PFIC VOICES®

Progressive Familial Intrahepatic Cholestasis

A Guide for Patients and Families

What is PFIC?

Progressive familial intrahepatic cholestasis (PFIC) is a spectrum of rare, inherited liver diseases that can lead to severe itching (pruritus), lack of sleep, slowed growth, and liver failure.

The itching can be so severe that children and infants may scratch through their skin.[1] Many patients turn to surgery, including liver transplant, to relieve the itching.[2,3]

PFIC affects 1 in 50,000 to 100,000 births.[4] It is caused by mutations on different genes, including ATP8B1 (PFIC1), ABCB11 (PFIC2), ABCB4 (PFIC3), and others.[5] PFIC1, PFIC2, and PFIC3 are the most common types.[4] In addition, other rare forms of PFIC exist. They have some differences, but all cause problems with bile flow.[5]

PFIC1 and PFIC2 usually appear in the first months of life. PFIC3 may also occur later in infancy, in childhood, or even during young adulthood.[4]

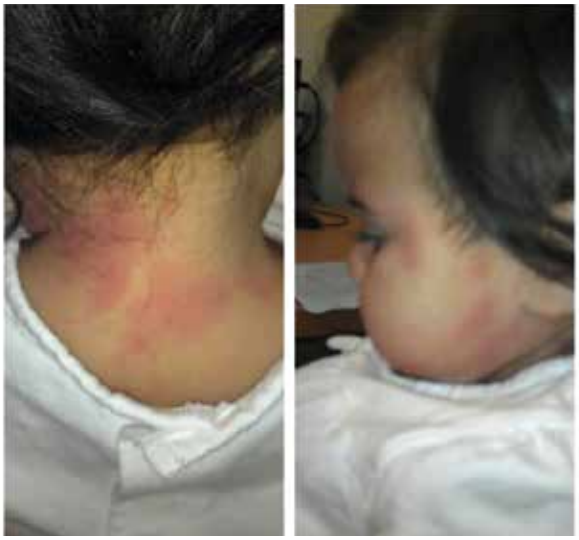
What Happens in PFIC?

The body naturally makes bile acids that help with digestion, including absorbing fats and some vitamins. In people with PFIC, the normal flow of bile acids is disrupted. Bile acids build up in the body, damaging the liver.[6,7]

What information is contained in this PFIC pamphlet, and who is it for?

PFIC stands for progressive familial intrahepatic cholestasis. It's a rare liver condition that requires medical attention and support. This pamphlet provides an overview of PFIC, how it is diagnosed and places you and your family can turn to for support. This overview is for the PFIC community and others who wish to learn basic information about this serious condition.

Signs and Symptoms



PFIC can cause signs and symptoms that may vary by person. Here are some of the most common.

Severe itching (pruritus). Itching can be disruptive, leading to loss of sleep, poor attention, and lower school performance.[1]

Jaundice. Yellowing of the skin and eyes may occur in the first months of life. In PFIC2 patients the jaundice may be permanent from the beginning, while in PFIC1 patients, jaundice may come and go at first, and become permanent later.[4]

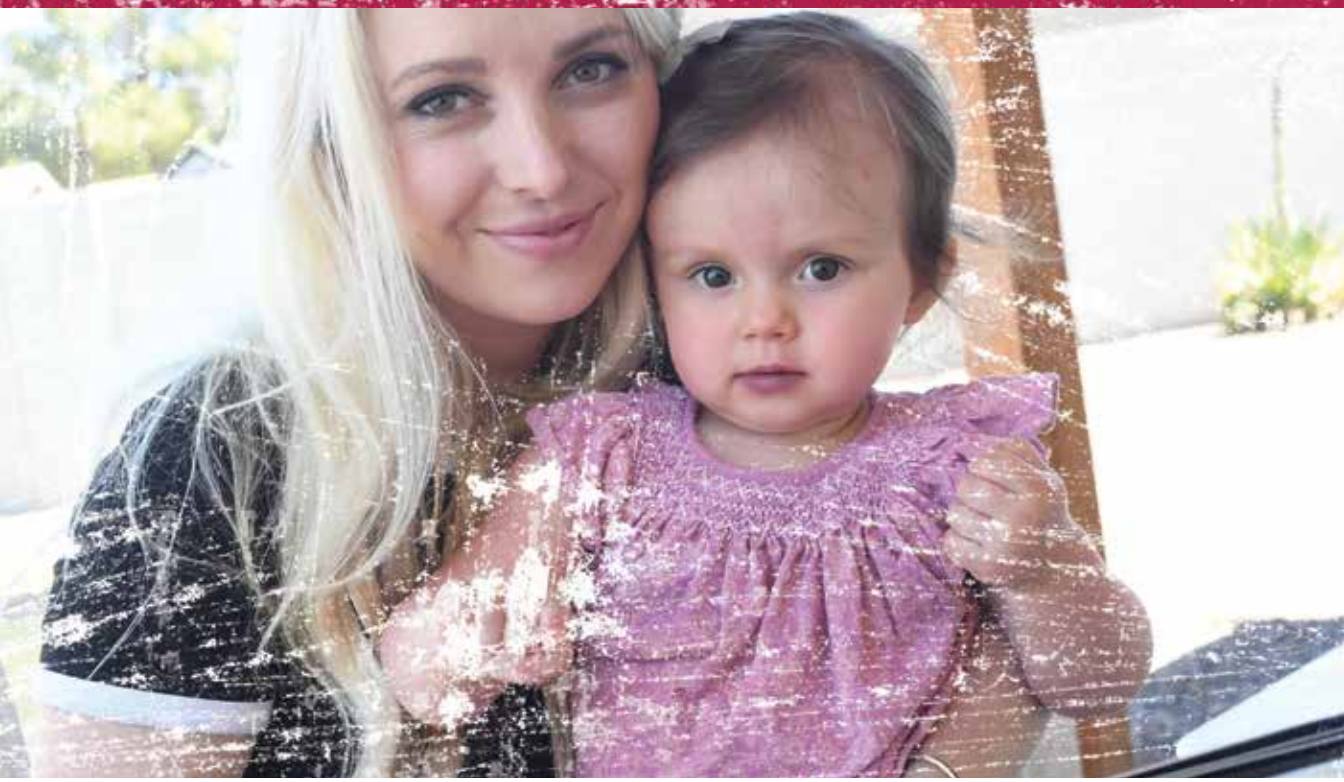
Nutritional problems. PFIC patients may have problems absorbing fats and fat-soluble vitamins (vitamins A, D, E, and K). As a result, height and weight may be below normal.[1]

Liver problems. Problems with bile flow can damage the liver, potentially leading to liver failure.[4]

Other signs and symptoms. Other problems may include diarrhea and pale or discolored stools.[8]

"The itching associated with PFIC is life-changing for the child and the family. Children with PFIC are unable to sleep, and their development and ability to learn and grow suffer. Parents have to restrain their child to try to prevent them from scratching until they bleed. It's heartbreaking. It can become so debilitating that the itching brings us to recommend liver transplantation for the child. The itching can be that bad."

Dr. Jaime Chu
Pediatric Hepatologist
Mount Sinai Medical Center
New York
Consultant to Albireo



A Parent's Perspective

"When Sylvie was three weeks old, I noticed that when she was drinking her bottle, she would itch extensively on her face and her eyes. And I thought that was odd. The more she would get into her feeding, the itchier she'd get. I told my pediatrician and the doctors at the hospital. All of them said it was eczema or dry skin, so I used lotion for a long time. Nothing worked. It almost made it worse, because she would wipe the lotion into her eyes, and then she'd start screaming.

After we got the diagnosis of PFIC, the itching was the most debilitating thing for us. To get that managed was so important for everyday life and quality of life. And we just don't have that yet. We have these amazing days and horrible days. And I think, if we can manage that itching and getting her stable, that would be a miracle."

Season, mother of a daughter with PFIC

How is PFIC Diagnosed?

Your child's doctor may suspect PFIC if your child has itching or jaundice that does not go away. The doctor will try to rule out other, more common causes of jaundice first. A pediatrician may recommend sending a patient to a liver specialist for special tests, including blood tests, imaging, or liver biopsy. Physicians who specialize in the digestive system or gastrointestinal system are called gastroenterologists. Physicians who specialize in the liver are called hepatologists.

Genetic testing can be relied on to support but not always definitively confirm the clinical diagnosis of PFIC.[9]

PFIC is an autosomal recessive disorder.[4] This means that a child must inherit an affected gene from both parents for the disease to be present. If the child only inherits the affected gene from one parent, he or she will be a "carrier" but will not have the disease.

Living with PFIC

Patients and their families should consult their healthcare providers for guidance on PFIC management. The following topics may be considered:

- **Skincare:** Patients with PFIC may have sensitive skin. It may be beneficial to cover skin as much as possible and to keep nails short.
- **Nutrition:** Talk with your doctor about possible ways to help manage nutritional deficiencies.

PFIC affects different people in different ways. Patients and parents should consult their healthcare providers for guidance on what may work best for them.

Surgical Interventions

When liver disease progresses, families may consider surgical options, including biliary diversion and liver transplantation.

Biliary Diversion. In surgical biliary diversion (or partial exterior biliary diversion, PEBD), bile is diverted out through the abdominal wall and, typically, collected in an ostomy bag outside the body. A less common approach called ileal exclusion (or internal biliary diversion), involves bypassing part of the small intestine and connecting it to the colon.

Liver Transplantation. Liver transplantation may be an option for some patients who experience progressing liver disease or severe itching.[1] Like all major surgeries, it has significant risks. Even when it is successful, it requires the patient to receive life-long immunosuppressive therapy. to prevent the body from rejecting the new liver.[10]

Medical Intervention

A class of medications called IBAT inhibitors has been approved to treat severe itching in PFIC. While it is not known exactly how IBAT inhibitors work, it is thought that by reducing bile acids in the blood, they may reduce the amount of itching PFIC patients experience. Talk to your doctor about whether this approach is right for your child.

Hope for Patients and Families

PFIC Advocacy and Resource Network aims to improve the lives of patients and families worldwide affected by PFIC.
PFIC.org

Childhood Liver Disease Research Network (ChiLDReN) offers medical and patient advocacy support with clinical sites and research labs in the U.S.
Childrennetwork.org

Children's Liver Disease Foundation (CLDF) is a UK-based charity dedicated to pediatric liver diseases. Download the CLDF PFIC brochure here: https://www.childliverdisease.org/wp-content/uploads/2018/01/PFIC.pdf.
Childliverdisease.org

ClinicalTrials.gov provides the public with information on clinical studies on a wide range of diseases and conditions, including PFIC.
Clinicaltrials.gov

Global Genes is an advocacy organization committed to supporting the rare disease community.
GlobalGenes.org

American Liver Foundation (ALF) is a national, voluntary nonprofit organization dedicated to the prevention, treatment, and cure of hepatitis and other liver diseases through research, education, and advocacy.
LiverFoundation.org

The National Organization for Rare Disorders (NORD), an independent nonprofit founded over 35 years ago, is leading the fight to improve the lives of patients with rare diseases. It does this by supporting patients and organizations, accelerating research, providing education, driving public policy and spreading awareness.
Rarediseases.org

About Albireo

Albireo is committed to supporting people with PFIC, their families, and healthcare providers with resources to better understand and manage this devastating disease. The company is focused on the development of novel bile acid modulators to treat rare pediatric liver diseases, such as PFIC.

albireopharma.com

Special thanks to these organizations and the families living with PFIC for their support and contributions.

References

1. Srivastava A. J Clin Exp Hepatol 2014;4:25-36. 2. Bjørnland K et al. Eur J Pediatr Surg. 2020. 3. van Wessel DBE et al. Hepatology. 2021;10.1002/hep.31787. 4. Davit-Spraul A et al. Orphanet J Rare Dis. 2009;4:1. 5. Amirneni S et al. World J Gastroenterol. 2020;26(47):7470-7484. 6. Kamath BM et al. Liver Int. 2020;40(8):1812-1822. 7. Karpen SJ. Clin Liver Dis. 2020;15(3):115-119. 8. Baker A et al. Clin Res Hepatol Gastroenterol. 2019;43(1):20-36. 9. Bull LN et al. Clin Liver Dis. 2018;22:657–669. 10. Stapelbroek JM et al. J Hepatol. 2010;52(2):258-271.

Global Genes® Allies in Rare Disease

Children's Liver Disease Foundation fighting childhood liver disease

NORD® National Organization for Rare Disorders

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