

# ADULT POLYGLUCOSAN BODY DISEASE

Patient-Led Listening Session with the FDA

October 28, 2021

A SUMMARY

By APBD Research Foundation



**APBD**  
ADULT POLYGLUCOSAN BODY DISEASE  
RESEARCH FOUNDATION

**FDA**

**U.S. FOOD & DRUG  
ADMINISTRATION**

# APBD Patient Listening Session Summary

## What is a Patient Listening Session?

The Patient Listening Sessions are small, informal, non-regulatory, non-public teleconference meetings that allow participants to connect with the United States Food & Drug Administration (FDA) staff first-hand.

These Sessions help the FDA inform medical product development, clinical trial design, patient preferences, and shape regulatory thinking. During a Patient Listening Session, FDA staff will either ask questions or simply listen to better understand your experiences and perspectives. Only the FDA, patients, caregivers, advocates, and community representatives participate in the Session.

The FDA's Office of Patient Affairs works in partnership with the National Organization for Rare Disorders and the Reagan-Udall Foundation for the FDA to organize these Listening Sessions.

## The APBD Patient Listening Session

On October 28, 2021, representatives from the APBD Research Foundation and the broader community met with the FDA to share the patients' perspective of Adult Polyglucosan Body Disease (APBD), its burden, symptom progression and heterogeneity, and potential issues related to therapeutic development.

The APBD Listening Session was patient-led. Our Foundation applied for and received approval from the FDA to host the APBD Listening Session.

## Opening Statement from the FDA

FDA staff thanked the APBD Research Foundation for contacting the Agency to hold this meeting. They stated that meetings like this are crucial to helping the FDA understand the burden of APBD, from the perspective of patients and their loved ones. The FDA assured us that patient and family perspectives are carefully considered in regulatory decisions to enable the availability of both safe and effective therapies.

After the opening statement from FDA, the APBD Research Foundation led the discussion, sharing the perspectives and concerns of the APBD community, as well as what constitutes, from the patients' perspective, meaningful outcomes in response to potential therapies.

## **Jeff Levenson, DDS | APBD Research Foundation**

Jeff Levenson, DDS, co-president of the APBD Research Foundation opened the Session with an introduction to the Foundation and the strides we are making in bringing the community together and preparing for clinical trials. He also shared the significance of this meeting for each of the speakers, and the broader APBD community, as they rallied together to share their most vulnerable experiences of life with APBD, the goal being to illuminate for FDA staffers how APBD impacts and destroys lives.

Additionally, Dr. Levenson described his personal battle with APBD that started in the 1980s. For 20 years, he watched helplessly as a mysterious disease stole his father's and his uncle's professional lives and their golden years. It was only towards the end of their lives that they received the APBD diagnosis. It was at one fateful meeting in 2005, with the Weiss brothers and Dr. Edwin Kolodny (Research Professor and Professor Emeritus, Department of Neurology, NYU Langone Medical Center), that Dr. Levenson was invited to volunteer with the newly formed APBD Research Foundation. Fifteen years later, Dr. Levenson was appointed co-president of the Foundation, joining current co-president Emil Weiss.

## **Michio Hirano, MD | Columbia University Irving Medical Center**

Michio Hirano, MD, Lucy G. Moses Professor of Neurology at Columbia University Irving Medical Center, provided a clinical description of APBD, including the biological pathway and the heterogeneity of both the symptomatic onset and progression of APBD. He posed both the opportunities and challenges in the current APBD landscape.

Dr. Hirano explained that APBD is an ultra-rare, genetic, neurodegenerative disease affecting the brain, spinal cord, and peripheral nerves. The age-at-onset, symptomatic presentation, and progression are variable.

In addition, Dr. Hirano shared that APBD results from mutations in the GBE1 gene, which encodes glycogen branching enzyme (GBE). These mutations impair GBE activity, which leads to accumulation of abnormal chains of sugar (polyglucosan bodies) in nerves, skeletal muscles, and other cells. The polyglucosan bodies are particularly toxic to neurons causing central and peripheral nervous system degeneration, which manifests as trouble urinating (neurogenic bladder), stiff and weak legs that impair walking, numbness in the legs, fatigue, and, in some cases, late cognitive decline. Through the course of this disease, patients suffer great disability as they progress and lose the abilities to control their bladder, walk, and conduct normal activities of daily living. Median survival is 70 years, which is eight years less than the general population.

Having diagnosed and provided medical care for over 15 patients over the course of ten years, Dr. Hirano expressed his frustration about having no treatment options and watching how this disease affects his patients as well as their family members. Nevertheless, he acknowledged how committed the patients, families, and medical community are to finding treatments and a cure.

## Testimonies from Patients, Individuals Diagnosed Preclinically, and Caregivers

Members from the APBD community, including people who were diagnosed preclinically, shared openly about how APBD has impacted their lives. The themes that follow offer insight into the shared as well as unique challenges we face:

### ❖ Early Onset of Symptoms Before Diagnosis

All patients and caregivers shared that, in looking back, they could identify the constellation of symptoms that mimicked more common diseases (i.e., multiple sclerosis and neuropathy, among others) many years before they received a confirmatory APBD diagnosis.

- “My symptoms began in my late 40s. I became increasingly aware of difficulty walking at a fast pace, numbness in my feet, and an inability to run. I had always been athletic, and walking was a passion of mine. I would walk for miles from one part of New York City to the other. I lost my ability to do that over time.”
- “My APBD journey began in 1998 when I noticed numbness in my hands and feet... My symptoms included cramps in my feet, stiffness and heaviness in my legs, muscle twitching, foot drag, and stumbling. I was also experiencing numbness in my hands. Additionally, I noticed that I was having urinary issues. While these symptoms were a nuisance, they didn't affect my ability to work and live a normal active life.”
- “I noticed my husband’s gait had become unsteady. I remember a golfing buddy mentioning that he seemed excessively tired and was having a hard time getting around on the golf course. I also noticed that he had trouble urinating -- I would hear the stream of urine start and stop and start and stop. I knew something wasn’t right.”

### ❖ The Diagnostic Odyssey

Most patients and caregivers shared the considerable length of time, often exceeding the cited average of 6.8 years ([Hellmann et al., 2015](#)), to receive their APBD diagnoses.

- “I had a full battery of tests, including several MRIs, which revealed multi-system atrophy. I was diagnosed with Charcot-Marie-Tooth Disease in 2006, the same diagnosis that my brother had. Several years after a follow-up and repeat MRI, the neurologist added a diagnosis of Multiple Sclerosis. I carried these diagnoses for eight years until my brother was correctly re-diagnosed with APBD by a blood test. I, too, was tested and the diagnosis was confirmed.”

- “It took nearly thirteen years for me to get this diagnosis. During that time, I was diagnosed with several different types of neuropathies, to include idiopathic, hereditary, and demyelinating.”
- “We saw a neurologist who, after many tests, gave [my husband] an MS diagnosis. This was devastating news to us. Something didn’t sit right with me about the MS diagnosis. I knew that we needed to dig deeper. Finding an accurate diagnosis for [my husband] became my priority.”

## ❖ Range of Symptoms and Progression

APBD symptoms include numbness and tingling in feet/legs and hands/arms (peripheral neuropathy), progressive muscle weakness and stiffness (spasticity), increasing difficulty starting or stopping the flow of urine (neurogenic bladder), fatigue, and cognitive difficulties.

Individuals with APBD can begin experiencing symptoms as early as age 35. They eventually lose the ability to walk, stand, stay continent, stay awake, perform at work, and socialize. They are robbed of nearly every aspect of their independent adult lives.

During the Listening Session, the patients and caregivers described a variety of symptoms that significantly impact their daily life. The range of experiences described highlighted the heterogeneity of APBD symptoms. And, while many could look back and identify points in time when specific symptoms began, their narratives also highlighted that the rate of progression varied from patient to patient.

- “APBD affects the peripheral nervous system of every patient in different ways – including ways that are very personal and difficult to discuss. One very serious issue is the loss of sex drive and the inability to perform. APBD has made it impossible to enjoy intimacy with my wife for more than two years now. This has had a significant impact on our relationship.”
- “I have severe muscle wasting and osteoporosis. I am at highest risk of fracture. I have poor balance; I have lost my ability to stand or walk freely. I have had frequent falls, and have broken my sternum, hip, and pelvis. I have a neurogenic bladder, significant loss of bladder control and take medication multiple times a day to prevent and treat frequent urinary tract infections. I catheterize several times a day. In addition, I have significant, immobilizing bouts of fatigue where walking up the steps is an impossibility. I now use a motorized wheelchair.”
- “More recently, I’ve also reduced my driving because I no longer feel safe behind the wheel. My fear of falling has grown, as I have had several falls and near falls over the past several months. I now wear braces and use a rollator to aid in my walking.”

In addition to the patients and caregivers who spoke during the Listening Session, we gave voice to patients who could not join us by sharing some of their dire challenges, including:

- Bladder and bowel incontinence
- Loss of balance and the ability to stand
- Loss of ambulation
- Difficulty swallowing and choking (on food, liquids, and saliva)
- Extreme fatigue
- Loss of vision
- Pressure sores, aspiration pneumonia, and related complications, requiring repeated hospitalizations
- Loss of independence
- Isolation
- Inability to work
- Suicidal thoughts
- Need for a full-time caregiver, whether it is a spouse, a parent, or a paid assistant
- Need for significant home modifications or relocations
- Astronomical cost of adjustments to life with APBD (including care products, wheelchair accessible vans, stair gliders and Hoyer lifts, electric scooters and wheelchairs, and physical therapy, among others).

### ❖ **The Challenges for Those with a Preclinical Diagnosis**

Due to the increased use of genetic screening, including pre-pregnancy screening, several individuals have received a genetic, preclinical, diagnosis of APBD -- before the onset of any symptoms. Three individuals shared the emotional toll of a preclinical diagnosis and how it impacts their families and their outlook on life.

- “I fear the day I will be forced to sit to the side and watch all things around me... The sacrifices I will make to find a cure are miniscule to the sacrifices I may have to make if I become symptomatic.”
- “The present changes I’ve been forced to make in my life are minor compared to many of the participants here today who are suffering from symptoms from this terrible disease. Still, what I want you to know is that APBD affects both the young and the old, both the symptomatic and asymptomatic, and their families as well. There are so many of us who are waiting for a treatment before it hits us later in life. And I am one of them; a young woman in her thirties, with a less than two-year-old child, hoping that I will not develop symptoms one day.”



## ❖ Caregivers' Perspective

The caregiver burden is strikingly high in this community. Two caregivers, both spouses, shared their concerns and fears as they watched their loved ones' diseases progress. They also shared their own unmet needs in addition to those of their loved ones.

- “I taught myself to sit [my husband] up and transfer him to a wheelchair and then to the toilet... Sometimes, everything would happen so quickly that he would fall on the floor before I could get him to the toilet. I was left to clean him and the bathroom, and to figure out how to get him off the floor and back to bed. This was physically and emotionally exhausting – it was my life for years, until I got a caregiver to help us.”
- “I make every financial and life decision. I run every errand. I arrange and make sure we're on time for every appointment, every visit to or from a friend. I assess what's safe and what's too risky. I break the news to [my husband] that he can't drive anymore because he falls asleep in the blink of an eye. I hide problems and my own fatigue.”

## ❖ A Motivated Community

The speakers shared their motivation, echoing others in the community, to participate in clinical trials if it meant the treatments would alleviate or reverse any of their symptoms and help other patients.

- “We in the APBD community are overcome with a sense of desperation. Our members are rapidly deteriorating and dying. What do we need to do to advocate for more research to be directed to our illness? We want you to know that we are willing to work with you in any way to help research move forward.”
- “[My husband]’s passing has only intensified my passion for finding a cure for APBD. I have my family to consider, given their risk for inheriting APBD. I also have my friends who are living through this devastating disease as we speak. I’m more aware of the time we have – and don’t – to find treatments and a cure. We need your help to develop a more creative and fast-tracked approach to review and approve therapies for APBD. And we’re willing to do whatever it takes to make it happen.”
- “It’s my hope that the future holds a cure or least treatments or therapies for my APBD symptoms. I am 57 but I feel like I’m trapped in the body of a senior citizen. Like the other APBD patients that I speak to, I would welcome and readily volunteer for any clinical trials that may become available in the future.”

## ❖ Treatments That Make a Difference

There are no treatment options for people with APBD. Patients and caregivers thoughtfully expressed what would be meaningful impacts when it comes to a potential therapy.

- “For my husband and all patients who have cognitive decline, if there were a treatment that would address the underlying issue here and bring improvement to their cognitive functions, we family members would get back the people we love.”
- “I catheterize several times a day in order to function outside of the home. I need treatments that would address these issues.”
- “Looking back, I began experiencing APBD symptoms in my thirties. I am 57 years old now. I’ve noticed that over the past two years, APBD has robbed me of several abilities. The worsening neurogenic bladder symptoms and the increasing pain and numbness in my legs has affected every facet of my life. I used to enjoy running and taking long walks; they helped me deal with most stresses in life. The ability to run and take long walks are slowly disappearing now. An effective treatment for these progressive symptoms would be great.”

## Closing Statement by the APBD Research Foundation

Harriet Saxe, a member of the APBD Research Foundation’s Board of Directors and spouse of an APBD patient, shared that APBD symptoms resemble aspects of MS and ALS, but the disorder has no name recognition. She emphasized that there are no treatments and no cure for APBD.

The community has assets that will help us to find treatments and cures: a multinational study of the natural history of APBD and its imaging features, animal models, and therapies in preclinical stages. She urged the FDA to:

- ❖ prioritize and accelerate drug reviews and apply regulatory flexibility on behalf of people who have a very poor quality of life and no time to spare;
- ❖ allow access to potential therapies that may halt the progression of the symptoms or reverse them;
- ❖ ensure our perspectives are included at every stage of drug development and approval;
- ❖ ensure the natural history study data is used and shared to make informed decisions.

Saxe thanked the patients and caregivers and Dr. Hirano for sharing the burden of APBD. As a community, our hope is that this is only the beginning of an ongoing conversation with the FDA.



## Closing Statement by the FDA

The Office of Patient Affairs (OPA) thanked the APBD Research Foundation for their work in organizing this Patient-Led Listening Session on Adult Polyglucosan Body Disease, which allows FDA staff to better understand how APBD impacts the lives of patients and caregivers. OPA also thanked each of the speakers for their willingness to share their experiences through this virtual forum and acknowledged that sharing personal perspectives about patient experiences and health is not always easy.

The Office of Patient Affairs at FDA is a resource for patient communities who want to connect with the FDA. Patient Affairs can keep patient communities informed about upcoming patient activities and meetings at the Agency and can help address future questions by connecting with communities with the appropriate FDA Centers, divisions, and offices. Patient Affairs encouraged the APBD patient community to reach out to OPA if there are additional comments or perspectives that they wish to share. Patient advocacy communities who want to connect with FDA's Office of Patient Affairs can do so by emailing [PatientAffairs@fda.gov](mailto:PatientAffairs@fda.gov).

## Participants and Organizers

### **FDA Centers and Offices That Attended the Listening Session:**

#### **Office of the Commissioner (3 offices)**

- ❖ Office of Clinical Policy and Programs/Office of Patient Affairs (*organizer*)
- ❖ Office of Clinical Policy and Programs
- ❖ Office of Clinical Policy and Programs/Office of Orphan Products Development

#### **Center for Biologics Evaluation & Research (1 office)**

- ❖ Office of the Center Director

#### **Center for Devices and Radiological Health (1 office/division)**

- ❖ Center for Devices and Radiological Health/Office of Strategic Partnership and Technology Innovation/Division of All Hazards Response Science & Strategic Partnership

#### **Center for Drug Evaluation and Research (4 offices/divisions)**

- ❖ Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment

- ❖ Office of New Drugs/Office of Neuroscience/Division of Neurology I
- ❖ Office of Surveillance and Epidemiology/Office of Medication Error Prevention and Risk Management/Division of Risk Management
- ❖ Office of Translational Sciences/Office of Biostatistics/Division of Biometrics II

**Non-FDA:**

**Reagan-Udall Foundation for the FDA**

**Patients Represented**

- ❖ 3 adults diagnosed with APBD
- ❖ 2 adults diagnosed preclinically with APBD
- ❖ 1 spouse of an adult diagnosed with APBD
- ❖ 1 spouse of a deceased patient with APBD
- ❖ 1 parent of an adult diagnosed preclinically with APBD
- ❖ 1 adult relative of deceased family members with APBD

**Disclaimer**

Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects APBDRF's account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of Adult Polyglucosan Body Disease, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire Adult Polyglucosan Body Disease patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

## About the APBD Research Foundation

Founded in 2005, the APBD Research Foundation is the only US-based nonprofit supporting people with APBD. As the trusted APBD hub for medical providers, healthcare industry, and APBD families, we are the #1 source for patient information and support through our website, social media, e-newsletters, and patient and caregiver Chat events.

Our mission is four-fold:

- ❖ Improve the diagnosis and treatment of APBD;
- ❖ Support affected individuals and families;
- ❖ Increase awareness of APBD among health professionals and the public;
- ❖ Facilitate the translation of research into treatments and a cure for APBD.

*To learn more about APBD and our Foundation's work  
to find treatments and a cure, visit [apbdrf.org](http://apbdrf.org).*



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