LIVING WITH APDS:

What to know about activated PI3K delta syndrome (APDS)

This guide can be a helpful resource for people living with APDS and their support network. Inside, you will find information on the underlying cause of APDS, common symptoms, family genetic testing, and how to work with your healthcare team to better manage symptoms.

APDS is also known as PASLI.

Pharming

WORDS TO KNOW

You will see these boxes throughout this guide providing definitions for terms you may hear in conversations with your healthcare team.

EXPERT INSIGHT

This icon will appear wherever APDS experts Dr Wu and Dr Siri have provided their insight on topics within this guide.

Dr Eveline Wu
A pediatric rheumatologist and immunologist at the University of North Carolina School of Medicine

Dr Dareen Siri
A pediatric and adult allergy, asthma, and immunology specialist and the founder of Midwest Allergy Sinus Asthma (MASA) in Illinois

What is APDS?

The full name for APDS is activated PI3K delta syndrome. The name stems from the underlying cause of APDS—hyperactivation of a signaling pathway in the body known as the PI3K delta pathway.

APDS is one disease in a group of over 400 rare genetic conditions known as primary immunodeficiencies (PIs). A common characteristic of all PIs is that they impair the body's immune system.

Each person living with APDS may experience the disease differently because an impaired immune system can cause lots of different problems. The most common symptoms are frequent and/or severe infections of the ear, sinuses, or respiratory tract. However, numerous other symptoms can occur due to APDS.

Quick facts about APDS

- APDS is a rare disease that **affects about 1 to 2 people per million** (In the US, there is estimated to be around 500 people with APDS).
- Symptoms of APDS can begin at any age and can vary from person to person—even among members of the same family.
- The median time to diagnosis for APDS after symptoms first appear is **7 years.** A genetic test early in the journey can ensure APDS is detected sooner and is the only way to definitively diagnose APDS.
- APDS is caused by **variations in your genes,** so it is with you from the very beginning—although symptoms may not appear until later in life.

As a genetic disease, APDS can be passed from a parent to their child. It's important for relatives of anyone diagnosed with APDS to **talk to their doctor about family genetic testing.**

PI3K: phosphoinositide 3-kinase.

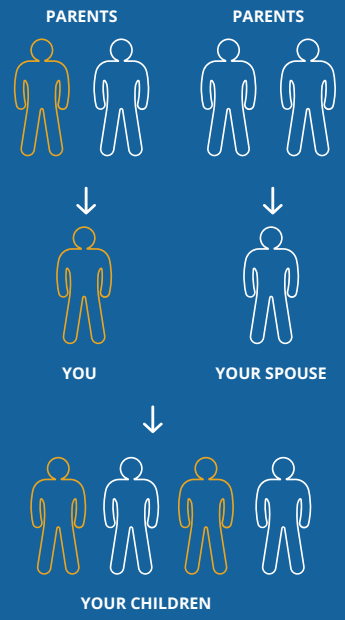
APDS can be passed from parent to child

APDS is an autosomal dominant disease—meaning **if either parent has APDS, there is a 50% chance their child will inherit the disease.** It's important to note that the genetic variants causing APDS can also occur randomly, without the child inheriting one from a parent (this is called a *de novo* variant).

HOW YOU COULD HAVE INHERITED APDS

If you have been diagnosed with APDS, you may have inherited the disease from one of your parents.

If you are a parent with APDS, there is a 50% chance your child will have APDS.



"In some families, APDS may manifest differently in one relative compared to another. They may have had different infections or autoimmune symptoms. We strongly encourage family screening." —Dr Siri

Family testing for APDS is strongly recommended

If you have been diagnosed with APDS, it is likely that other relatives also have the same genetic variations that cause the disease. Genetic testing could provide answers for any family members who have been undiagnosed or misdiagnosed for years.

"Prior to genetic testing being available, I had some patients who had been sick for 20 years without a diagnosis." —Dr Wu

Diagnosed with APDS?
Talk to your doctor about genetic testing for your children, your siblings, and other relatives who may be affected.

Parent of a child with APDS?
Talk to your doctor about genetic testing for you, your child's other parent, your child's siblings, and other relatives who may be affected.

Related to someone living with APDS?
Ask your doctor if you or your family members should undergo genetic testing.

SCAN WITH YOUR PHONE

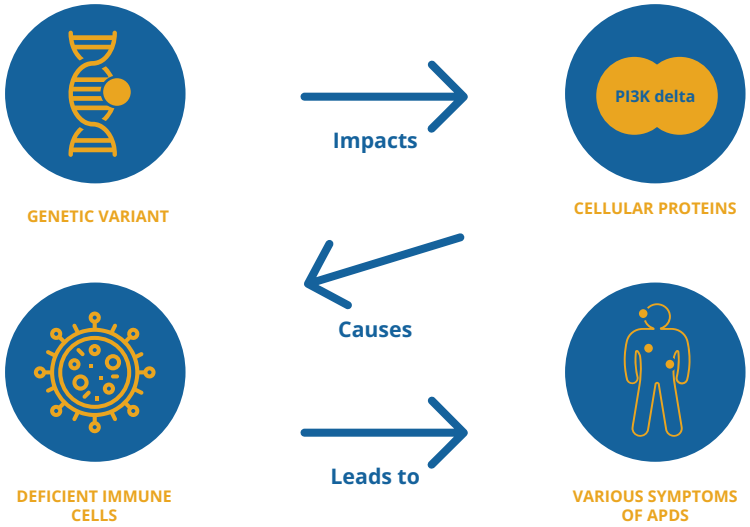
Download a customizable family tree to fill out and show to your doctor.

If you or a loved one has been diagnosed with APDS, learning the cause and symptoms is important →

The underlying cause of APDS

APDS occurs when there is a genetic variation in either the *PIK3CD* or *PIK3R1* gene. These genes provide the instructions for making a group of proteins in the cells of the immune system known as PI3K delta.

PI3K delta proteins control the development and function of B and T cells (immune cells). These are cells that help you fight infections. In APDS, PI3K delta proteins are overactive, leading to your body having too many immune cells that are either too old or too young to help your body fight off infections.



What are B and T cells?
Types of white blood cells that play important roles helping your body fight diseases. B cells produce antibodies and can activate other immune cells. T cells kill infected host cells and also activate other immune cells.

Signs & symptoms of APDS

An improperly functioning immune system can lead to many symptoms. Some people may experience few or mild symptoms, while others can have many severe symptoms that get steadily worse over their lifetime. Read below for some of the typical signs and symptoms.

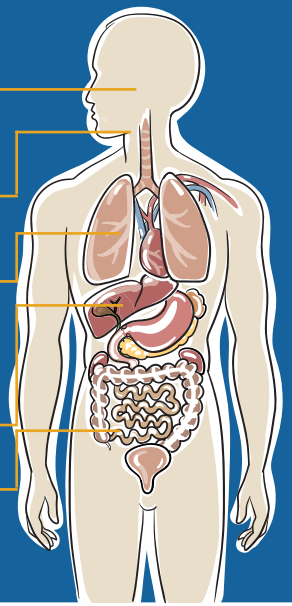
Frequent and severe respiratory tract, sinus, or ear infections

Persistent painful or swollen lymph nodes

Coughing phlegm (mucus), wheezing, difficulty breathing, chest pain (These symptoms can lead to a serious condition called bronchiectasis)

Enlarged spleen or liver

Diarrhea, abdominal pain, cramping, blood in stool, or malabsorption (a potential cause of weight loss)



Additional features:

- Frequent and severe herpesvirus infections, including Epstein-Barr virus and cytomegalovirus
- Fatigue, which can result from low numbers of red blood cells
- Developmental delay (speech and growth)
- Lymphoma occurs in 12-25% of people with APDS

What is lymphoma?
A cancer of the immune system that occurs when B or T cells change and grow out of control. When patients with APDS have lymphoma, they typically get it at around 18-23 years of age.

Clear communication between you and your healthcare team can help with managing APDS symptoms →

Partner with your healthcare team to manage APDS

With the varying symptoms and the uncertainty that can come with APDS, it's important to work closely with your healthcare team.

You may see multiple specialists, along with your primary care provider, to manage your specific symptoms. It's important that your specialists are made aware of the therapies you are taking for symptom management. This can help them have a more complete picture of your overall health and better help you to manage your symptoms.

Below are some steps you can take to be proactive in communicating with your healthcare team:

Take notes	...at your medical appointments and at home when you're experiencing symptoms. Noting the frequency and severity of your symptoms in a daily journal can give you detailed information to share with your healthcare team.
Talk with your doctor about how you are feeling	...not just your symptoms, but how you are doing emotionally and socially in your daily life. Your healthcare team wants to know if you are struggling, and they may be able to help.
Track your treatments and symptoms	...and record any progress or setbacks in your symptoms to share with your different healthcare specialists. It's important for them to know what is working and what isn't so they can coordinate effectively.

"Medical providers can really partner with families—not just for their physical health, but for their mental health too. It helps to know you have someone in your corner fighting for you." —Dr Wu

Questions to ask your doctor

Sometimes it can be hard to know where to start when trying to understand a new diagnosis. Below is a list of some questions you can bring to your healthcare team:

- Knowing how my APDS symptoms have been impacting my life, how can we better manage my symptoms?
- Are there certain activities I need to discontinue or modify due to APDS?
- How often should I come in for checkups?
- Are there any tests I should be getting for diseases I'm at increased risk for?
- Which specialists should I be seeing, and will you be working with them to help manage my symptoms?
- Are there any groups you can connect me with for social support?
- Which of my family members should be tested and how do we go about getting this done?

Consider genetic testing for family members
APDS can be inherited. So if you or a family member have been diagnosed with APDS, it's recommended that you discuss genetic testing with your doctor.

navigateAPDS by Pharming

navigateAPDS offers no-charge sponsored genetic testing and counseling for individuals who meet specific criteria.*

*Available in the United States and Canada only.

You and your support system could benefit from additional resources and services →

Support for people affected by APDS

Whether you have been diagnosed with APDS or are caring for a loved one who has, finding necessary support can get you answers to questions and provide a sense of community.

Looking for more information on primary immunodeficiencies like APDS?

Primary Immune Deficiency Treatment Consortium

The Primary Immune Deficiency Treatment Consortium (PIDTC) offers connections to primary immunodeficiency patient support groups, experts, and educational resources, and also provides information to physicians on immune disorders, treatment options, and research studies.

IPOPI
INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

International Patient Organisation for Primary Immunodeficiencies (IPOPI) is a nonprofit international organization dedicated to improving awareness and access to early diagnosis and optimal treatments for primary immunodeficiency patients through global collaboration.

jm Jeffrey Modell Foundation

At the Jeffrey Modell Foundation (JMF) website, you can access patient-friendly e-books and other information about primary immunodeficiencies, as well as find doctors and connect with other patients and caregivers.

IDF Immune Deficiency Foundation

The Immune Deficiency Foundation (IDF) provides information about primary immunodeficiencies, treatments, awareness, and advocacy. Connect with other patients and caregivers to share your experiences.

Want insight on genetic testing and genetic disease?

GeneMatters™
Genetics Care. Reimagined.
A Genome Medical Company

GeneMatters provides genetic counseling services and has genetic counselors who can help you make the best decisions for your family. This service is free for those who have undergone genetic testing through the navigateAPDS program.

Looking to connect with the rare disease community?

Global Genes®
Allies in Rare Disease

At the Global Genes website, you can find other patients with rare diseases, access information and resources, connect to researchers, and learn to advocate.

RARE REVOLUTION

Through *Rare Revolution* magazine, you can hear from people affected by rare diseases and the groups that support them.

Want additional information on APDS?

All about APDS

You can find more APDS information and resources at **AllaboutAPDS.com.**

YouTube

Detailed videos from APDS experts are also available on the **All about APDS YouTube page.**

Your guide to understanding APDS

This booklet covers information on APDS, including:

The underlying cause of APDS

Typical symptoms of this rare and complex disease

Tips for better communication with your healthcare team

How APDS can be inherited in families

Resources and information on family genetic testing

Register for more information on APDS at our website, AllaboutAPDS.com.

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