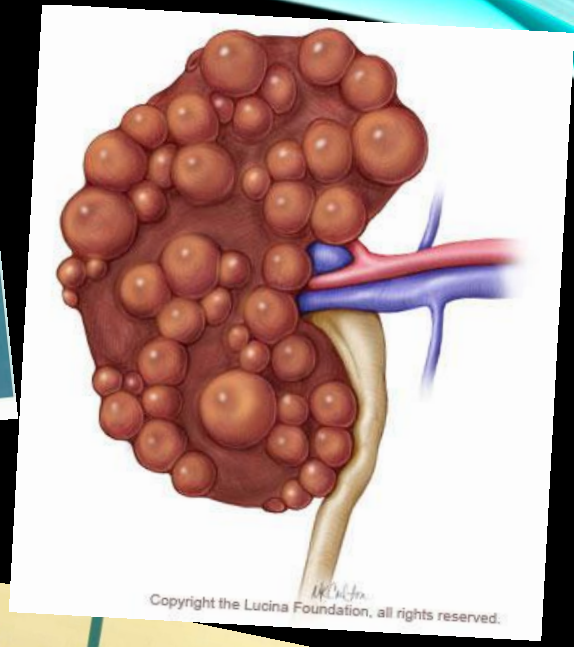
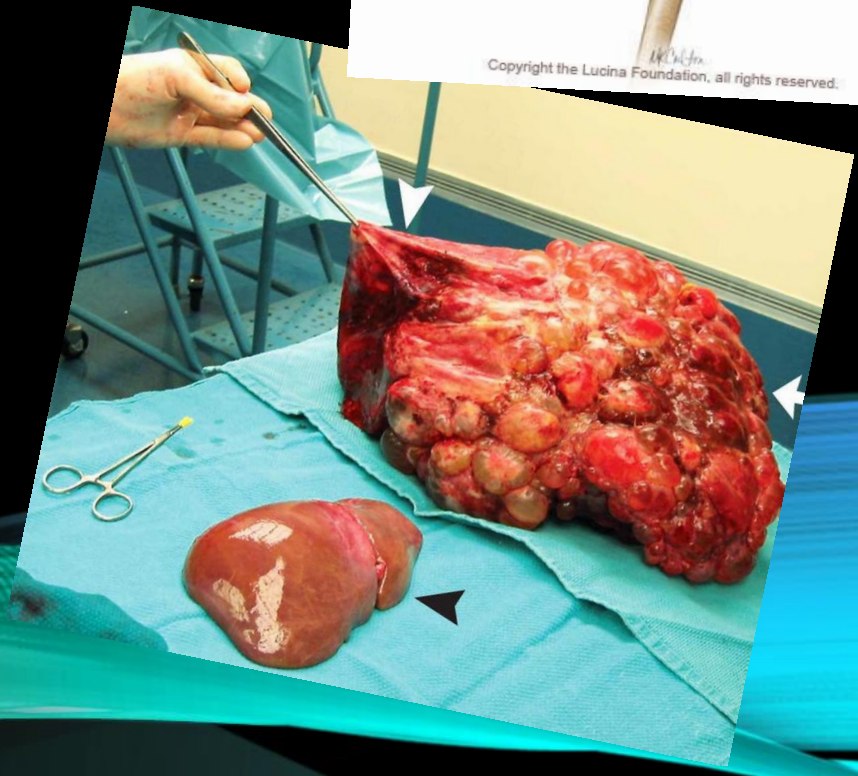
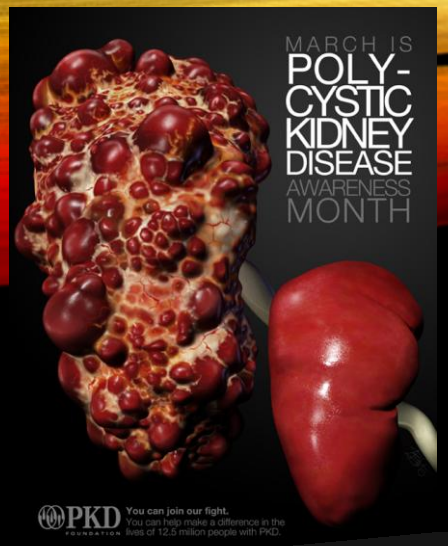
POLYCYSTIC KIDNEY DISEASE

By Suhbat Shugan



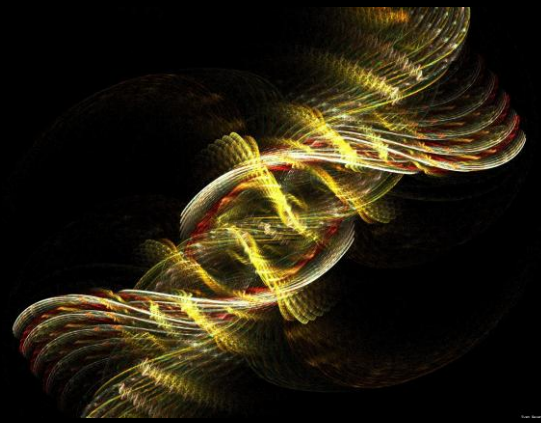




Physiology

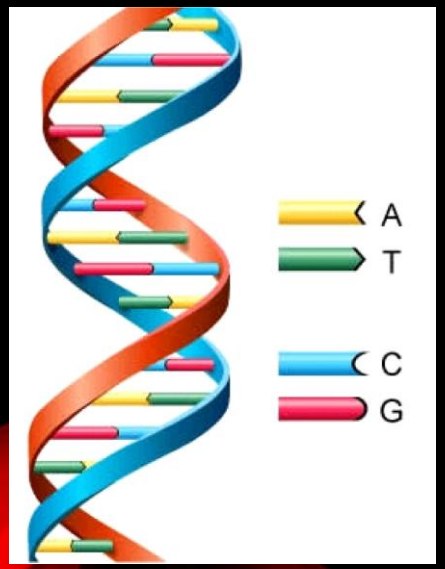
SOME GENERAL PHENOTYPIC INFORMATION ABOUT PKD

- It affects about 600,000 people in the US.
- Polycystic Kidney Disease (PKD) is a genetic disease that affects the kidneys, specifically the renal tubules. These are the tubes that create urine within the kidneys. These tubes swell and create cysts, which are sacs filled with pus.
- PKD has two forms, dominant and recessive. The dominant version is often referred to as the adult PKD because it develops during adulthood.
  - ❑ Onset for PKD dominant is usually around the 20s to 30s
  - ❑ Onset for PKD recessive in during childhood.
- PKD causes an extremely enlarged kidney.
- PKD can also cause different levels of pain which can escalate quickly.
- Individuals diagnosed have frequent urinary tract infections and in the kidney cysts, and usually have hematuria.
- The cysts often spread to other organs, such as the liver, and pancreas. Usually abdominal organs, but can spread to heart as well as the brain.
- Abnormal heart valves are sometimes present.
- Some other symptoms include high blood pressure, kidney stones, aneurysms, and diverticulosis.



MOLECULAR CAUSE

The Genetics Behind The Killer Kidney Conundrum



There are two types of Polycystic Kidney Disease. There is a Dominant type as well as a Recessive type.

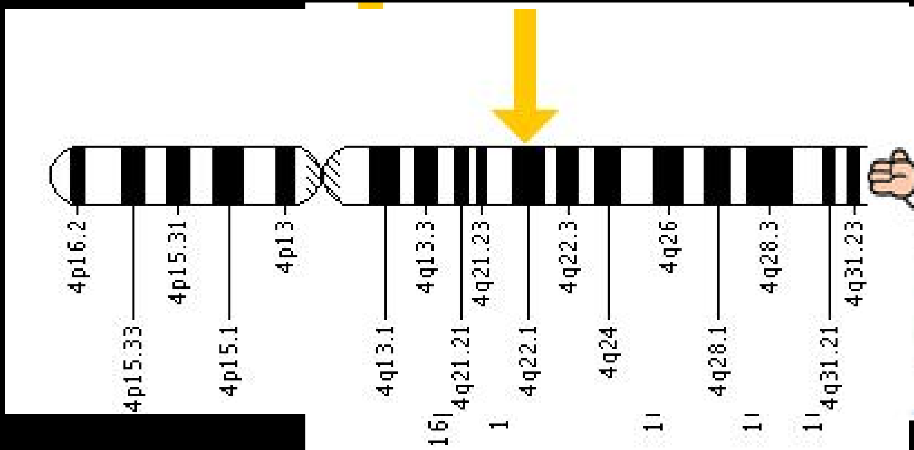
Both are very different and are caused for different reasons, but they are known under the same disease because the phenotypes are the same.

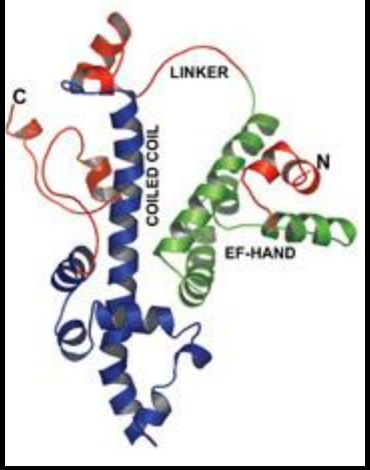
Autosomal Dominant PKD

- ➢ Polycystic Kidney Disease 1
- ➢ Polycystic Kidney Disease 2

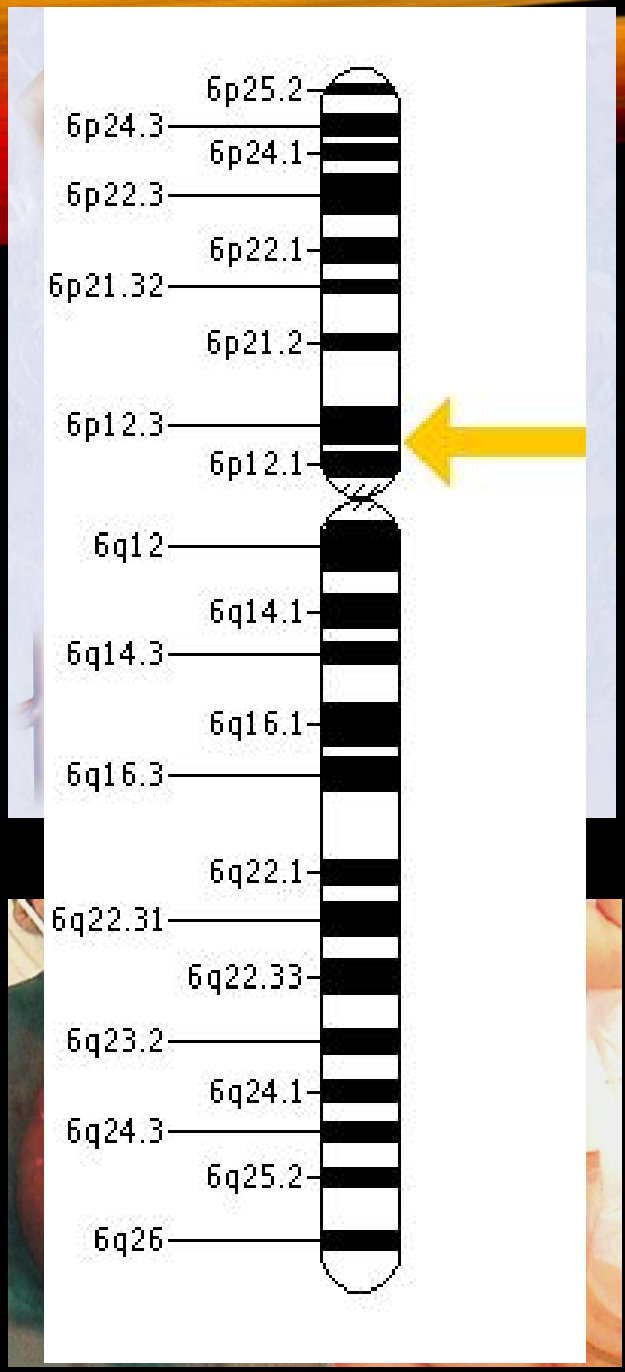
Autosomal Dominant PKD is caused by a mutation in either the gene Polycystic Kidney Disease 1 (PKD1) or the gene Polycystic Kidney Disease 2 (PKD2).

- PKD1 produces protein called Polycystin1.
- ... the part outside the cell interacts with ...
- ... PKD2 ...
- ... chemical changes within the cell.
- ... they help kidney cells control cell growth and division as well as cell movement and ...
- Over 250 different mutations in the PKD1 gene associated with PKD.
- ... also found in ... adulthood ... time.
- ... to the formation of Cysts.





Autosomal Recessive PKD



- Autosomal Recessive PKD is caused by a mutation in the PKHD1 gene.
- The PKHD1 gene is located on chromosome 6 at the location 12.2.
- PKHD1 produces a protein called Fibrocystin (aka Polyductin).
- There are over 270 different mutations in the PKHD1 gene that is associated with the development of autosomal recessive PKD. Unlike PKD1 and PKD2, there is no trend in the resulting mutant protein, it is completely random in PKHD1. The end result is the same, the fibrocystin becomes useless.
- Fibrocystin is located in both fetal and adult kidney cells. It is also located in liver and pancreas cells.
- Fibrocystin, like PKD1 and 2, is a membrane spanning protein. It is a receptor protein that helps cells interact and respond to the environment it is in. It helps to regulate growth, cell adhesion, and cell repulsion.
- Firbrocystin is also found in primary cilia, but the role of fibrocystin in the primary cilia is not known.
- As you know, ARPKD is very severe, and the onset is during fetal development, and life expectancy is low.

Current Treatments and Limitations

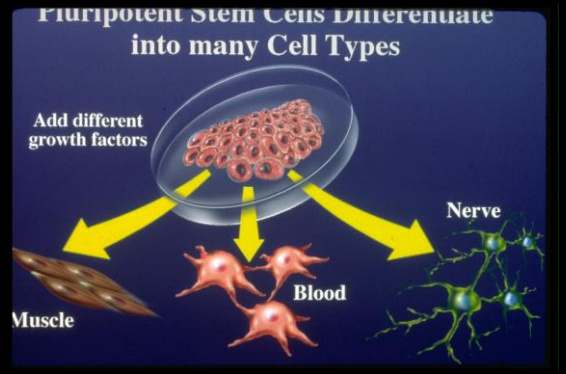
Treatment of Autosomal Dominant PKD

- Doctors usually tackle all the symptoms individually.
- Pain is treated with pain relievers (Tylenol or aspirin). Can also be treated through surgery that drains the cysts within the kidneys.
- Headaches often occur, but they are difficult to treat because it could be because of high blood pressure or because of aneurysms. If because of high blood pressure is the cause, medication can be given to reduce the high blood pressure, but aneurysms must be treated with brain surgery (clipping).
- Antibiotics are prescribed in order to prevent urinary tract infections.
- Diet control and an exercise regimen are usually prescribed. The patients are usually told to avoid certain food which may upset their kidneys or increase their blood pressure. Caffeinated beverages are one example.
- End stage renal disease is the final stage of PKD, kidneys lose all their functionality, the cure is usually to perform dialysis or to perform a kidney transplant, the latter being better because once it is complete, the disease is relatively cured.

Treatment of Autosomal Recessive PKD

- Although many babies with this disease die because of the severity of the disease due to respiratory complications, some are able to survive.
- The main solutions to ARPKD is for the child to undergo organ transplants.
- There are other symptoms associated with ARPKD, such as short stature due to the kidneys being extremely important during development. To treat this, a special diet extra rich in nutrients is prescribed.
- There are also cysts that form in the spleen and liver that cause low blood cell counts and result in hemorrhoids and varicose veins. These organs also have to be replaced.

Proposed Cure



To cure Polycystic Kidney Disease, the population should be checked for kidney cysts every year or so through a sonogram. It is cost effective and can help to detect Polycystic Kidney Disease earlier.

The next step is to teach the public about PKD, the reasoning is to encourage the donation of more organs, which would not only help PKD patients, but also other individuals who need organ transplants.

The final and main part is the development of kidneys through stem cell growth.

- Stem cells would have to be acquired from another individual and grown within laboratories. Cannot be an individual's own cells because they contain the defective gene.
- Does not need to be umbilical, can be obtained from marrow or fat cells.

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