP production in the kidneys. In addition, it is generally suggested that PKD patients limit caffeine intake, since caffeine slows degradation of cAMP. Finally, generous water intake helps maintain a dilute urine and decreases the risk of kidney stones, which are seen at increased frequency in PKD patients.

It is important to understand that the benefit or risk of high water intake have never been formally studied in PKD patients, and therefore results cannot be predicted or guaranteed. In addition, as kidney function deteriorates, generous water intake can be problematic and even dangerous. Thus, it is important to discuss appropriate water intake with your doctor.

Table 2

Caffeine content of beverages:

Beverages	Serving Size	Caffeine (mg)
Coffee, drip	5 oz	110-250
Coffee, perk	5 oz	60-125
Coffee, instant	5 oz	40-105
Coffee, decaf	5 oz	2-5
Tea, 5-minute steep	5 oz	40-100
Tea, 3-minute steep	5 oz	20-50
Hot cocoa	5 oz	2-10
Coca-cola	12 oz	45

Will caffeine damage my kidneys?

There is no direct evidence that **caffeine** will damage your polycystic kidneys. However, studies of PKD cells grown in a lab have shown that caffeine-like substances promoted cyst growth in PKD. At this time, it may be wise to limit caffeine intake to less than 200 to 250 mg (i.e. two to three cups of coffee) a day.

What about potassium?

Potassium is essential to all living cells and is important for muscle and nerve functions in the body. It is found in most foods including legumes, whole grains, fruits, green vegetables, potatoes, meats, milk and yogurt. Although potassium is vital to the body, it is not wise to take potassium supplements in pill or liquid form without consulting your doctor and/or your renal dietician, especially if your kidney function is reduced.

What about calcium and magnesium?

In non-PKD settings, a deficiency of calcium and magnesium has been associated with high blood pressure. Dietary **calcium** and **magnesium** are best provided by dairy products and are important in maintaining a normal mineral balance as part of healthy diet.

Essentials for a balanced and healthy diet

Given the current obesity epidemic that is prevalent in all developed countries, the following provides a simple conceptual framework for a balanced and healthy diet:

Tips for a healthy diet:

- High fiber: fresh vegetables and nuts
- Carbohydrates: minimize intake of bread and pasta
- Protein: moderation of red meats
- Fat: moderate intake may actually decrease hunger drive (Olive oil in salad dressing to increase fat intake)
- Avoid: processed food and sugary drinks with fructose syrup
- Decrease food portion size if you are overweight

If you have moderate to advanced kidney failure, further modification of the above will be required and consultation with your doctor and a dietitian experienced with kidney disease is recommended.

DASH diet

Studies in high blood pressure patients without PKD have shown that the so-called DASH diet (Dietary Approach to Stopping Hypertension), which consists of lots of fruits and vegetables combined with low-fat dairy, may lower blood pressure. A diet based on these guidelines could also seem appropriate for you. Look in the resources section at the back of the book for web resources on the DASH diet. Talk to your doctor before significantly altering your diet.

Exercise and sports

Exercise is an important part of maintaining good, overall health. Regular exercise can decrease your blood pressure and stress as well as improve muscle strength, heart function and stamina. It can also enhance a sense of well-being. In general, you will do much better on dialysis and with a transplant if you are physically fit.

What kind of exercise is best?

There is no one best kind of exercise. The key is to find an activity that is comfortable for you and that you enjoy doing. Generally, PKD patients can do any activity they want unless they get blood in the urine or it causes back, flank or abdominal pain. The exercises that are least jarring to the kidneys include walking, swimming and biking.

Be sure to talk with your doctor before starting an exercise regimen, as he or she may have guidance about what will be most effective for you, or what to avoid. Remember to always keep well hydrated when exercising, and do your best to be active on a regular basis.

Are sports dangerous to my kidneys?

In general, most sports do not affect kidney function. However, PKD does present unique circumstances and so there are some issues that need to be considered. Given the unique nature of PKD, where kidneys are enlarged and cysts can rupture, there are some simple precautions to take. Contact sports where the kidneys may be traumatized (flank /side or lower back impact) should either be avoided or protective pads should be worn. Examples of these types of sports include football, rugby, basketball, hockey and particularly boxing or kickboxing. Horseback riding and cross-country biking are other sports with repetitive impact that could potentially cause issues with your kidneys. There is no evidence that these activities worsen renal function, but they can result in pain and/or blood appearing in the urine.

Types of Doctors

Internist
general practitioner (G.P.) or family doctor

Nephrologist
kidney specialist

Hepatologist
liver specialist

Transplant surgeon
doctor who performs transplants

Renal dietician
Nutrition and diet specialist focusing on kidney and dialysis patients

Pharmacist
Expert in drug chemistry and how drugs may interact with each other

Regular visits to your doctor

What kind of doctor should I see?

In addition to your general practitioner (also called an internist), you should also see a doctor who specializes in kidneys. A **nephrologist** (kidney specialist) will be able to advise you best on how to care for your polycystic kidneys and the other related symptoms. Ideally you would find a nephrologist with experience treating PKD, but this could be difficult depending on where you live.

If you have more than one doctor, they should all be working together in a coordinated approach to your health care. This does not always happen so you must not be afraid to vocalize your concerns and ask your doctors to talk to each other, especially if you are getting conflicting advice from them. If you are being prescribed medication by multiple doctors, keep track of this and be sure to tell each doctor about all of your prescriptions to ensure no adverse effects arise.

Find a doctor(s) who you trust and with whom you work well. Don't be afraid to "shop around" or visit with several different doctors until you find one you like and trust. Be involved in your own health care and become your own expert by gathering as much information as possible about PKD and any other health concerns you may have. This will assist you in knowing your choices and allow you to make well-informed decisions. Pay attention to symptoms and write them down, including details like: when symptoms started; what time of day they occur and how frequently; how long they last and what makes them better or worse. This will give you and your doctor a clear picture of what is happening. Ask questions and make certain you understand the answers. Don't be afraid to ask them to repeat the answer if you don't understand the first time.

What about prescription medications?

Know about the medications you are taking. When one of your doctors prescribes a drug, be sure to ask questions like:

- What does this drug do?
- What are the advantages of this drug?
- What are the possible side effects?
- Is it dangerous to take this drug with any foods, beverage or other medications
- I'm taking other (including over-the- counter medications), is this a problem?
- Will any other condition I have be aggravated or made worse by this drug?
- Are there alternatives to this drug (generic brand, other medication, different treatment)?

In addition to talking to your doctor, ask your pharmacist questions regarding over-the-counter medications and your medical condition. NEVER take medications that were prescribed for a friend or other family member.

WHAT SHOULD I KNOW ABOUT MY KIDNEYS?

Typically, each of us is born with two kidneys. They are located in the back of the body on each side of the spine, tucked under the rib cage. Each kidney is about 5 inches long (12 cm), 3 inches wide (8 cm), 2 inches thick (5 cm) with each one weighing 10 to 12 ounces (280 to 340 grams). Both kidneys are affected by PKD. The number of cysts that are detectable by imaging tests increases with age and can range from just a few to too many to count. The size of individual cysts also increases with age and may range from that of a pinhead to a grapefruit. On average, your **total kidney volume (TKV)** as measured by MRI will increase by about 5 percent per year despite your kidney function remaining within the normal range for several decades. Recent studies have shown that TKV expansion to 1000 to 1500 mL (normal TKV: 250-350 mL) is associated with a significant risk for a future decline in kidney function. Thus, TKV is being used as a surrogate disease outcome measure in clinical trials of novel drug treatments for PKD.

Surrogate disease outcome measure

- Measures the effect of a specific treatment
- Substitutes for a clinical endpoint, a symptom or sign of the disease that is the target of the trial

Your kidney is a filter

Each of your kidneys contains about one million tiny filters called **nephrons**. The nephrons are made of a tuft of thin blood vessels in a spherical structure called the **glomerulus** which is connected to a series of tubules. Almost a quarter of the blood your heart pumps every second passes through the nephrons. Red blood cells, white blood cells, and large substances like proteins do not normally pass through, staying inside the glomerular blood vessels instead. The 180 liters (approx. 47 gallons) of fluid that passes through the filters of your kidneys each day is made up of water, electrolytes (sodium, potassium, calcium, and phosphorus) and other small substances. Most of the fluid that passes through the glomerulus is modified and reabsorbed during transit through the tubules of the nephron. This leaves 1 to 2 liters (a quart to a half-gallon) as **urine** each day.. The process of filtering and reclaiming fluid along the nephron enables normal kidneys to perfectly maintain your body's fluid composition with electrolytes and blood pH regulated within a specific concentration or range. Your kidneys also filter and excrete waste products generated from your diet and body metabolism each day.

Each kidney is about 5 inches long (12 cm), 3 inches wide (8 cm), 2 inches thick (5 cm) with each one weighing 10 to 12 ounces (280 to 340 grams).

Waste products of the kidneys

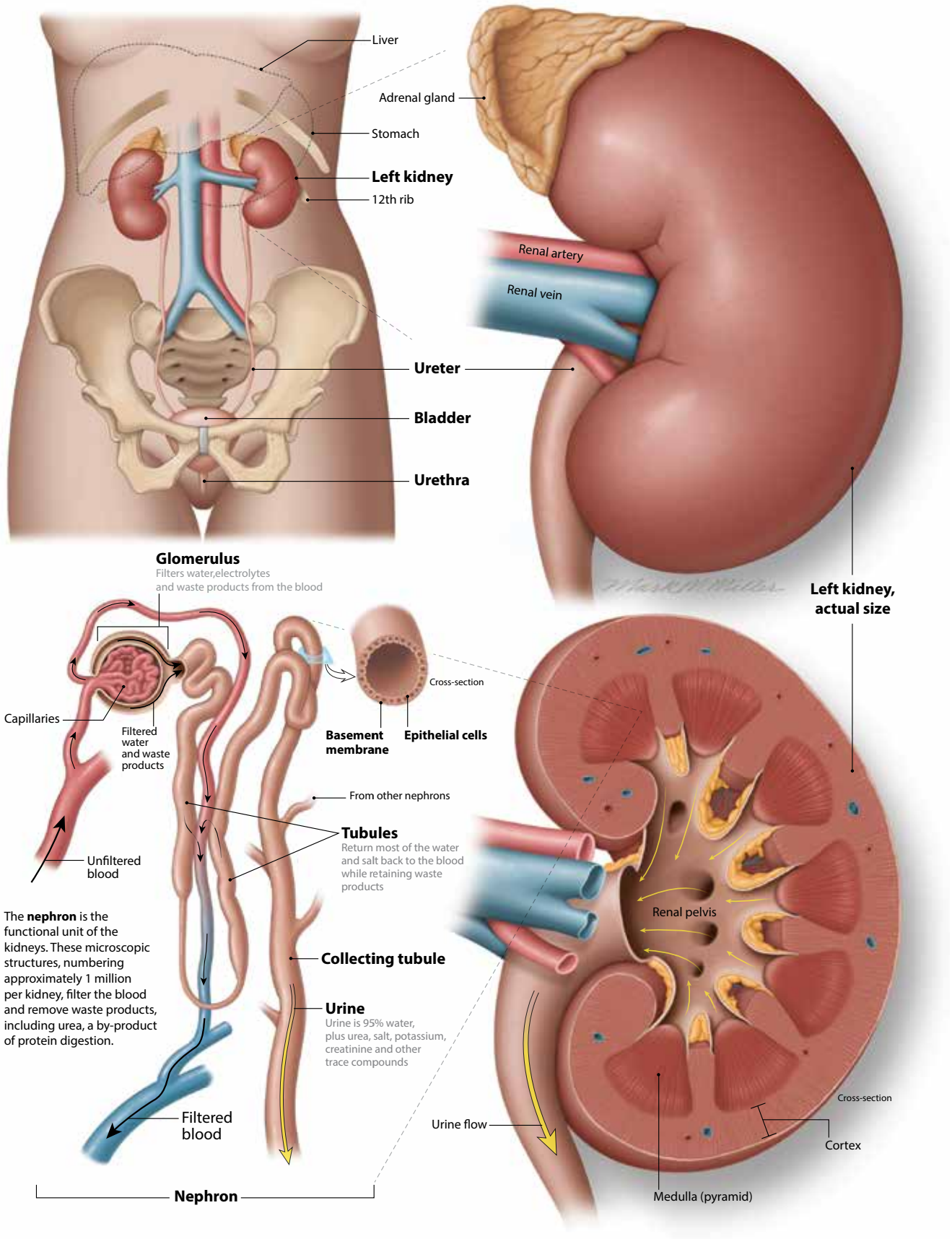
Blood Urea Nitrogen (BUN) and **creatinine** are two waste products removed by the kidneys. In particular, creatinine is removed so efficiently that an estimate of actual kidney function can be made by the level of this substance in the blood. Your doctor can calculate approximately how much actual kidney function you have with a blood test for creatinine compared to a 24-hour urine collection, height and weight. This is called **creatinine clearance** and is approximately equal to the true **glomerular filtration rate (GFR)** of your kidneys which can be measured precisely for clinical and research purposes.Your creatinine clearance tells your doctor the approximate percent of "normal" kidney function you have.

Hormones and your kidneys

Your kidneys also make several essential hormones and enzymes. One of these is renin, an enzyme that facilitates the production of other hormones such as **angiotensin** (helps regulate blood pressure) and **aldosterone** (aids in the body's handling of salt and potassium). Another hormone made in the kidneys is **erythropoietin**, commonly known as EPO. This hormone tells the bone marrow to make red blood cells. If your kidneys are surgically removed or if they fail because of kidney disease, EPO is no longer produced and blood transfusions must be given to the person every five or six weeks. The EPO gene was discovered almost three decades ago. A genetically engineered form of EPO is available that patients can take to avoid the need for blood transfusions.

The kidneys also modify vitamin D to its active form, which helps the body absorb calcium from the diet. In this way, the kidneys help control the blood calcium and phosphate levels and thus bone formation.

Figure 4


Liver
Adrenal gland
Stomach
Left kidney
12th rib
Renal artery
Renal vein
Ureter
Bladder
Urethra
Left kidney, actual size
Glomerulus
Filters water,electrolytes and waste products from the blood
Capillaries
Filtered water and waste products
Unfiltered blood
Cross-section
Basement membrane
Epithelial cells
From other nephrons
Tubules
Return most of the water and salt back to the blood while retaining waste products
The nephron is the functional unit of the kidneys. These microscopic structures, numbering approximately 1 million per kidney, filter the blood and remove waste products, including urea, a by-product of protein digestion.
Collecting tubule
Urine
Urine is 95% water, plus urea, salt, potassium, creatinine and other trace compounds
Filtered blood
Nephron
Renal pelvis
Urine flow
Cross-section
Cortex
Medulla (pyramid)

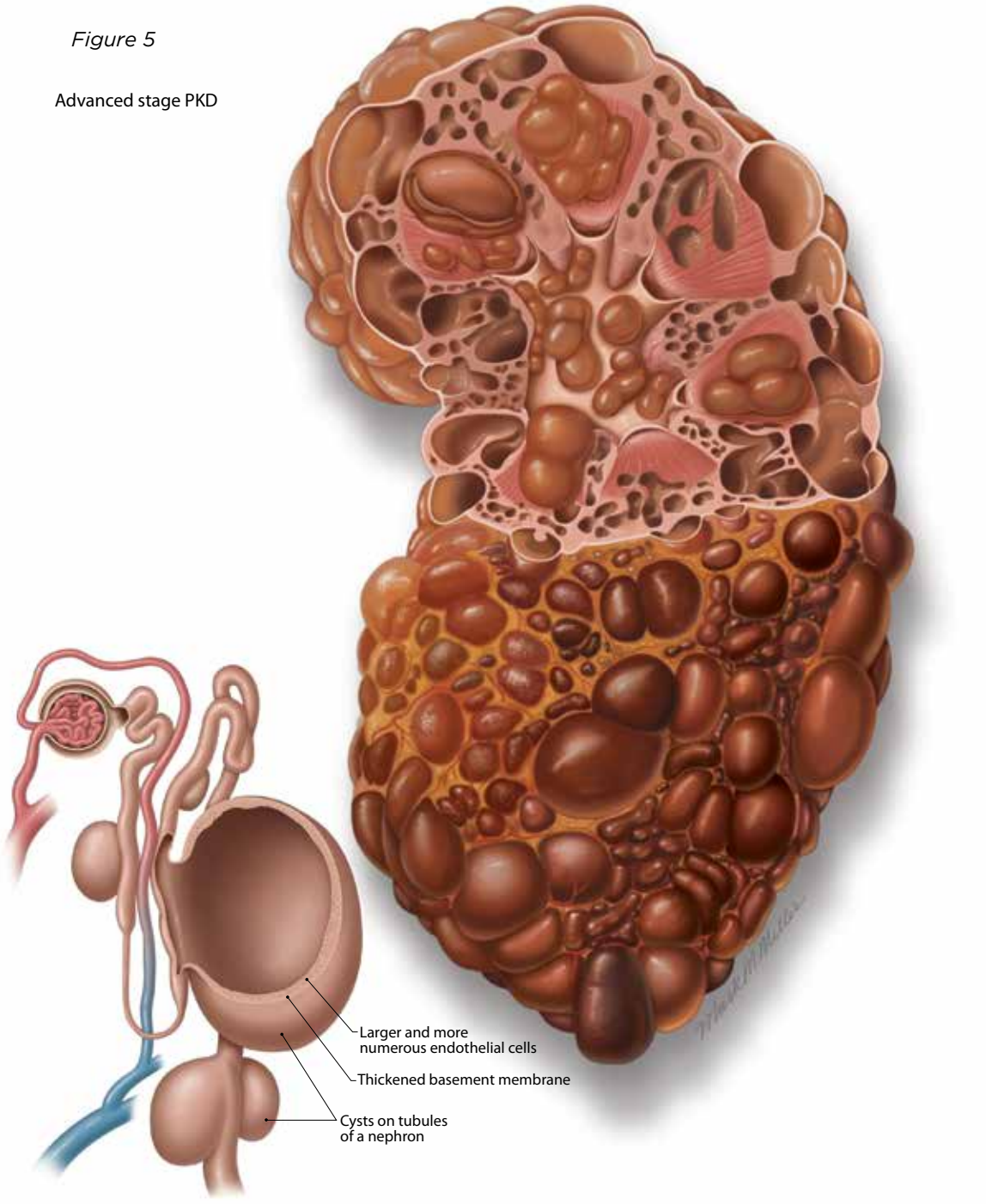
What is a cyst?

A cyst in the kidney begins as an outpouching of the nephron, similar to a blister, and can occur any where along the length of the nephron (Fig. 5). The fluid inside the cysts often reflects the area in the nephron that the cyst began.

Approximately 70 percent of cysts detach from the nephron once they reach 2 mm (1/8 inch) in diameter. Over time, the cysts enlarge and can become filled with clear fluid or blood. Cysts can also form in other organs, with the liver being the most common site. Liver cysts are derived from the bile ducts or tubules.

Figure 5

Advanced stage PKD



What causes cysts to form?

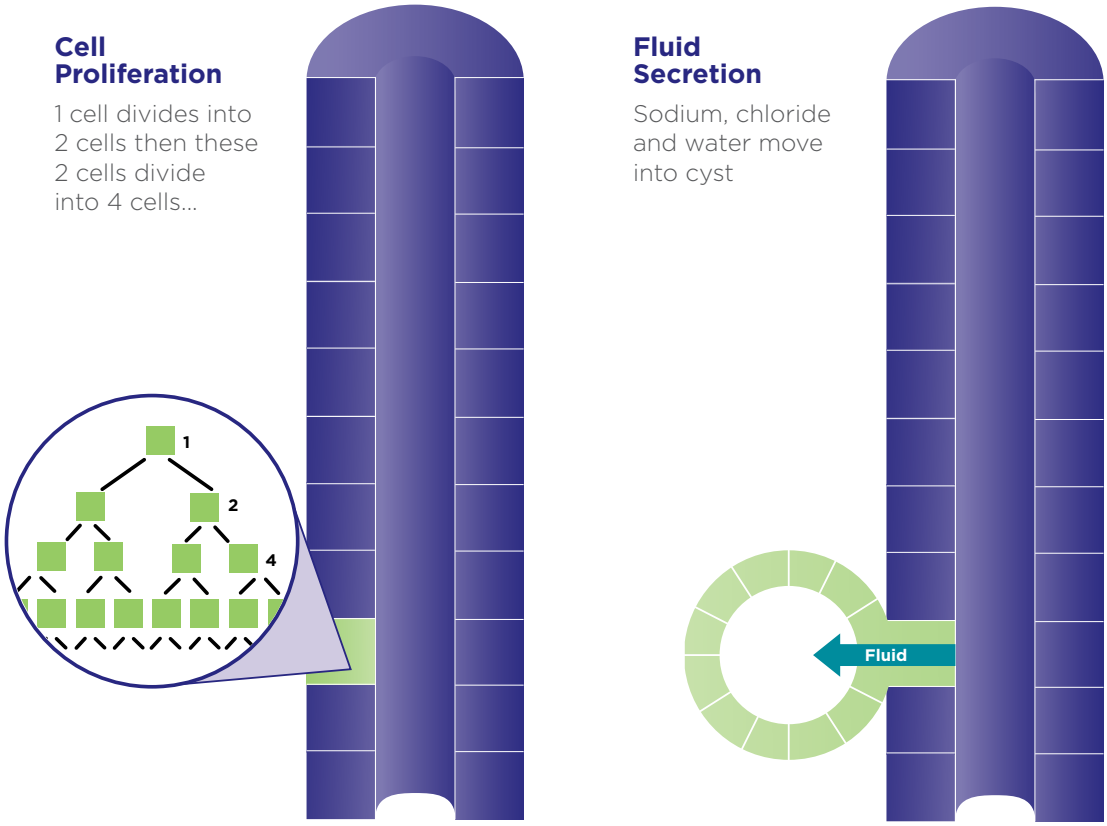
Mutations of the *PKD1* or *PKD2* gene reduce the normal level of **polycystins**, which regulate many important tubular cell functions. Recent research has highlighted a central defect in PKD related to dysregulation of calcium levels and a signalling molecule called **cyclic AMP (cAMP)** within the cells that form tubules in the kidneys and other target organs. These abnormalities in turn can lead to cyst formation through at least three important mechanisms (Fig. 6):

- **Cell proliferation** (growth) – the cells lining a cyst reproduce themselves more than normal kidney cells do, making them grow in size. This process is essential to growth and replacement of the old cells.

- **Fluid secretion** – the lining cells secret fluid into the empty sac which expands the cyst. Without fluid secretion a cyst would collapse like a deflated balloon.

Figure 6

Two basic processes simultaneously occur in the formation of cysts:

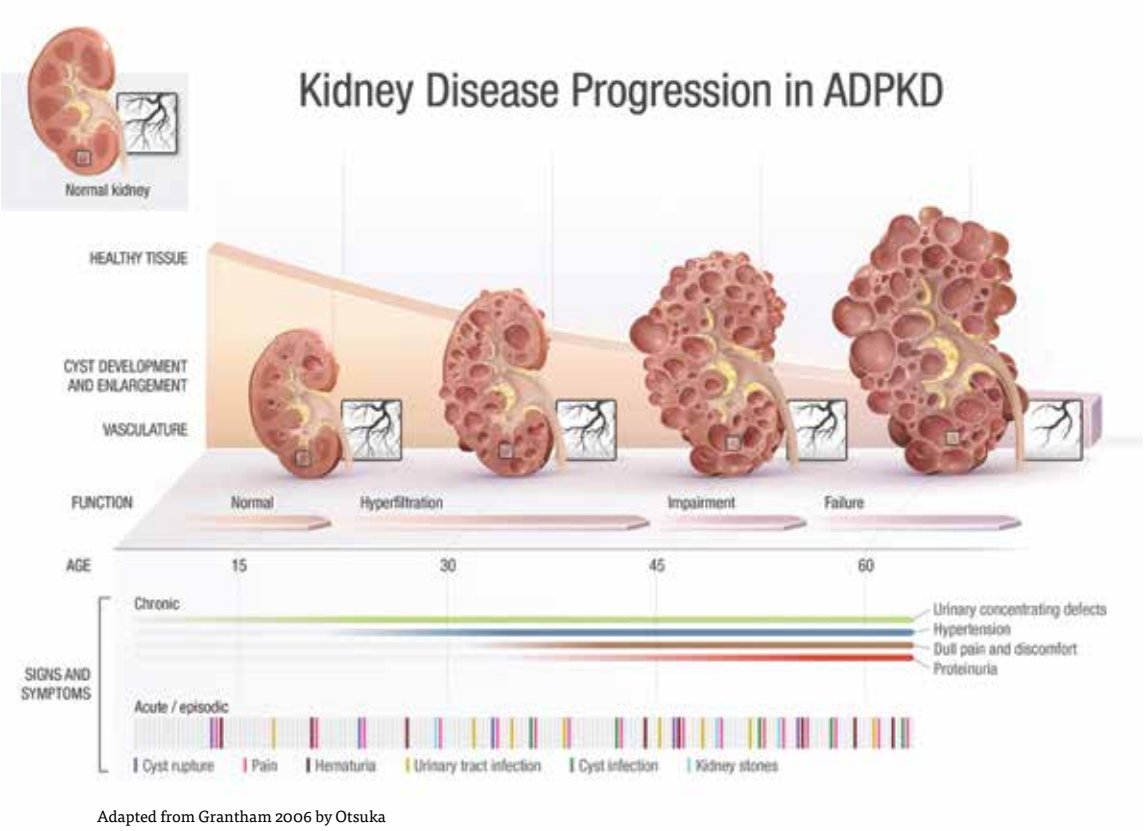


How do cysts cause problems?

In general, cysts cause problems because of their size and the space they occupy (Fig. 7). Many of the symptoms you may have are dependent on how large your kidneys are, detailed below:

- Kidneys over 15 cm (6 inches) are more likely to cause pain than smaller kidneys
- Patients with bigger kidneys are more likely to experience high blood pressure than those with smaller kidneys,
- Patients with bigger kidneys are more likely to have bleeding into their urine than those with smaller kidneys, and
- Patients with bigger kidneys are more likely to experience more rapid loss of renal function than those with smaller kidneys.

Figure 7



Adapted from Grantham 2006 by Otsuka

STAGES OF CHRONIC KIDNEY DISEASE

If you have kidney damage and/or a decrease in kidney function for three or more months, it is called chronic kidney disease (CKD). There are five stages of CKD, with progressive symptoms.

Stage 1: Includes signs of mild kidney disease, with a normal GFR showing 90 percent or higher kidney function.

Stage 2: Includes signs of mild kidney disease with a GFR showing 60-89 percent kidney function.

Stage 3: Includes signs of moderate kidney disease and a GFR showing 30-59 percent kidney function

Stage 4: Includes signs of severe kidney disease and GFR showing 15-29 percent kidney function

Stage 5: Includes signs of severe kidney disease and kidney failure, with a GFR showing less than 15 percent kidney function

These indicators can occur in all stages

- May have some blood in urine
- May have UTIs
- May have kidney stones
- Can have aneurysms in brain

Treatment Options to discuss with your doctor

- Limit protein intake
- Limit salt intake
- Consider hypertension medication (see box on HALT study on page 10).

The stages of CKD in PKD have specific indicators including:

PKD Stage 1-2

- Few physical symptoms
- Labs may show slightly elevated creatinine

PKD Stages 3-4

- May have no physical symptoms or may have:

- Fatigue
- Back pain
- Puffiness or swelling
- Loss of appetite
- Food may taste funny
- Hypertension
- Abdominal swelling

PKD Stage 5

- Physical symptoms include:

- Anemia
- Weak, tired, drowsy
- Headaches
- Confusion, difficulty concentrating
- Nausea, vomiting, decreased appetite
- Itching
- Muscle cramps
- Swelling and puffiness
- Shortness of breath
- Hypertension
- Change in skin color (grayish or yellowish)
- Women may experience changes in menstrual cycle

KIDNEY FAILURE

How can I tell if my kidneys have failed?

End-stage renal disease (ESRD) is when normal kidney function declines and needs to be replaced by dialysis or transplant. This is also known as kidney failure. At this point, GFR is at 10 or less, and kidneys can no longer balance electrolytes and acids in the blood or remove wastes and excess water.

Symptoms that some people experience during this time could include:

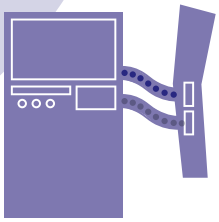
- Decreased energy
- Weakness
- Shortness of breath
- Weight loss
- Nausea and/or vomiting
- Metallic taste in the mouth
- Mild to moderate depression
- Decreased ability to think problems through.

It is important to keep your doctor informed of your symptoms so she/he can help you decide when it's time to start dialysis or be evaluated for transplant.

Blood tests will show that your blood urea nitrogen (BUN) and creatinine are not being properly eliminated by the kidneys and are building up in the blood. These tests may also show that your electrolytes and pH are out of balance.

Generally, planning for kidney replacement therapy (dialysis) is done when your kidney function is at about 25 percent. If you wait until you are very sick, it will take you much longer to recover and may require hospitalizations.

What options are there for me if my kidneys fail?



1. Dialysis

Dialysis is a kidney replacement option that does some of the things healthy kidneys do. It is needed when your own kidneys fail or can no longer function well enough to take care of your body's needs.

There are multiple types of dialysis: hemodialysis and peritoneal dialysis

▶ **Hemodialysis (Hemo)** – uses a machine to clean waste from your blood. Your blood flows on one side of a natural or artificial membrane, with special fluid on the other side. The membrane permits waste molecules (extra fluid, electrolytes, etc.) that have built up in the blood to pass into the fluid and be removed, thus cleaning your blood.

- **Home hemodialysis** – dialysis that is done at home with an assistant and your own dialysis machine
- **In-center, self-care hemodialysis** – dialysis done in a center with you doing as much as possible with the assistance of staff at the dialysis center
- **In-center hemodialysis** – dialysis that is done in a center with the staff providing all of the care.

Required for hemodialysis:

Dialysis access port

When you are in need of dialysis, your doctor will require you to have a vascular access surgically placed. This will provide a port for your blood to flow through to be cleaned by the dialysis machine. It will stay with you as long as you are on dialysis. There are two types of vascular access designed for long-term use.

An **arteriovenous (AV) fistula** is a surgically created connection from an artery to a vein. Your surgeon will typically place an AV fistula in the forearm or upper arm as an outpatient procedure; occasionally doctors require patients to stay overnight after the procedure. The procedure is done under local anesthesia, only numbing the area where the AV fistula is created. An AV fistula generally requires two to three months to mature before it can be used; if it fails to mature, the procedure must be repeated.

This type of access is recommended because it:

- Provides good blood flow for dialysis
- Lasts longer than other types
- Is less likely to get infected or cause blood clots

An **arteriovenous graft** is a looped, plastic tube that connects an artery to a vein. This type of access is also placed in an outpatient procedure using local anesthesia. You can generally use an AV graft two to three weeks after surgery. It is generally more likely to have issues with infection and clotting but a well cared for graft can last several years.

A third type of access, a **venous catheter** is not intended for long-term use. It is a tube inserted into a vein in your neck, chest, or groin area. The tube splits in two after it exits your body to carry blood to the dialyzer and then back again. A venous catheter will be used if you progress to kidney failure quickly and there is not enough time for placement of a permanent access before starting dialysis. This type of access is more likely to become infected, cause clots, etc. It is preferential to begin hemodialysis with a fistula or graft.

Caring for your vascular access is key to your health

- Keep the access area clean at all times
- Use the access only for dialysis
- Do not bump or cut the access
- Check the "thrill" in the access daily. The "thrill" is the rhythmic vibration a person can feel over their access
- Report any signs of infection including redness, tenderness and/or pus
- Do not let anyone put a blood pressure cuff on your access arm
- Do not let anyone draw blood from your access arm
- Do not wear jewelry or tight clothes over the access site
- Do not sleep with the access arm under the head or body
- Do not lift heavy objects or put pressure of any kind on the access arm

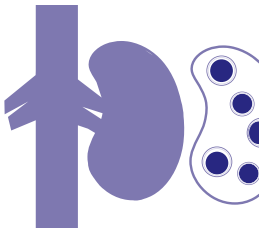
▶ **Peritoneal dialysis (PD)** – a type of dialysis that removes extra fluid, electrolytes and wastes using the lining of the abdominal cavity (peritoneum). PD requires a soft plastic tube be surgically placed in your belly. A sterile cleansing fluid is then put into your belly via the tube to filter the fluid.

There are two ways to do peritoneal dialysis:

- **Continuous ambulatory peritoneal dialysis (CAPD)** – this is done on a continuous basis. It is machine-free and happens while you go about your normal life, including work, school, or social activities. It is done by hooking a plastic bag of cleaning fluid to the tube in your belly then raising the bag to shoulder level. This allows gravity to pull the fluid into your belly. When the bag is empty, it is removed and thrown away. After 30 to 40 minutes, the fluid is drained from your belly (through the plastic tube) and discarded. This process is usually done three, four, or even five times each day.
- **Continuous cyclic peritoneal dialysis (CCPD)** – the process for CCPD is the same as for CAPD, but it is done during the night using a machine to make the exchanges while you sleep.

How will I choose the dialysis type for me?

When your kidney function has declined to the point that replacement therapy is needed, your doctor and the dialysis team will discuss in detail all the options available to you. When you get close to needing dialysis, you'll take a tour of the dialysis facilities, and talk to others on dialysis and the nursing staff to get a sense of what will work best for you.



2. Transplant

When your GFR nears 20, you can start considering a transplant. Making the decision to be evaluated for a kidney transplant should be considered carefully with your doctor and/or nephrologist and your immediate family. Because of the way kidneys are allocated (read more on this below) combined with the progressive nature of PKD, it is important to consider being listed early – before dialysis begins. Although you cannot be officially listed until your GFR is at 20 or below, it is important to gather information early. You may have to start the conversation with your physician; don't wait for them to bring it up!

What happens during a transplant evaluation?
When you and your doctor agree it is time for you to be evaluated for a transplant, you undergo a series of tests to assess your options. You'll be evaluated for potential issues like heart disease, obesity, and diabetes. A social worker or transplant coordinator will discuss the logistics with you as well; things like transportation, housing, financial and family support will all be considered.

Screening tests:
There are several screening tests to determine your blood and tissue type which are needed to match you to a donor kidney. In addition to the tests below, other tests may be required depending on your age, medical history, etc. A mammogram, colonoscopy, or other tests may be required.

Blood type is the first test; it will tell you which of the four blood types – A, B, AB, or O, you are. You must have a blood type that is compatible with your donor for the transplant to be successful.

Compatible blood types:

- If your blood type is A, donor blood type must be A or O
- If your blood type is B, donor blood type must be B or O
- If your blood type is AB (universal recipient), donor blood type must be A, B, AB or O
- If your blood type is O (universal donor), donor blood type must be O

The Rh type (+ or -) is not a factor in donor matching.

Human leukocyte antigens (HLA) (also called tissue typing) is the second blood test you'll undergo. The HLA are found mostly on white blood cells; they are markers that let your immune system know which cells belong to your body and which do not.

Crossmatch is another blood test you will undergo. This test tells you what antibodies you have in your body. Antibodies are produced by your immune system when it attacks foreign substances. You make antibodies when you have an infection, are pregnant, have a blood transfusion or undergo a kidney transplant. If you have antibodies to the donor kidney, your body will fight that kidney until it is destroyed. The crossmatch test is done by mixing your blood with cells from your donor. If the crossmatch is positive, you have antibodies against your donor and should not receive the kidney.

All of these blood tests, along with the discussions mentioned above, are all required before you can be considered for a transplant. Once the results from all the tests are back, your transplant team will meet to discuss your results. They will discuss your

medical and social history (history of drug or alcohol abuse, level of family and financial support, etc.) and make a decision. If they decide you should be listed for a transplant, you are then placed on the United Network for Organ Sharing (UNOS) waiting list.

How do I get a transplant?
There are two ways to receive a new kidney – through a living donation or through a deceased donation.

Living donation

Living donation is when a living person decides to donate a kidney (or other organ) to someone who needs a transplant. 6,000 organ transplants a year are made possible by living donors. The kidney is the most commonly transplanted organ from a living donor.

Positive aspects of living donation:

- A living donation makes it possible to schedule the transplant surgery at a time convenient for both the you and your donor.
- Better genetic matches between you and your donor decrease the risk of organ rejection.
- Kidneys from living donors usually work immediately, as the kidney is removed from a healthy donor and transplanted right away in an operating room.
- A living donor transplant may reduce or eliminate your time on dialysis and/or years of waiting for a deceased donor organ.

Who can be a living donor?
Potential living donors must be in good overall health, both physically and psychologically. Gender and race are not factors.

Types of living donor transplants

▸ Directed donation

Directed donation is the most common type of living donation. In a directed donation, the donor names the specific person to receive the transplant. The donor may be:

- Related: your biological relative, such as a parent, brother, sister, or adult child
- Non-related: a biologically unrelated person who has a personal or social connection with you, such as a spouse or significant other, a friend or a coworker

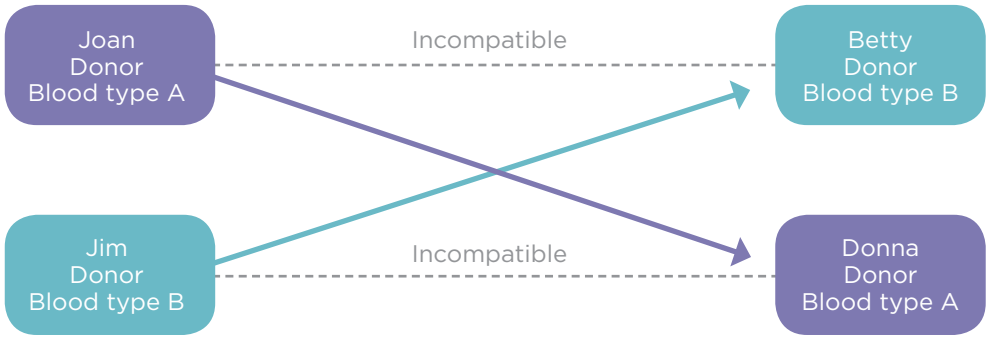
▸ Non-directed/altruistic donation

In a **non-directed** or **altruistic donation**, the donor does not name a specific person to get their organ. The match is arranged based on medical compatibility with a patient in need. Some non-directed donors choose never to meet their recipient. In other cases, the donor and recipient may meet at some time, if they both agree, and if the transplant center policy permits it.

Paired donation or paired exchange

Paired donation involves two or more pairs of living kidney donors and transplant candidates who do not have matching blood types. The candidates "trade" donors so that each candidate receives a kidney from a donor with a compatible blood type. For example, in figure 8, Joan wants to donate to her sister Betty, but they do not have matching blood types. Jim wants to donate to his wife Donna, but they are also not compatible. By "swapping" donors so that Jim matches Betty and Joan matched Donna, two transplants are made possible. This type of exchange often involves multiple living kidney donor/transplant candidate pairs.

Figure 8



Blood type incompatible

Blood type incompatible donation allows you to receive a kidney from a living donor who has an incompatible blood type. To prevent rejection of the kidney, you undergo specialized medical treatment before and after transplant including the possible removal of your spleen during the transplant. This type of transplant is only done at highly specialized centers.

Positive crossmatch donation

Positive crossmatch donation occurs when you and your living donor do not match due to your antibodies. These antibodies will immediately react against your donor kidney's cells and cause rejection. Specialized medical treatment is required. This type of donation is only considered when no other living donors match.

Since PKD is a hereditary disorder, can family members be kidney donors?
Your family member can be a kidney donor if that individual does not have PKD. The first step for a potential donor is to have an ultrasound of his or her kidney. 83 to 90 percent of people at risk for inheriting PKD can be diagnosed with an ultrasound by age 40. In the younger at-risk individuals who are deemed negative by ultrasound, an MRI or genetic testing can be used to provide further certainty in excluding milder forms of PKD. If your family member does not have the disease, the transplant team will further evaluate to make sure there are no other risks for that individual to donate their kidney.

Other considerations for living donation

Costs

Most medical costs associated with living donation are covered by your (the recipient) insurance. The government requires all certified transplant centers to charge your insurance an "acquisition fee" when you receive a transplant. The medical costs related to your donor's medical evaluation, transplant procedure and postoperative care, called the "donor protocol" are covered by this fee. Anything that falls outside of this protocol is not covered. These non-covered and, thus, out-of-pocket costs could include annual physicals, travel, lodging, lost-wages, dependent care and other non-medical expenses. Your donor must agree to pay these expenses and must prove that they have the financial capacity to do so.

Disability pay

If your job provides disability insurance coverage, then you will most likely be entitled to disability pay. Check with your employer for details.

When will the transplant take place?

This decision is made jointly by the transplant team, by you, and by your donor. The transplant team, particularly the doctors involved directly in your care, will determine as accurately as possible the best time to do the transplant, based on your medical condition.

Once the transplant is scheduled, will it definitely happen?

A number of events could happen that may change the date of the transplant. For example, your condition might deteriorate to the point that you are too sick to receive the transplant. Or, the recipient or donor might develop an infection or some other condition that would need to be treated before the transplant could be done. Additionally, your donor has the right to change their mind at any point. This is why it is so important to encourage your donor to take the time and give the consideration necessary to explore the process and fully understand all the benefits and risks.

Deceased donation

In the United States, most kidney transplants come from deceased kidney donors. Deceased donors are most often individuals who die from accidents, or sudden death, and their next of kin consent to organ donation.

Donor organs are matched to waiting recipients by a national registry called the **Organ Procurement and Transplantation Network (OPTN)**. This registry is operated by an organization known as the **United Network for Organ Sharing (UNOS)**.

▶ When should I start the process to be listed on the registry?

When your GFR is right at or just above 20, you should ask your doctor about the steps it takes to be listed for a transplant. There are many steps, including an evaluation by a transplant center that is affiliated with OPTN.

Kidney Allocation System (KAS)

The current **kidney allocation system** aims to provide recipients with longer function with their transplanted kidney by matching the donated kidney that has the longest potential life with the recipient who has the longest potential life with that kidney.

Once you are approved to be listed for a transplant, you will be assigned an **estimated post-transplant survival score (EPTS)** – a percentile score that ranges from zero to 100. The score is based on how long you will need a functioning kidney as compared to all other transplant candidates on the list. If you have an EPTS of 20, it means that you will need a kidney longer than 80 percent of all other candidates. Your EPTS will be electronically updated daily.

To determine your EPTS, four factor values are entered into a mathematical formula:

1) whether or not you are diabetic
2) Your current age
3) If you are on dialysis and, if so, for how long
4) Have you had a previous transplant of any organ

Each available deceased kidney available for transplantation is assigned a **kidney donor profile index (KDPI) score** – a percentile score ranging from zero to 100. The KDPI is associated with how long the kidney is likely to function as compared to other kidneys, based on information about the donor. A KDPI score of 60 means that the kidney is likely to function longer than 40 percent of other available kidneys.

The KDPI is calculated based on factors including:

- Age
- Height
- Weight
- Ethnicity
- Cause of death
  - Loss of heart function?
  - Loss of brain function?
  - Stroke?
- History of high blood pressure
- History of diabetes
- Exposure to Hepatitis C
- Serum creatinine

How do the EPTS and KDPI allocate kidneys?

When a kidney becomes available and it is given a KDPI score, the EPTS scores of all recipients are considered. The 20 percent of kidneys expected to last the longest (those with a KDPI score of 20 or less) will first be offered to patients likely to need a transplant the longest (those with an EPTS of 20 or less). If a kidney with a KDPI of 20 or less is not accepted for any of these patients, it will then be offered to any other person who would match, regardless of their EPTS score.

Kidneys with high KDPI scores are expected to function for a shorter amount of time than others. They may be best used to help candidates who are less able to stay on dialysis for a long time, thus needing a kidney very quickly.

Does the KAS negatively impact PKD patients?

A common concern is that as a PKD patient, you receive fewer transplants because you would not be accumulating time on dialysis, as your kidney function declines more slowly. However, the remedy for this is to be evaluated and listed at a GFR of 20 percent. In this case, based on the natural rate of progression of PKD, most patients should have at least several years of waiting time before being faced with dialysis, and so **"pre-emptive" (before dialysis begins) transplantation** should still be a common option.

A second concern is that "all the young donors' kidneys will be given to other groups." This is a valid concern because PKD patients are often older on average when you reach stage 4-5 CKD. However, two points must be considered:

1) Even people into their 60s can have an EPTS under 20

2) 80 percent of kidneys donated are allocated to people with an EPTS over 20, and the vast majority of those kidneys will serve their recipient extremely well.

Will my kidneys be removed before or after I have a transplant?
Removal of a polycystic kidney, a process called **nephrectomy**, before a kidney transplant is generally not performed unless you have a history of:

- Kidney cyst infections
- Severe bleeding from the cystic kidney
- Cancer of the cystic kidney
- Kidneys so large there is no room for a new kidney to be transplanted
- Kidneys are very uncomfortable or cause a lot of pain due to their size.

If one or both of your kidneys are removed, the timing will depend on your individual case as well as the center where you are having your transplant. They can remove one or both kidneys before, during, or after transplant.

Does everyone with PKD eventually need to have dialysis or a transplant?
Although everyone with the PKD gene develops kidney cysts, not everyone progresses to kidney failure, and if you do it is generally not before age 40. More than 50 percent of people with PKD will develop kidney failure by age 50. Some PKD patients have relatively normal kidney function until their 40's or 50's, but when function does begin to decline, it can drop rapidly – in the course of just a few years, rather than the slow decline seen in other kidney diseases.

Many people with a very mild form of PKD are unaware of their status and thus are never diagnosed.

Although we still don't know exactly how kidney failure happens in PKD, we do know some of the risk factors associated with more rapid progression ESRD. These risk factors include include:

- **Inactivating *PKD1* mutations** (see genetics section for more information) as opposed to ***PKD2*** and **non-inactivating *PKD1* mutations**
- Being male may be associated with more severe disease than females
- Diagnosed with cysts at a young age
- High blood pressure
- Large kidneys
- Multiple episodes of blood in the urine
- Being a woman with high blood pressure and four or more pregnancies

The burden of kidney disease in America:

- More than 20 million Americans have kidney disease
- Nearly all patients with kidney failure are Medicare beneficiaries, regardless of age, income or disability
- ESRD patients account for nearly 7 percent of Medicare costs but comprise less than 1 percent of Medicare patients
- PKD is the fourth leading cause of kidney failure
- More than 50 percent of people with PKD will develop kidney failure by age 50

How are the costs associated with dialysis and transplant covered?
In general, Medicare covers a significant amount of the cost of dialysis and transplantation. To be eligible, a person must have earned Social Security benefits or be the spouse or dependent of someone who has. About 93 percent of those with ESRD are eligible for this benefit.

Medicare covers immunosuppressive drugs for 36 months (three years) after the month of transplant. Medicare will continue to pay for your immunosuppressive drugs with no time limit if:

- You were already entitled to Medicare because of age or disability before you got ESRD
- You became entitaled to Medicare because of age or disability after getting a transplant that was paid for by Medicare or paid for by private insurance that paid primary to your Medicare Hospital Insurance coverage.

For more detailed information regarding Medicare and payment of costs associated with dialysis and transplant, call your local Social Security Medicare office or visit the website of the U.S. Department of Health and Human Services (see page 55 for a list of resources). Medicaid may cover those who do not qualify for Medicare. A social worker or financial counselor in the dialysis unit or transplant program at your hospital will help you work through the financial issues.

PKD AND CHILDREN

Pregnancy: Can I safely have children if I have PKD?

The diagnosis of PKD is most commonly made by pre-symptomatic screening of at-risk patients with a positive family using ultrasonography which is inexpensive, safe, and readily available. Alternatively, incidental findings of kidney cysts in at-risk patients who undergo imaging studies for other indications may also lead to the diagnosis of PKD. In both scenarios, early diagnosis of PKD has become increasingly more common and has important implications for family planning.

Generally, women with PKD who have normal blood pressure and normal kidney function have uneventful pregnancies and deliver healthy babies. Risk factors associated with pregnancy and PKD are due to increased blood pressure. Some women with PKD will develop hypertension during their pregnancy and are more likely to have continued elevations in their blood pressure after delivery. Women who have high blood pressure prior to becoming pregnant have the risk of further elevations in their blood pressure while pregnant and women with complications in their first pregnancy are more likely to have complications in future pregnancies.

It is important for a woman with PKD to be closely monitored during pregnancy whether she has hypertension or not. Increases in blood pressure as well as protein in the urine could signal a serious complication of pregnancy called preeclampsia – a condition where the placenta can be prevented from getting enough blood. If the placenta doesn't get enough blood, the growth of the fetus can be compromised resulting in low birth weight, premature birth, and other problems for the baby. Most women with preeclampsia still deliver healthy babies.

Pregnancy does not seem to affect the growth of kidney cysts but there appears to be a slight increase in the rate of loss of kidney function in women with hypertension and four or more pregnancies, as compared to PKD women with hypertension who have fewer than four pregnancies.

The decision to have children is a very personal one. Both parents need to discuss the risks involved and the joy associated with having a child. With an affected parent, there is a 50 percent probability of having a child who has inherited the gene for PKD (see "Genetics" section on page 46). Pre-implantation genetic diagnosis (PGD) is now feasible and has been successfully applied in more than 300 genetic disorders for selecting healthy embryos created by in-vitro fertilization (IVF) for implantation. The utility of this new approach in PKD in the context of family planning has not been formally assessed. Should you be interested in learn more, please contact your physician for referral to specialized centers experienced in PGD.

ADPKD and children

ADPKD can be diagnosed at a very young age or even before birth. Diagnostic tests performed during pregnancy should be done in conjunction with medical counseling so the test results can be completely understood. For example, knowing your baby could have (or does have) an ADPKD gene does not determine the course or severity of the disease.

There are two different groups of children with ADPKD – those diagnosed before birth or in their first year of life with large cystic kidneys and those who are diagnosed after their first year.

Children who are diagnosed in the first year of life have some special characteristics:

- One parent may have severe ADPKD
- Some of these severely affected infants may have a related syndrome which causes a genetic disease called **tuberous sclerosis complex** which can also cause kidney cysts. Many will not have a family history of having ADPKD or tuberous sclerosis complex.
- Most are diagnosed in-utero with large kidneys cysts.
- Most develop high blood pressure (hypertension) in childhood which should be monitored and treated by a doctor/pediatric nephrologist.
- Some patients could develop end stage renal disease (ESRD) by their teenage years.

Children who are diagnosed after one year of age:

- Usually, one of the parents is known to be affected with typical ADPKD.
- Often have kidney cysts without kidney enlargement.
- These cases most likely represent incidental findings due to widespread use of ultrasounds and improved resolution of the scans to detect smaller sized cysts.

Almost all children who are diagnosed after the first year of life will have perfectly normal kidney function throughout childhood.

What kind of medical treatment should a child with ADPKD have?

Children who have (or who may have) ADPKD should have their blood pressure measured at least every six months. Normal blood pressure varies for different ages and between boys and girls. All children with ADPKD and high blood pressure require treatment and should be seen by a pediatric nephrologist.

Although less common than in adults, signs and symptoms of infection, blood in the urine and/or pain also need to be evaluated by a doctor.

Should I limit the physical activity of a child who has ADPKD?

There is no information to support limiting physical activity in any child simply because he or she has ADPKD. It is possible that children with large kidneys and/or large cysts may have more episodes of blood in the urine if they play contact sports such as football, however each child should be evaluated by a doctor on an individual basis.

Do children with ADPKD have involvement of organs besides the kidney?

Just as in adults, children who have ADPKD are more likely to have mitral valve prolapse (MVP) and hernias than children who do not have ADPKD. Approximately 12 percent of all ADPKD children will have MVP, but unlike adults, it is unusual for them to have any symptoms. If your child has a hernia, they should be treated as they would in any other child. Children rarely have any of the other manifestations of ADPKD.

Should I tell my children they have or are at risk of having ADPKD?

To date, no research has been done on the effect such knowledge would have on children. Generally speaking, there is no need to burden children with information they are too young to understand. Children have a tendency to ask questions when situations arise and, at that time, usually want simple honest answers. There is no need to go into great detail unless a child asks more questions on the subject.

Children of affected parents need not be tested for ADPKD. They should be monitored by their doctors for hypertension, and have screening urinalyses performed as part of general health visits without actually making the ADPKD diagnosis. **The decision parents make to test a child should include understanding that a negative result in childhood may not exclude the diagnosis later in life.** For example, cysts may develop after the imaging study was performed. The added consequences of making the diagnosis in childhood may give the child a label, which could result in discrimination in employment and potentially in life and disability insurance. Children can be informed of their risk for ADPKD but routine screening is not recommended at this time. When and if therapies become available to prevent the progression of PKD, the decision to screen may change.

ARPKD

What is ARPKD?

Autosomal recessive polycystic kidney disease, ARPKD, is a rare genetic disorder occurring in approximately 1 in 20,000 children. It affects boys and girls equally and can cause death in the first month of life. If a child with ARPKD survives the newborn period, the chances of survival are good. For these children, approximately one-third will need dialysis or transplantation by the age of 10.

What can I expect if my child has ARPKD?

Previously thought to be a fatal condition, the prognosis for children with ARPKD has improved dramatically. Twenty years ago, only half of the children born with the disease survived to their 10th birthday, but now that percentage has increased to 85.

The immediate life-threatening issue for infants with ARPKD is lung immaturity. Lung immaturity is caused in part by insufficient **amniotic fluid**, produced by the kidneys, due to poor prenatal renal function. Severely enlarged kidneys caused by ARPKD also limit breathing by preventing adequate lung expansion. Death in the **neonatal period** can be as high as 30 to 50 percent. If an infant with ARPKD survives this critical period, kidney failure can become the most prominent life threatening issue. When the newborn's life isn't at risk, the biggest health concerns are often regulating blood pressure and the chemical balance of blood.

The improved prognosis for ARPKD may be attributed to improved prenatal **sonogram** technology which allows doctors to diagnose many cases of ARPKD prior to birth. Accordingly, the birth of an affected child is better planned so the necessary specialists can be alerted. Importantly, the doctors are able to discuss with the parents what they should expect once the baby is born, advising them that the infant may need a breathing tube, may require dialysis, may have severe liver disease, and will require multiple evaluations and treatments to handle associated complications.

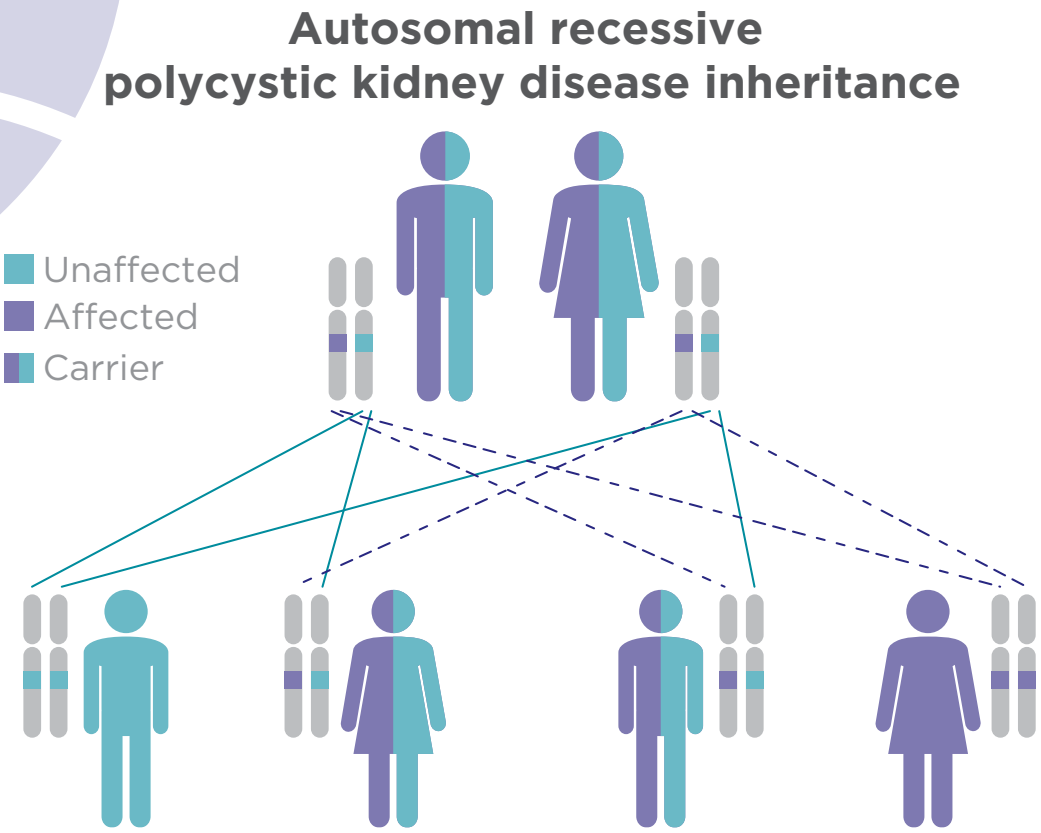
What causes ARPKD?

In recessive disorders such as ARPKD, the child must inherit a copy of the ***PKHD1* gene** from each parent. Since the parents each have only one copy of the disease gene, they do not have the disease and are referred to as "**carriers.**" Parents carrying the mutated *PKHD1* gene have a 25 percent chance that each child with have ARPKD. There is also a 50 percent chance each child will not have ARPKD but will be a carrier of the disease. See Figure 12

How is ARPKD Diagnosed?

Typically in ARPKD, the kidneys appear to be larger than normal. In some babies, prenatal ultrasound can detect the enlarged kidneys as early as 18 weeks after conception. Some families may also hear their doctor say the kidneys look "echogenic" (more white) during an ultrasound, which can be an indicator of kidney problems such as ARPKD.

Figure 9



Prenatal genetic testing is possible using samples from either **chorionic villus sampling** or **amniocentesis**. These genetic tests can either involve a direct search of the gene for mutations or an indirect association using linkage analysis. For linkage analysis, DNA samples are required from the fetus, a previously affected child, and the parents.

Another option for pre-natal diagnosis in affected families is a recently developed procedure called **pre-implantation genetic diagnosis, or PGD**. This is an early form of genetic diagnosis that involves the detection of specific genetic abnormalities in single cells taken from fertilized human embryos. The PGD procedure involves in vitro fertilization whereby eggs harvested from a mother are fertilized in a laboratory with the father's sperm. Then, the fertilized embryos are tested for ARPKD by removing one or two cells for genetic analysis. Embryos that are diagnosed as free of the disorder are then placed in the uterus with the intent to initiate a pregnancy.

What happens to my child's kidneys when they have ARPKD?

In ARPKD, small cysts form in the last section of the nephron called the collecting tubule. A cyst is a balloon-like widening of the tubule. Due to the numerous nephrons with small balloon-like dilatations, the kidneys can become quite enlarged. In addition, the normal function of the collecting tubule is disrupted. In the normal kidney, the collecting tubule fine-tunes the amount of water and acid in the tubular fluid so that the body retains an appropriate amount of water and eliminates excess amounts of acid. In ARPKD, the cystic collecting ducts cannot retrieve water efficiently, causing much more urine production than in children with normal kidneys.

For reasons that are not completely understood, the majority of children with ARPKD have a progressive loss of kidney function. However, the age at which kidney failure develops varies greatly among patients, and, for reasons still unknown, the size of the kidneys does not necessarily correlate with the severity of the disease.

Are other organs affected by ARPKD?

ARPKD affects both kidneys and the liver. Affected children may have significant kidney involvement at the time of birth. In-utero, urine production is a critical factor in maintaining normal amniotic fluid levels. When amniotic fluid levels are very low, lung development can be impaired. In some newborns with low levels of amniotic fluid, impaired lung development can result in serious breathing difficulties that require ventilation upon birth and sometimes can cause death.

Children with ARPKD often produce very large volumes of urine and must urinate much more frequently than children with normal kidneys. Given the kidney abnormality, urine production in ARPKD children does not slow down at night or even when liquid intake is limited.

High blood pressure is very common in children with ARPKD, and current information indicates that untreated high blood pressure can lead to kidney failure more quickly than if the blood pressure is kept within the normal range with medications.

Children with ARPKD also have the liver abnormality called **congenital hepatic fibrosis (CHF)** that may lead eventually to enlargement of the liver and spleen. In the liver, the abnormality can impede the return of blood from the intestine to the liver. This condition, called **portal hypertension**, can lead to distention and increased pressure in the veins around the esophagus, the stomach, and the intestine. This can rupture, leading to possibly life-threatening gastro-intestinal bleeding. In addition, portal hypertension can cause spleen enlargement and hypersplenism resulting in low red blood cell, white blood cell and platelet counts.

GENETICS

How does disease inheritance work?

Your body is composed of about forty trillion cells, almost all of which have two basic parts: the **nucleus** and the **cytoplasm** (Fig.10). The nucleus is the control and operational center of the cell while the cytoplasm is vital to proper cell function. Each of your cells contains a genetic blueprint inherited from your parents that determines what your cells do.

Each cell's nucleus contains tiny threads called **chromosomes**. All the necessary information required to direct the formation and function of a human being is contained in 23 pairs of chromosomes. In turn, each chromosome contains hundreds to more than a thousand **genes** – the basic units of heredity. Genes are pieces of DNA so small they are barely visable, even under a powerful **electron microscope**.

The building blocks of genes are chemical substances called **nucleotides**. There are four nucleotides: **adenosine**, **thymidine**, **cytosine**, and **guanine**, commonly expressed as A, T, C, and G. Ultimately, the genetic code that programs our cells is made by these four nucleotides. A sequence of three nucleotides is called a codon. Each gene is made up of hundreds to thousands of codons which form the template for a messenger **RNA (mRNA)**. Each mRNA in turn provides the instruction for the cellular machinery to make a protein.

Each protein has a unique function within a cell by providing structural support, regulating metabolic processes, or coordinating communication between cells. **In a genetic disease such as PKD, there is a mistake or mutation within a gene which can lead to an altered protein with abnormal function or a decreased level of a normal protein.**

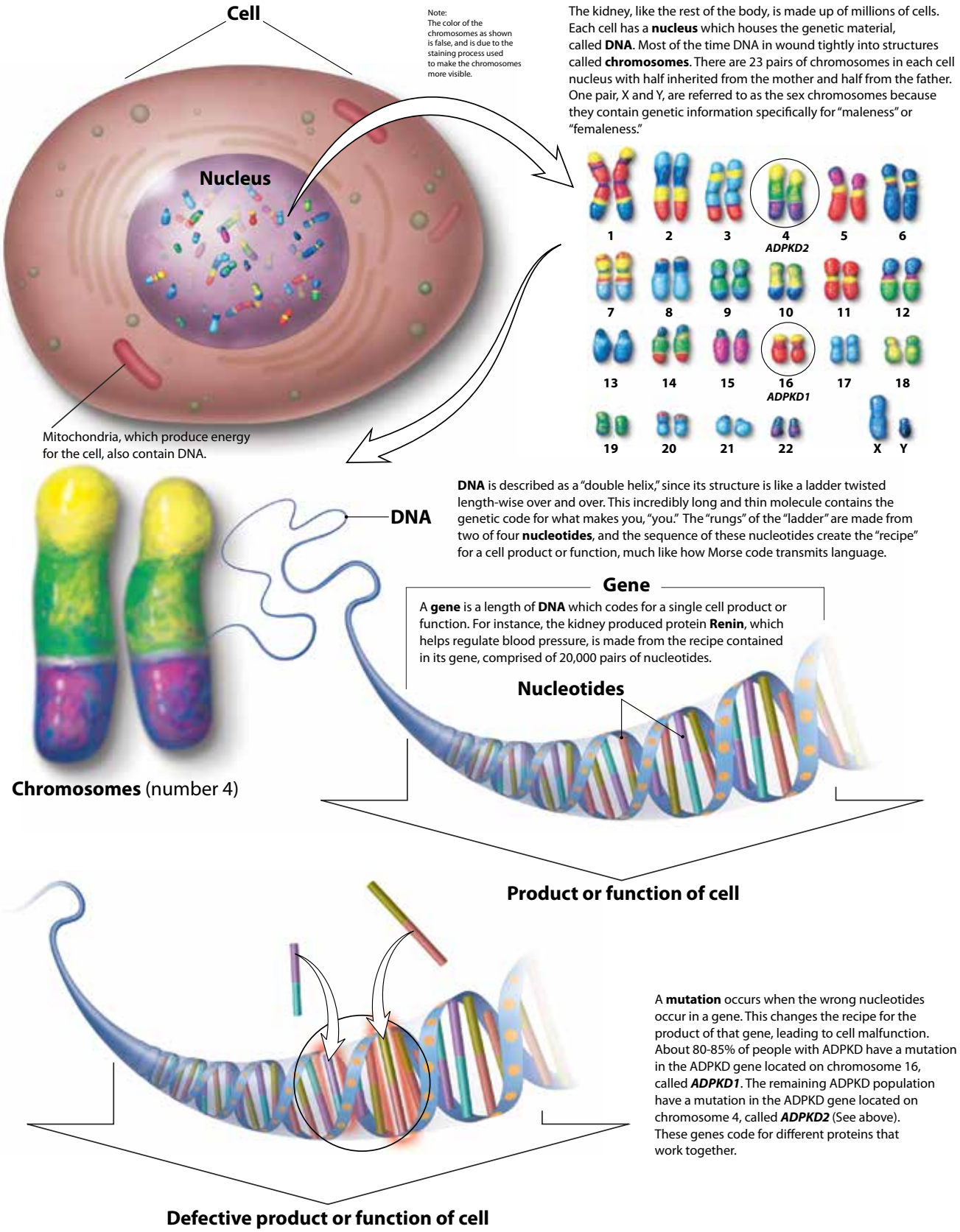
A single nucleotide change is enough to cause the gene to code for an abnormal protein and cause a disease.

The goal in treating a genetically inherited disease is to find out how the abnormal protein alters the normal cell function and to partially or fully restore the aberrant function using specific drug(s). In the future, it may be possible to replace the defective gene.

PKD research has a two-pronged approach:

1. **Discovery research** focuses on understanding certain cell functions and pathways and their implications for the whole organism
2. **Drug development** focuses on applying the knowledge gained in discovery research to develop medicine or biomedical technology that will alter or correct the anomalies caused by the PKD genes.

Figure 10


Cell
Note:
The color of the chromosomes as shown is false, and is due to the staining process used to make the chromosomes more visible.
Nucleus
Mitochondria, which produce energy for the cell, also contain DNA.
The kidney, like the rest of the body, is made up of millions of cells. Each cell has a **nucleus** which houses the genetic material, called **DNA**. Most of the time DNA in wound tightly into structures called **chromosomes**. There are 23 pairs of chromosomes in each cell nucleus with half inherited from the mother and half from the father. One pair, X and Y, are referred to as the sex chromosomes because they contain genetic information specifically for "maleness" or "femaleness."
1 2 3 4 ADPKD2 5 6
7 8 9 10 11 12
13 14 15 16 ADPKD1 17 18
19 20 21 22 X Y
DNA
DNA is described as a "double helix," since its structure is like a ladder twisted length-wise over and over. This incredibly long and thin molecule contains the genetic code for what makes you, "you." The "rungs" of the "ladder" are made from two of four **nucleotides**, and the sequence of these nucleotides create the "recipe" for a cell product or function, much like how Morse code transmits language.
Gene
A **gene** is a length of **DNA** which codes for a single cell product or function. For instance, the kidney produced protein **Renin**, which helps regulate blood pressure, is made from the recipe contained in its gene, comprised of 20,000 pairs of nucleotides.
Nucleotides
Chromosomes (number 4)
Product or function of cell
A **mutation** occurs when the wrong nucleotides occur in a gene. This changes the recipe for the product of that gene, leading to cell malfunction. About 80-85% of people with ADPKD have a mutation in the ADPKD gene located on chromosome 16, called ***ADPKD1***. The remaining ADPKD population have a mutation in the ADPKD gene located on chromosome 4, called ***ADPKD2*** (See above). These genes code for different proteins that work together.
Defective product or function of cell

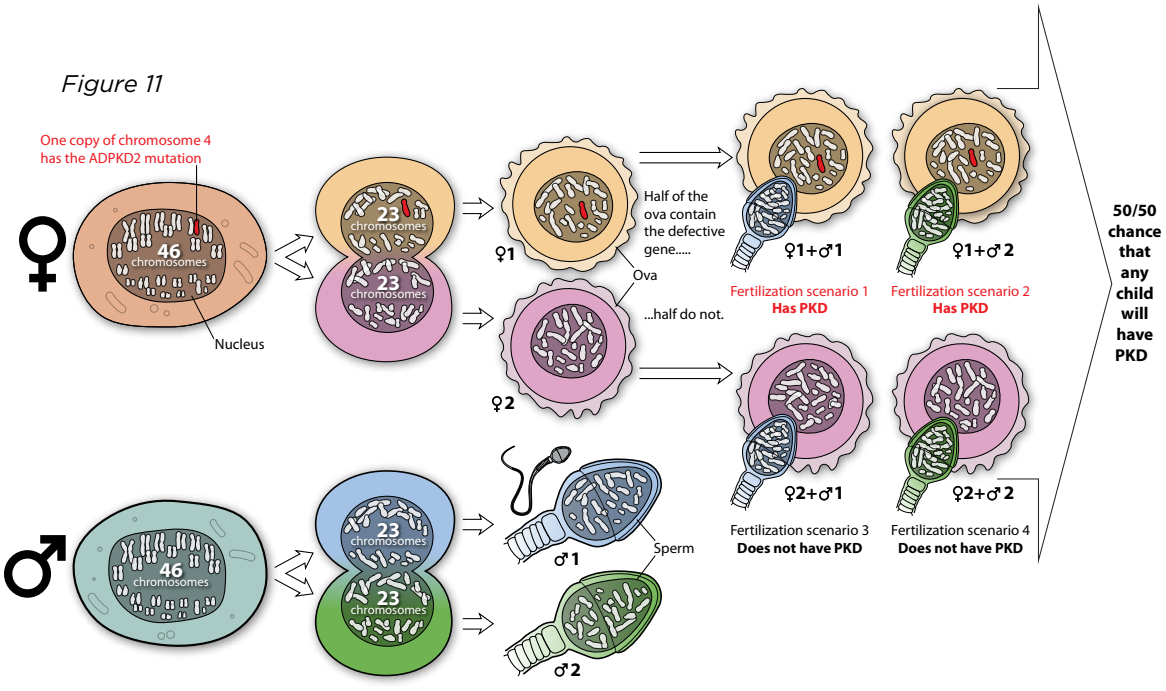
What do we know about PKD genes?

PKD is caused by **mutations** (unintended change or typo) in two genes. Mutations of the first gene, *PKD1*, accounts for about 85 percent of patients affected by PKD, while mutations of the second gene, *PKD2*, account for the remaining patients. There are no other PKD genes that have been identified to date. The *PKD1* and *PKD2* genes encode the proteins **polycystin-1** and **polycystin-2**, respectively. These two proteins interact to regulate cells in the kidneys and liver to maintain their orientation to form tubular structures as well as their growth and fluid secretion function. Mutations of the *PKD1* or *PKD2* gene leads to a wide array of cellular abnormalities associated with normal polycystin function and ultimately result in PKD.

There is a marked difference in kidney disease severity associated with mutations that inactivate the *PKD1* compared to the *PKD2* gene. Specifically, patients with **inactivating *PKD1* mutations** have bigger kidneys, more kidney related-complications and require dialysis at an earlier age compared to those with ***PKD2* mutations** (55 versus 75 years, respectively). More recent studies have also identified a subset of PKD1 patients with milder kidney disease in which their mutations do not seem to completely inactivate polycystin-1 function; this is called a **non-truncating *PKD1* mutation**.

Determining the specific gene mutation you have requires genetic testing. This type of testing is not typically covered by health insurance and could be costly (several thousand dollars). If you or someone you know chooses to explore this option, Athena Diagnostics (athenadiagnostics.com) was the first lab to begin PKD genetic testing and they continue to do so today.

Figure 11



Mutation types:

Inactivating mutation: a change in the DNA that leads to a reduced or complete loss of function of a protein

Non-inactivating mutation: a change in the DNA that does not lead to a loss of function of a protein

Truncating mutation: a change in the DNA that can truncate or shorten the protein

Non-truncating mutation: a change in the DNA that does not truncate or shorten the protein

De novo or spontaneous mutation: a mutation that arises naturally and is not inherited from parents

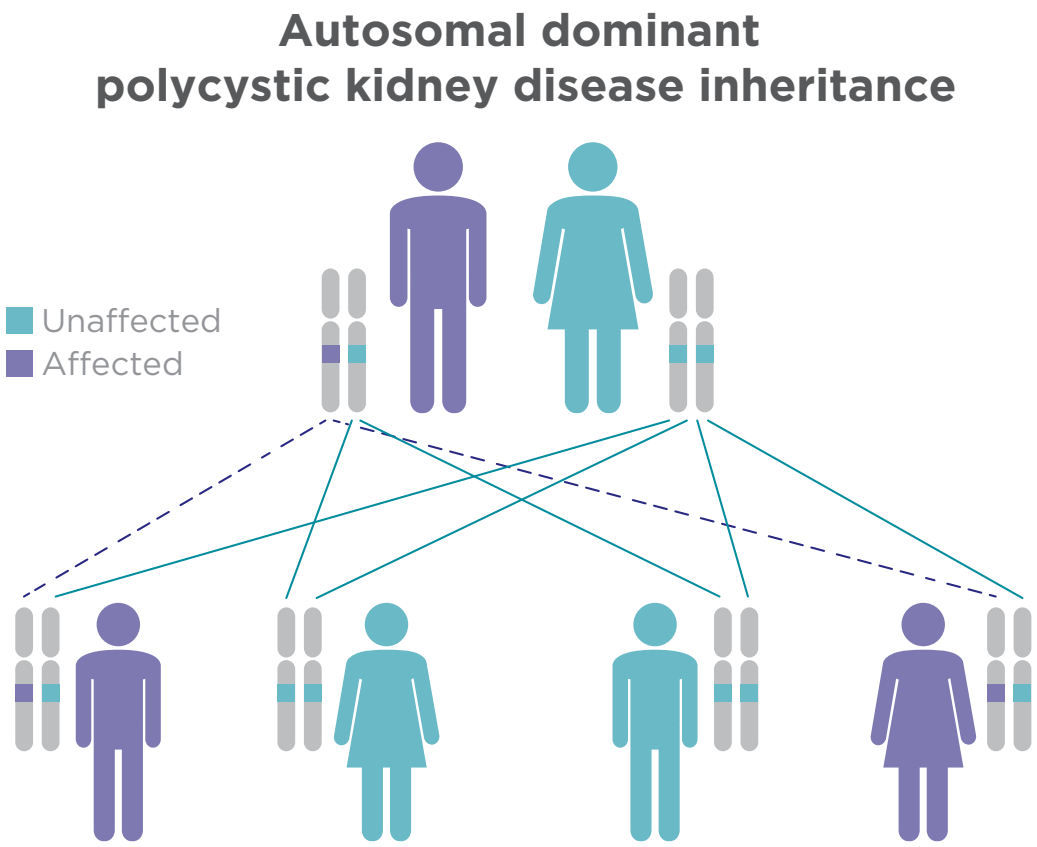
How is PKD inherited?

Most cells in our body inherit one set of 23 chromosomes from each parent to make a total of 46 chromosomes (Fig. 11). Twenty-two pairs are called **autosomes**; the remaining pair are called the **sex chromosomes** since they contain genes that determine gender. The only exception to the above are the **germ cells** (eggs in females and sperms in males), each of which only has a set of 23 chromosomes that are inherited from our parents. Upon fertilization of an egg by a sperm, the full complement of 46 chromosomes is restored. The fertilized egg develops into an embryo and eventually a fully-grown being. The term "**autosomal dominant**" in ADPKD refers to two important features of the disease. First, because the disease genes reside on an **autosome** (i.e. *PKD1* on chromosome 16 and *PKD2* on chromosome 4), both male and female at-risk patients have an equal chance of inheriting PKD. This means that the possibility of transmitting PKD from an affected parent to a child is 1 in 2, or 50 percent (like flipping a coin) when a large number of families are studied. However, the number of affected children within a single family is entirely due to chance and may or may not be 50 percent. Second, the disease is dominant because inheritance of one copy of the mutated *PKD1* or *PKD2* gene from one parent is sufficient to cause disease. By contrast, the inheritance of a copy of a mutated gene from both parents is required for a **recessive** disease.

Four to 10 percent of patients with PKD may have "**de novo**" disease due to a **spontaneous mutation**. Typically these patients do not have a family history of PKD. Their disease is due to a spontaneous mutation of the *PKD1* or *PKD2* gene in one of the germ cells (i.e. egg or sperm) of one of their parents that then gets passed on to them. Individuals with "spontaneous mutations" thus become the founders of a bloodline which is continued into the next generation with 50 percent chance of disease transmission. Most of your body cells carry one normal and one mutated copy of the PKD gene. However, when sperms or eggs are formed in that person, only one of the two copies of a PKD gene is passed on, typically with equal chance. Only the sperms or eggs that carry a mutated PKD gene can pass on the disease. Therefore, the chance of disease transmission to your children is typically 50 percent.

Carrying two copies of the same PKD gene (two *PKD1* or two *PKD2*) is generally not compatible with life, if the mutations are truncating on inactivating.

Figure 12



If I have four children, does this mean that two of my children will have PKD and two will not?

No, this is not necessarily the case. The risk of having a child who inherits the PKD gene is always 50 percent **with each individual pregnancy**, no matter how many children a couple has. It's like the flip of a coin – there is always a 50 percent chance of getting heads and a 50 percent chance of getting tails. In some families, all of the children are affected, while in other families, none are. Many families with multiple children will have both affected and unaffected children.

Will a person with a mutation for PKD always have the disease?

Yes. The genes for PKD are dominant, which means that inheriting only one mutated copy of the *PKD1* or *PKD2* gene from an affected parent is sufficient to cause the disease. **There is no carrier state with a dominant disease, and it does not skip a generation.** This means that the disease will eventually manifest as you get older and that all generations have the potential to be affected. If you have a mutation, at some point in your life at least some of the symptoms of the disease will probably occur, although they could be very mild. **When an at-risk individual does not have a mutation for PKD, he/she is not affected and the disease cannot be passed to the next generation.**

This does not mean that everyone who gets the PKD gene will have the same signs or symptoms or the same course of the disease. There is a wide spectrum of severity within PKD. At one end are children who are diagnosed before birth or in the first year of life with cysts or big kidneys, at the other end are people who have few symptoms, even when they are much older. It is important to note that some individuals (especially those with a *PKD2* or non-inactivating *PKD1* mutation) are more likely to live a normal life span and die of other causes before there is a need for dialysis or transplantation. A majority of patients with PKD will fall in the middle and at some point in their life will have some signs or symptoms associated with PKD.

Will everyone with a mutation in the same family have the same type of PKD?

Yes, all affected PKD patients with the same mutation in a family will have the same type of PKD. However, their signs, symptoms and course of the disease are often different. The most dramatic example of this occurs in families with children who are diagnosed before birth or in the first year of life. These children have symptoms long before their parents. Sometimes the parent may not even be aware they have PKD until after their child is diagnosed. Significant kidney disease variability within PKD families suggest other genetic and environmental factors can modify the severity of this disease.

Core Resources:

PKD Foundation
8330 Ward Parkway Dr
Suite 510
Kansas City, MO 64113
1.800.PKD.CURE
pkdcure.org

PKD Foundation of Canada (for those living in Canada)
3-1750 The Queensway, Suite 158
Etobicoke, ON M9C 5H5
endpkd.ca

PKD United Kingdom (for those living in the U.K.)
pkdcharity.org.uk

Additional Resources:

American Kidney Fund
11921 Rockville Pike
Suite 300
Rockville, MD 20852
1.800.638.8299
kidneyfund.org

American Society of Nephrology
1510 H Street, NW
Suite 800
Washington, DC 20005
202.640.4660
asn-online.org

American Society of Transplantation
1120 Route 73
Suite 200
Mt. Laurel, NJ 08054
856.439.9986
myast.org

Clinicaltrials.gov – A service of the U.S. National Institutes of Health
clinicaltrials.gov/ct2/help/for-patient

DaVita Dialysis
2000 16th St.
Denver, CO 80202
1.888.484.7505
davita.com

DASH Diet
dashdiet.org

Fresenius Medical Care
920 Winter Street
Waltham, MA 02451-1457
1.800.662.1237
fmcna.com

Medicare
7500 Security Boulevard
Baltimore, Maryland 21244-1850
1.800.MEDICARE (633.4227)
medicare.gov

ESRD-specific Medicare Information
medicare.gov/people-like-me/esrd/getting-medicare-with-esrd.html
Medicare: Coverage of Kidney Dialysis and Kidney Transplant Services
Medicare Handbook (CMS Publication #10128)
medicare.gov/Pubs/pdf/10128.pdf

Organ Procurement and Transplantation Network
P.O. Box 2484
Richmond, VA 23218
optn.transplant.hrsa.gov

United Network for Organ Sharing
P.O. Box 2484
Richmond, VA 23218
804.782.4800
unos.org

U.S. Department of Health
and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
1.877.696.6775
hhs.gov

Affordable Care Act
(part of HHS)
hhs.gov/healthcare/facts/timeline/index.
html

Published Research Articles:

Chang MY, Ong A.
New treatments for autosomal
dominant polycystic kidney disease.
Br J Clin Pharmacol 76: 524-535, 2013.

Cornec-Le Gall E, Audrézet MP, Chen JM, et al.
Type of PKD*1* mutation influences renal outcome in PKD.
J Am Soc Nephrol. 2013; 24: 1006-1013.

Harris PC, Torres VE.
Strategies targeting cAMP signaling in the treatment of polycystic kidney disease.
J Am Soc Nephrol. 2014; 25(1):18-32.

Pei Y, Lan Z, Wang K, et al.
A missense mutation in PKD1 attenuates the severity of renal disease.
Kidney Int. 2012; 81: 412-417.

Rossetti S, Kubly VJ, Consugar MB, et al.
Incompletely penetrant PKD*1* alleles suggest a role
for gene dosage in cyst initiation in polycystic kidney disease.
Kidney Int 2009; 75: 848-855.

Torres VE, Bankir L, Grantham JJ.
A case for water in the treatment
of polycystic kidney disease.
Clin J Am Soc Nephrol 4: 1140-1150, 2009.

GLOSSARY

24-hour urine collection
A test done in combination with the blood creatinine test to determine kidney function, called creatinine clearance and is an approximation of glomerular filtration rate

A

ACE inhibitors
Angiotensin converting enzyme (ACE) inhibitors; a group of drugs commonly used to treat hypertension in PKD patients

ADPKD
Autosomal dominant polycystic kidney disease; the more common form of PKD, it occurs in approx. 1 in 500 live births

Aldosterone
A hormone that causes the body to retain salt and lose potassium

Amniocentesis
A test used in prenatal diagnosis of chromosomal abnormalities in which a small amount of amniotic fluid, which contains fetal tissues, is sampled from the amniotic sac surrounding a developing fetus, and the fetal DNA is examined for genetic abnormalities

Amniotic fluid
The protective fluid contained in the amniotic sac of a pregnant female; the fluid is partially supplied by fetal urine which is produced by the fetal kidneys; in ARPKD, poor prenatal renal function causes a reduction in this fluid

Aneurysm
An outpouching in a blood vessel which can leak or rupture

Angiogram
Procedures that utilize contrast dye injected into the blood vessels in order to clearly visualize them; it is typically used when an aneurysm is suspected or to look for blockages in heart vessels

Angiotensin
A powerful constrictor of blood vessels; it stimulates the production of aldosterone

Angiotensinogen
A substance in the blood that forms a hormone called angiotensin

ARB's
Angiotensin receptor blockers (ARBs); a group of drugs commonly used to treat hypertension in PKD patients

ARPKD
Autosomal recessive polycystic kidney disease; occurs in approx. 1 in 20,000 live births.

arteriovenous (AV) graft
A looped, plastic tube that connects an artery to a vein

arteriovenus (AV) fistula
A surgically-created connection from an artery to a vein

Aspirate
To draw fluid by suction

Autosomes
A chromsome that is not a sex chromosome; most cells in our body have 22 sets of autosomes

B

Bladder
A muscular sac in the pelvis that collects urine

Blood pressure
A measurement of the force of the blood as it flows through the body.

Blood type
A classification of blood based on the presence or absence of antigens on the surface of red blood cells; there are four major blood types - A, B, AB, and O; your blood type must be compatible with a potential kidney donor

Blood type incompatible
A transplant option that allows you to receive a kidney from a living donor who has an incompatible blood type; specialized medical treatment is required before and after transplant to prevent rejection

Blood urea nitrogen (BUN)
A measure of kidney function; urea nitrogen is the waste product of dietary protein, so if the urea nitrogen builds up in the blood, it is a sign of decreased kidney function

C

Caffeine
A substance found in coffee, tea, soft-drinks, etc.; it is generally considered best for PKD patients to limit caffeine intake to less than 200-250 mg daily

Calcium
A mineral that the body needs for strong bones and teeth. Calcium may form stones in the kidney.

Calcium oxalate
A common type of crystal that can lead to kidney stones

Carrier
An individual who carries one copy of a recessive gene like that for ARPKD; they do not have the disease but can pass the mutation on to their offspring.

Cell proliferation
Cell growth

Chorionic villus sampling
A test used in prenatal diagnosis of chromosomal abnormalities in which a sample of chorionic villi is removed from the placenta for testing; also called CVS

Chronic pain
Pain that is constant over a long time; long-term pain

Computed tomography (CT)
A screening test that may involve radiation or iodinated contrast dye, which can be toxic to kidneys.

Congenital hepatic fibrosis
A liver abnormality common in children with ARPKD; it may lead eventually lead to enlargement of the liver and spleen

Creatinine
A waste product of muscle metabolism; the level of creatinine in the blood is a measure of kidney function

Creatinine clearance
A test to calculate approximately how much actual kidney function you have

Crossmatch
A bloodtest that tells you what antibodies you have in your body

Cyclic AMP (cAMP)
Signalling molecule in cells that form tubules in the kidneys; abnormalities can lead to cyst formation

Cystitis
A UTI with infection in the bladder

D

Diastolic pressure
The bottom/second number of the blood pressure reading; it measures the pressure when the heart is relaxing between beats

Direct mutation analysis/ DNA sequencing
A type of DNA testing requires only a single sample from the person being tested. An analysis of the DNA sequences of the *PKD1* and *PKD2* genes is performed.

Directed donation
The most common type of living donation; when a living donor (see living donation) names the person who will receive their organ

Diverticula
outpouchings on the large intestine

Diverticulitis
Can occur when diverticuli rupture or become infected

DNA testing
A way to find out if you have a PKD gene. See also gene linkage testing and direct mutation analysis

E

Echocardiogram
An ultrasound of the heart

End-stage renal disease (ESRD)
When normal kidney function declines and needs to be replaced by dialysis or transplantation; also known as kidney failure; typically considered to occur when GFR is at 10 or less

Erythropoietin
Also called EPO; a hormone made in the kidney that tells the bone marrow to make red blood cells; if your kidneys fail or are removed, you must be given EPO via blood transfusions or a synthetic supplement

Estimated post-transplant survival score (EPTS)
A percentile score that ranges from zero to 100 and is assigned to each potential transplant recipient; the score is based on how long you will need a functioning kidney as compared to all other transplant candidates on the list

G

Gadolinium
A special dye used to improve visualization in MRIs

Gene linkage testing
A type of DNA testing that can determine if you have PKD with 99 percent probability in those with a family history. It requires samples from several family members and looks for "markers" in the DNA. A detailed family history is also required.

Glomerular filtration rate (GFR)
The test used to check how well the kidneys are working; it estimates how much blood passes through the glomeruli each minute. Glomeruli are the tiny filters in the kidneys that filter waste from the blood.

Glomerulus
A small tuft of blood capillaries in the kidney, responsible for filtering out waste products.

H

Hematuria
Blood in the urine

Hemodialysis (Hemo)
A procedure that removes extra fluid, electrolytes and waste from blood using a dialysis machine

Hernia
Occurs when the contents of a body cavity buldge out of the area where it is normally contained. Two types of hernia, inguinal and umbilical, are more common in those with PKD

Human leuocyte antigens (HLA)
Markers that let your immune system know which cells belong to your body and which do not; used in tissue typing

Hypertension
High blood pressure; it affects about 60-70 percent of PKD patients and begins early in the course of the disease

I

Inactivating mutation
A change in the DNA that leads to a reduced or complete loss of function of a protein

Intercranial aneurysm
An aneurysm that occurs in the blood vessels of the brain

K

Kidney Allocation System (KAS)
The system that allocates deceased kidney donations to waiting recipients

Kidney donor profile index (KDPI)
A percentile score that ranges from zero to 100 and is assigned to each available deceased kidney; the score is associated with how long the kidney is likely to function as compared to other kidneys, based on information about the donor

Kidney stones
Small, hard deposits made of minerals and acid salts that form inside the kidneys

L

Lithotripter
A machine that uses ultrasound waves to treat large kidney stones

Liver function tests
Blood tests that help determine how well the liver is functioning

Living donation
When a living person choses to donate their kidney (or other organ) to someone who needs a transplant

M

Magnesium
A mineral in the body that is important for metabolism; a deficiency has been associated with high blood pressure

Magnetic resonance arteriogram (MRA)
A type of MRI used to visualize the blood vessels in the brain to screen for aneurysms; it is similar to an MRI scan but does not use contrast dye or radiation

Magnetic resonance imaging (MRI)
A screening test that uses a powerful magnetic field, radio frequency pulses and a computer to produce detailed pictures of the inside of the body.

Microscopic hematuria
Small amounts of blood in the urine

Mitral valve prolapse (MVP)
Occurs when the valve between your heart's left upper chamber (left atrium) and the left lower chamber (left ventricle) doesn't close properly.

Mutation
An unintended change or typo in a person's genetic code

N

National Institutes of Health (NIH)
The agency of the U.S. government primarily responsible for biomedical and health-related research

National Organ Procurement and Transplantation Network (OPTN)
The national registry where donor organs are matched to waiting recipients

Neonatal period
The first month of life of a newborn

Nephrectomy
A surgical procedure to remove one or both kidneys

Nephrogenic Systemic Fibrosis (NSF)
A rare but serious complication that can arise from the use of gadolinium

Nephrologist
A doctor who specializes in kidneys

Nephrons
Tiny filters in the kidney made of think blood vessels; each kidney has about one million nephrons

Neuroradiologist
The type of surgeon who repairs aneurysms

Non-directed donation
When a living donor (see living donation) does not name a specific person to receive their organ; also called altruistic donation

Non-inactivating mutation
A change in the DNA that does not lead to a loss of function of a protein

Non-truncating mutation
a change in the DNA that does not truncate or shorten the protein

NSAIDs
Non-steroidal anti-inflammatory drugs like aspirin or ibuprofen; these are not advisable for PKD patients to take

P

Pain clinic
A clinic or office that uses biofeedback and supports groups to help manage pain.

Paired donation
A transplant option for candidates who have a living donor who is medically able, but cannot donate a kidney to their intended candidate because they are incompatible (i.e. poorly matched); consists of two or more kidney donor/recipient pairs whose blood types are not compatible; the two recipients trade donors so that each recipient can receive a kidney with a compatible blood type.

Peritoneal dialysis (PD)
A type of dialysis that removes extra fluid, electrolytes and waste using the lining of the abdominal cavity

Peritoneum
The abdominal cavity

PKD
Polycystic kidney disease; a genetic disease which causes uncontrolled growth of cysts in the kidneys. There are two forms of PKD: ADPKD and ARPKD.

PKD1
The gene that provides instructions for the polycystin-1 protein; a mutation of the *PKD1* gene will cause a person to have ADPKD

PKD2
The gene that provides instructions for the polycystin-2 protein; a mutation of the *PKD2* gene will cause a person to have ADPKD

PKHD1
The gene that codes for ARPKD

Polycystic liver disease (PLD)
More than 80 percent of PKD patients will develop liver cysts; severe cystic liver disease is uncommon

Polycystin
A protein that is encoded by the *PKD1* and *PKD2* genes; regulates many important tubular cell functions

Polycystin-1
The protein that is coded by the *PKD1* gene

Polycystin-2
The protein that is coded by the *PKD2* gene

Portal hypertension
An abnormality in the liver which can impede the return of blood from the intestine to the liver; it can lead to distention and increased pressure in the veins around the esophagus, the stomach, and the intestine. This can rupture,

leading to possibly life-threatening gastro-intestinal bleeding. In addition, portal hypertension can cause spleen enlargement and hypersplenism resulting in low red blood cell, white blood cell and platelet counts.

Positive crossmatch
A transplant option that allows you to receive a kidney from a living donor who does not match you due to antibodies; specialized medical treatment is required before and after transplant to prevent rejection; this type of donation is only considered when no other option is available

Potassium
A substance essential to all living cells found in most foods; supplements should not be taken without consultation by your doctor or dietician

Pre-emptive transplantation
Having a transplant before dialysis is required

Pre-implantation genetic diagnosis
A form of early genetic diagnoses that uses vitro fertilization; eggs harvested from a mother are fertilized in a laboratory with the father's sperm then the fertilized embryos are tested for ARPKD; embryos that are diagnosed as free of the disorder are then placed in the uterus with the intent to initiate a pregnancy.

Proteinuria
Protein in the urine

Pyelonephritis
A UTI when the infection is in the kidney

R

Red blood cells (RBCs)
RBCs in the urine is called hematuria.

Regurgitation
When blood leaks back to the top part of the heart caused by MVP

Renal dietician
A dietician with special knowledge and experience in kidney disease

Renin
An enzyme produced in the kidneys

Renin-angiotensin-aldosterone system
A hormone system in the body that regulates blood pressure and fluid balance.

S

Satiety
Feeling full; a common side effect of severe PLD

Sclerose
To harden

Sex chromosomes
The chromosomes that contain genes that determine gender

Sonogram
See ultrasound

Spontaneous mutation
A mutation that arises naturally and is not inherited from parents; also called a de novo

Systolic pressure
The top/first number of the blood pressure reading; it measures the pressure when the heart is pumping

T

Therapeutic coil
A device surgically placed in an aneurysm to repair it

Total kidney volume (TKV)
The total volume your kidney holds and is typically measured by MRI

Truncating mutation
A change in the DNA that can truncate or shorten the protein

Tuberous sclerosis complex
A rare, multi-system genetic disease that causes benign tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin; can affect infants who have ADPKD

Tubules
The filtering part of the kidney

U

Ultrasound
The most common and least costly screening method for PKD; a screening method that uses sound waves to develop images of the inside of the body.

United Network for Organ Sharing (UNOS)
The organization that sets transplantation policy and who operates NOTA (see National Organ Procurement and Transplantation Network)

Ureters
The tubes from the kidneys to the bladder

Urethra
The tube that goes from the bladder to the outside

Uric acid
A common type of crystal that can lead to kidney stones

Urinalysis
An analysis of the urine to determine the type of baceria that is causing infection

Urinary tract infection
Commonly called a UTI, an infection caused by bacteria in the bladder, kidneys, or cysts.

Urine
Liquid by-product of the body secreted by the kidneys

Urine citrate
A substance that prevents formation of kidney stones; it may be decreased in some PKD patients

V

Venous catheter
A tube inserted into a vein in your neck, chest, or groin area; not intended for long-term use

W

White blood cells (WBCs)
WBCs are typically present in the urine in small numbers; large numbers in the urine could suggest a UTI

Notes:

Notes:

Notes:

Notes:

This handbook made possible by an education grant from Otsuka America Pharmaceutical, Inc.

PKD FOUNDATION
Polycystic Kidney Disease

pkdcure.org
1.800.PKD.CURE