
# Patient Information Resource

#PFICAwareness #ItchingForACure

**Progressive Familial Intrahepatic Cholestasis Advocacy and Resource Network, Inc.**

pfic network

# Diagnosis

# Progressive Familial Intrahepatic Cholestasis (PFIC) is a general term that represents a group of rare genetic disorders that cause a progressive liver disease and can lead to cirrhosis and end-stage liver disease. So what happens next?

**Much like artists set up brushes and canvases as they begin creating beautiful works of art, this was created as a first step in familiarizing what a PFIC diagnosis means for you.**

**Think of this as a road map in understanding the PFIC diagnosis and terminology. This is a starting point between you and a strong support network.**

## What Does PFIC Mean?

Progressive: getting worse over time
Familial: related to change in genes
Intrahepatic: disease inside the liver
Cholestasis: poor bile flow

Itis important to follow up and stay in contact with your provider and specialist. Close monitoring by a Liver Specialist is an important part of achieving the best quality of life for the PFIC patient.

## What to Expect

**Diagnostic Testing**

–Blood Tests: Liver enzymes, GGT and bile acid tests can be useful in identifying PFIC
–Genetic Testing: can be done with a blood sample and involves extracting code from DNA
–Liver Biopsy: a small piece of liver tissue is extracted and then examined under a microscope

## Possible Manifestations

**Symptoms of Cholestasis**

–Itching
–Jaundice (yellow of skin or eyes)
–Swollen abdomen
–Yellow or brown urine
–Acholic stools (stools that are pale, grey or white)
–Bleeding or easy bruising
–Poor growth
–Vitamin deficiencies

**Symptoms Related to Vitamin Deficiencies:**

– Vitamin A: can lead to problems with vision
– Vitamin D: can lead to poor bone formation and an increased risk of broken bones
– Vitamin E: can lead to problems with balance, strength and coordination
–Vitamin K: can lead to bleeding problems, which can be very dangerous especially if bleeding occurs in the brain

**Features of More Advanced Liver Disease**

PFIC can progress to liver failure. If left untreated or unmanaged, liver failure may happen sooner. It is important to understand the difference between signs of cholestasis and signs of advanced liver disease.
–Bruising related to low platelet counts
–Ascites (fluid in the abdomen)
–Esophageal varices (enlarged veins that may bleed)
–Enlarged spleen
–Portal hypertension (high blood pressure in the veins leading to the liver)

**Possible Blood Test Findings with Cholestatic Liver Disease**

–Elevated liver enzymes (AST, ALT, Alk Phos)
–Elevated bile acids
–Elevated bilirubin
–Decreased vitamin levels A,D and E
–Increased PT/INR (due to decreased vitamin K)

## Treatment

– Close monitoring of blood tests, liver ultrasound and frequent appointments with your hepatologists
– Using medications is the first line of defense, but if insufficient surgery may be necessary
– Surgical options aim to keep bile acids from entering the liver. They may include:
  » Partial External Biliary Diversion
  » Partial Internal Biliary Diversion
  » Ileal Exclusion
– Liver Transplant may be necessary if medical and surgical options do not work

## Understanding PFIC

*General symptoms and considerations for PFIC apply to all of the subtypes on this table. This table is intended to highlight some of the potential differences in each diagnosis. Please note, the course of PFIC can be variable and unique, not all patients will experience the disease as it is outlined.*

| Common Name | Protein Deficiency | Mutated Gene | Pruritus (itch) | Other Potential Manifestations | GGT Cholestasis | Potential Clinical Outcomes, Treatment and Complications of Treatment |
|---|---|---|---|---|---|---|
| **PFIC 1** | FIC1 | *ATP8B1* | Intense | •Extrahepatic Symptoms<br>•Diarrhea<br>•May have pancreatitis<br>•May have cough, wheezing<br>•May have hearing loss | Normal GGT Cholestasis | •Moderate rate of progression<br>•Can lead to cirrhosis and end stage liver disease typically in the second or third decade of life<br>•Post-transplant hepatic steatosis (fatty change) and diarrhea<br>•Extrahepatic symptoms can worsen and new ones can develop after liver transplant<br>•BRIC presentations have been recorded* |
| **PFIC 2** | BSEP | *ABCB11* | Intense | •Potential for developing heptocellular carcinoma and cholangiocarcinoma (liver cancer)<br>•Gallstones | Normal GGT Cholestasis | •Moderate to rapid progression<br>•Success of surgical biliary diversion may depend on the specific genetic defects<br>•Liver transplant in PFIC 2 patients may lead to antibody induced BSEP deficiency in some<br>•Potential for retransplant<br>•BRIC presentations have been recorded* |
| **PFIC 3** | MDR3 | *ABCB4* | Mild to moderate | •Reduced bone density<br>•Potential for developing hepato-cellular carcinoma and cholan-giocarcinoma (liver cancer)<br>•Gallstones | Elevated GGT Cholestasis | •Highly variable rate of progression<br>•Medical management: those retaining MDR3 expression respond better to ursodiol<br>•Biliary diversion may not be as effective as in other forms of disease<br>•Liver transplant is curative<br>•BRIC presentations have been recorded* |

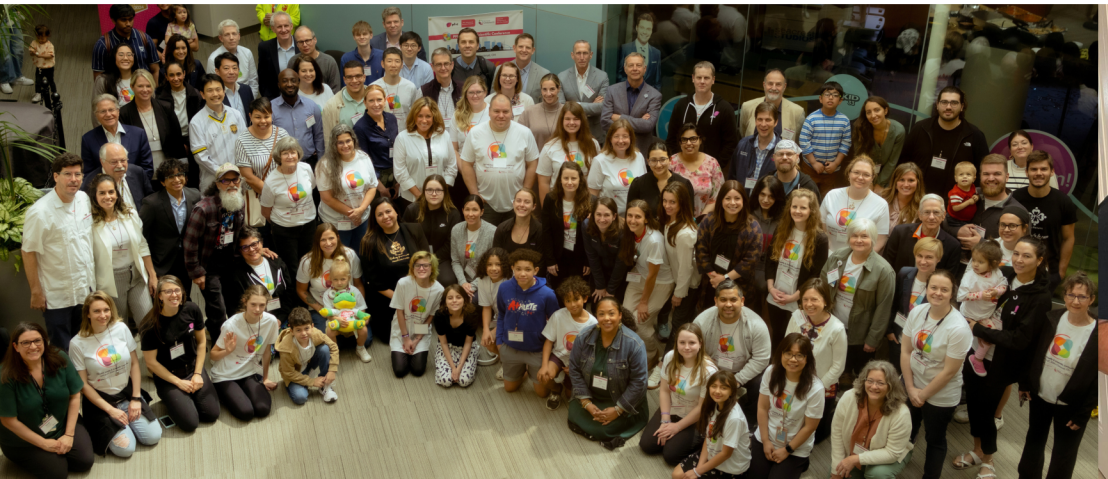
*(BRIC) Benign Recurrent Intrahepatic Cholestasis is a transient presentation of a known or unknown subtype of PFIC.

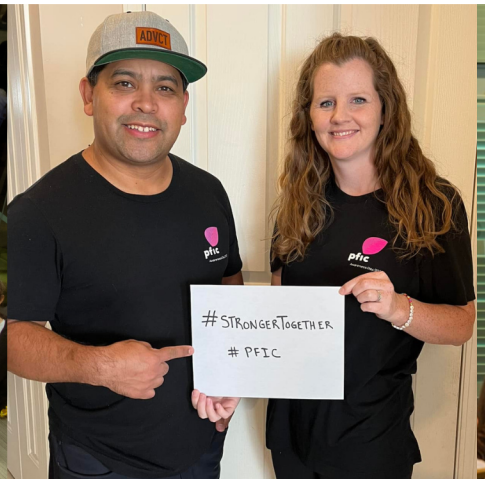


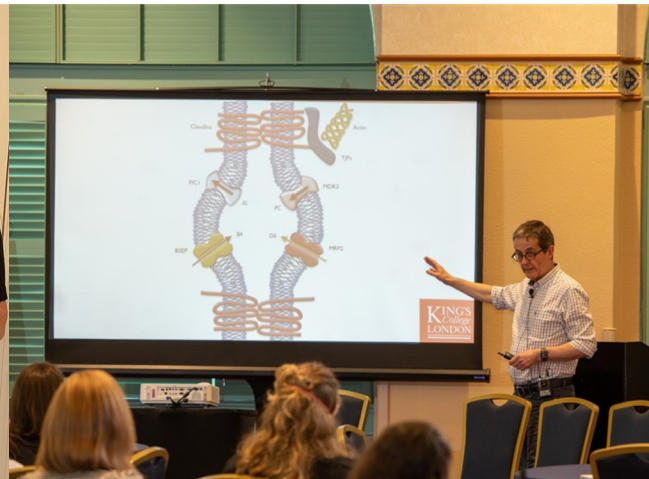
PFIC Subtypes

## Find additional resources at pfic.org

*Visit our website for additional resources, such as educational webinars, patient & family support programs, and research updates!*





## I've been diagnosed with PFIC, but they can't tell me what type?

Genetic studies are underway to try to identify genetic factors contributing to PFIC when mutations are not found in any of the below listed genes. Identifications of these genes is very complicated and require state-of-the-art genetic investigations. Doctors and scientists are working on finding more answers for these patients.

## New genes have been identified.

Not all genetic causes of PFIC have yet been discovered. Scientists continue to uncover new genes linked to PFIC. Please visit our website for an updated list of genes associated with PFIC.



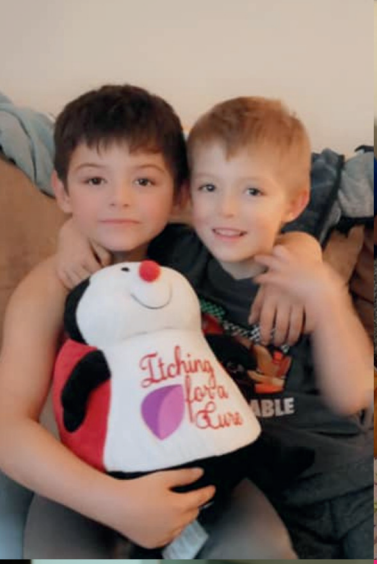


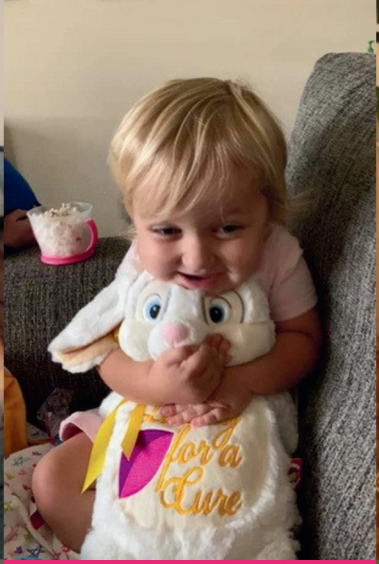
PFIC Subtypes

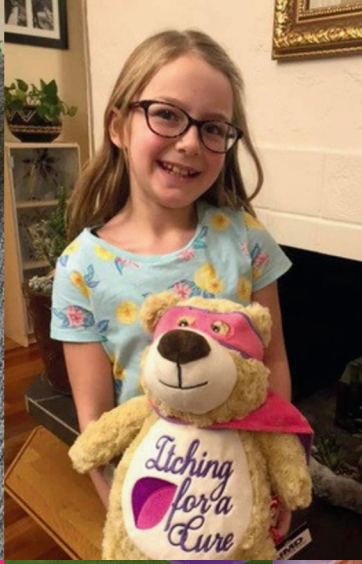
| Common Name | Protein Deficiency | Mutated Gene | Pruritus (itch) | Other Potential Manifestations | GGT Cholestasis | Potential clinical Outcomes, Treatment and Complications of Treatment |
|---|---|---|---|---|---|---|
| *The following subtypes are exceedingly rare in the reported literature (although being recognized more).* | | | | *This information is based on only a handful of patients in eachgroup and should be viewed with that in mind.* | | |
| **PFIC 4** | TJP2 | *TJP2* | Unclear/variable | •Hearing loss<br>•Neurological Symptoms<br>•Respiratory Symptoms | Normal GGT Cholestasis | •Moderate to rapid progression<br>•Some reports of hepatocellular carcinoma |
| **PFIC 5** | FXR | *NR1H4* | Unclear/variable | •Vitamin K independent coagulopathy<br>•Can mimic BSEP deficiency | Normal GGT Cholestasis | •Very rapid progression<br>•Post-transplant hepatic steatosis<br>•Very rare (Only eight cases reported as of December, 2020). |
| **PFIC Associated with MYO5B defects** | MYO5B | *MYO5B* | Mild to moderate | •Potential for congenital diarrhea | Normal GGT Cholestasis | •Slow progression<br>•MicroVillus Inclusion Disease (MVID) can be experienced<br>•Lifelong TPN with associated MVID<br>•Combined bowel liver transplants may prevent post transplant cholestasis |
| | USP53 | *USP53* | Mild to moderate | •Hearing loss<br>•Heart failure reported in one patient | Normal GGT Cholestasis | •Slow progression<br>•Age of onset is variable<br>•Continued follow-up is needed for all patients<br>•First published in seven patients, in September, 2020 |
| | MRP9 | *ABCC12* | Intense | •Intrahepatic bile duct paucity | Normal GGT Cholestasis | •Slow progression<br>•Uncertainty whether PFIC occurs with (one) heterozygous mutation in ABCC12<br>•Only one case published as of March, 2021 |

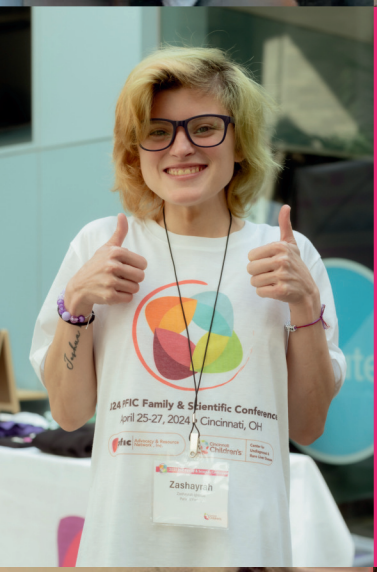
**PFIC Definition of Terms**

**ALT and AST:** Markers of liver injury.
**Antibody Induced BSEP Deficiency (AIBD):** cholestasis that can develop after transplant in some PFIC 2 patients related to the development of BSEP antibodies.
**Autosome:** Any chromosome that is not a sex chromosome.
**Benign Recurrent Intrahepatic Cholestasis (BRIC):** Is a transient presentation of a known or unknown subtype of PFIC.
**Bile:** Bile is a yellow fluid that contains a number of compounds including bile acids, phospholipids, cholesterol and waste products from the body.
**Bile Acid/Bile Salt:** Bile acids are chemicals made by the liver from cholesterol. In a healthy individual bile acids are transported from the liver to the intestines where they help to absorb fats, fat soluble vitamins and other fat-soluble nutrients. They are then circulated back to the liver such that they can be reused.
**Cholestasis:** Means poor bile flow and build-up of substances in the liver that would normally be carried out of the liver into bile and then the intestines.
**Cholestatic Pruritus:** Is the sensation of itch due to liver disease.
**Chromosome:** Chromosomes are large molecules that mainly consist of DNA.
**Dominant:** Dominant disorders are a single defective copy of a gene that can lead to disease. The impact of that defective copy is dominant over the other copy which is healthy.
**Familial:** Originally described in families and related to changes in genes.
**Gamma GT (GGT):** A type of liver enzyme which may help to distinguish between the types of PFIC.
**Genes:** Genes are short parts of a chromosome that contain the genetic code for heritable characteristics. Some characteristics such as height are influenced by many genes, and some just by one single gene. Humans have two copies for most genes including those associated with PFIC.
**Hepatic Steatosis:** Fatty change in the liver.
**Hepatocytes:** Liver cells, responsible for making bile.
**Hepatologist:** A doctor who specializes in liver disease.
**Icterus:** Yellowing of the skin, mouth, tongue, etc.
**Intrahepatic:** Involves disease inside the liver.
**Jaundice:** Yellowing of skin.
**Liver:** The Liver is the largest solid organ in the body. It plays an essential role in many different body functions, such as removing toxic substances from the blood, or producing proteins and bio- chemicals (bile) that are necessary for digestion and growth.
**Microvillus Inclusion Disease:** A disease caused by structural changes in the small bowel usually, but not always, causing severe diarrhea.
**Mutations:** A change in the genetic code.
**Offspring:** A person's child or children.
**Progressive:** Tending to get worse over time.
**Recessive:** Two abnormal copies of a gene to have disease.
**Scleral Incterus:** Yellowing of the eyes.

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