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# So... You're treating a Rare Bird?

**RARE BIRDS FOUNDATION** is a non-profit Patient Advocacy Organization that supports families living with ADSL Deficiency and other disorders of purine metabolism. We call our children Rare Birds because we know with the right supports, they can soar.

**WE KNOW THERE ARE MANY UNCERTAINTIES IN TREATING A CHILD WITH A RARE DISORDER. WE CAN HELP.**

Our advocacy group began on social media. Parents use this group to share stories, experiences, and ideas to help other families on what is often a scary and lonely journey. However, our doctors have not had access to this information.

**RARE BIRDS IS FOCUSED ON TRANSLATING PATIENT PERSPECTIVES INTO MEDICAL RESEARCH, AND MEDICAL RESEARCH INTO BETTER HEALTH OUTCOMES AND IMPROVED QUALITY OF LIFE FOR OUR KIDS.**
**THE MISSING PIECE IS YOU.**

We hope the following pages will help you move beyond "symptom management" to help your patient with the underlying cause of their symptoms–a genetic disorder of purine metabolism.

The following pages are designed to help spark conversations during your appointment, and to use patient perspectives to guide thorough care. We have included information on research studies, our Rare-X patient registry, and Patient Perspectives.

We recognize treating a child with a rare disorder when no treatments are available must be a lonely journey. Because of this, we are excited to announce the first Rare Birds Foundation Clinician Consortium.

Becoming a member of the consortium will provide:

- Full Access to De-Identified Rare-X Patient Registry Data
- Quarterly Meetings with Research Teams and Patient Ambassadors
- Your name/organization listed in our Clinician Directory
- Information on Research Opportunities

If you are interested in joining the Rare Birds Foundation Clinician Consortium, please send an email to Nicole@rarebirdsfoundation.org or contact (206)734-2293 for more information.

**THANK YOU FOR YOUR COMMITMENT TO HELPING OUR RARE BIRDS SOAR!**

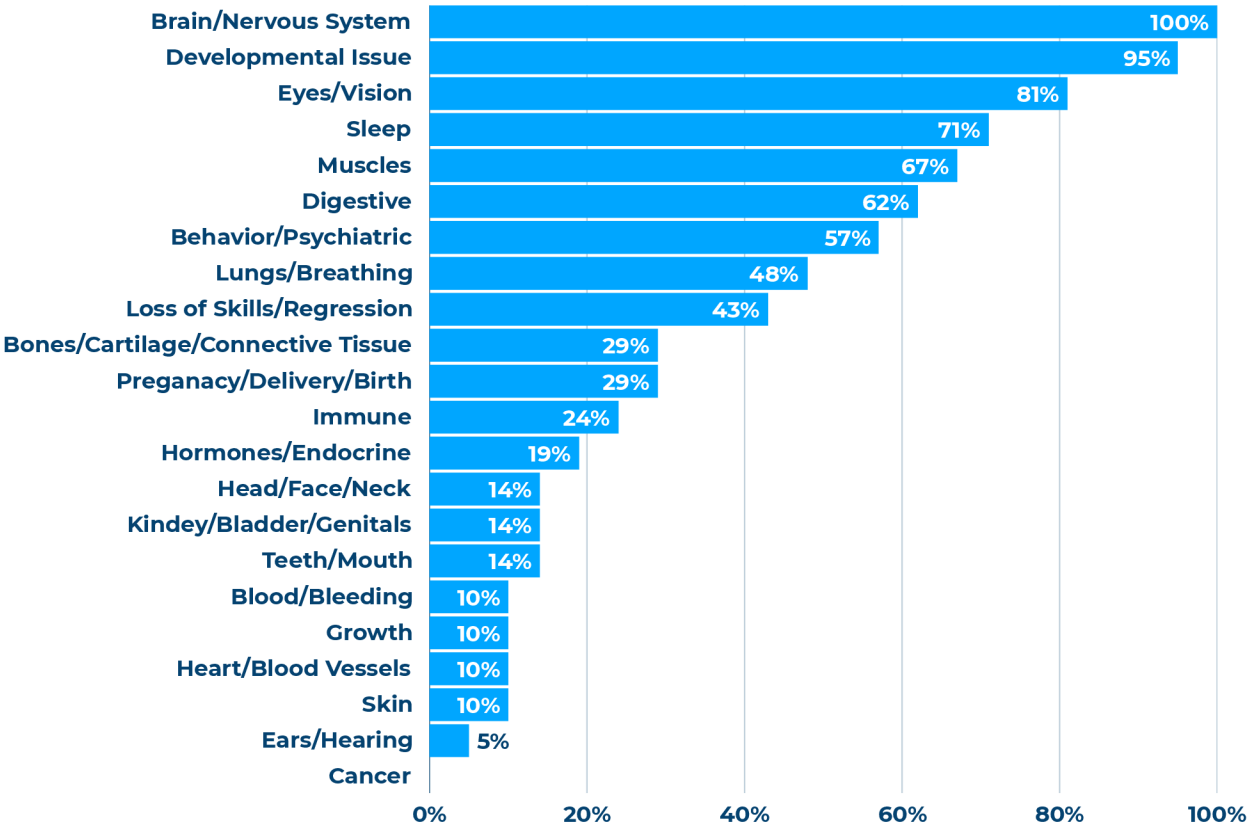
NICOLE LYTLE
President

rarebirdsfoundation.org

# Rare-X Patient Registry
# Head-to-Toe Survey: September 2024

FAMILY REPORTED SYMPTOMS

## Of 21 ADSL (Adenylosuccinate lyase) Deficiency respondents, what percentage reported yes to having issues in each of the following domains?




## My child experiences the following:

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# Head-to-Toe Breakdown

| | Symptom Detail | Family Notes |
|---|---|---|
| **Brain/Nervous System** | Abnormal EEG, Epilepsy, Neuro-irritability, Involuntary Muscle Movements, Sensory Processing Issues, Apraxia of Speech | |
| **Developmental Issue** | Missed Milestones, Global Delay, Intellectual Disability, Learning Disability | |
| **Eyes/Vision** | Cerebral Visual Impairment | |
| **Sleep** | Apneas, Insomnia, Hypersomnia, Nocturnal Seizures | |
| **Muscles** | Dystonia, Dyskinesia, Hypotonia, Hypertonia, Opisthotonos, Torticollis, Muscle Wasting | |
| **Digestive** | Dysphagia, Feeding Tube, Constipation | |
| **Behavior/ Psychatric** | Autism, Self-Injurious Behavior, Anger | |
| **Lungs/Breathing** | Obstructive and Central Sleep Apnea, Respiratory Distress | |

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## Head-to-Toe Breakdown (Continued)

| | Symptom Detail | Family Notes |
|---|---|---|
| **Loss of Skills/ Regression** | Often caused by seizures/ Metabolic Decompensation | |
| **Bones/Cartilage/ Connective Tissue** | Osteoporosis, Kyphosis, Scoliosis | |
| **Pregnancy/ Delivery/Birth** | Prematurity, Oligohydramnios, Polyhydramnios | |
| **Immune** | Slow Wound Healing, Slow Recovery from Illness, Immunodeficiency | |
| **Hormones/ Endocrine** | Early Puberty, Sterility | |
| **Head/Face/Neck** | Microcephaly, Dysmorphic Features | |
| **Kidney/Bladder/ Genitals** | Incontinence, Dehydration, Effects of Seizure Medication | |
| **Teeth/Mouth** | Abscess, Mouth Ulcer, Delayed Dentition or Exfoliation, Dental Injuries from Falls or Seizures | |

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# Research Partnerships and Initiatives

MAY 2025

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## NATURAL HISTORY STUDY AT THE NIH (U.S.A.)

A Natural History Study observes a patient over time to understand their lived experience and the progression of their disease. This study will contribute a vast amount of knowledge and serve as a baseline for further research going forward. Families in the U.S. are encouraged to participate!

- Dr. Oleg Shchelochkov is Head of the Purine and Pyrimidine Metabolism Unit at the National Institutes of Health (NIH). He is willing to consult with clinicians of study participants. See included flyer for more information.

## RARE-X PATIENT REGISTRY (GLOBAL)

We partner with Rare-X to collect data from patient surveys to learn more about ADSLD. These patient-owned data sets can be shared with research partners, doctors, and even with schools to improve care for our Rare Birds.

- Use the QR code to register:

## NEWBORN SCREEN INVESTIGATION AT BAYLOR (GLOBAL)

Dr. Sarah Elsea is investigating whether ADSLD can be detected in blood and included in Newborn Screening. You can participate in this study simply by mailing in dried blood spots. You may be able to request dried blood spot samples from the time of your child's birth.

- See included flyer for more information.

## OTHER RESEARCH PARTNERS:

- Dr. Wendy Hanna-Rose, Professor of Biochemistry and Molecular Biology, Penn State University
- Dr. Marie Zikanova, Head of the Purine Metabolism Disorders Group at Charles University, Prague

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
National Human Genome Research Institute

Building 10 CRC, Room 8D54A
10 Center Drive
Bethesda, Maryland 20892

# Clinical and Basic Investigations of Purine and Pyrimidine Metabolism Disorders NIH Protocol

We are doing this research to better understand the causes and medical complications of diseases called Disorders of Pyrimidine and Purine Metabolism (DPPMs). You are being asked to join this research study because your body has a different way of dealing with chemicals called pyrimidines or purines. We are trying to find out more why your body handles these chemicals differently and the medical problems that you can have when it happens. We can learn more about DPPMs by seeing you and doing some tests. During the course of this study, we plan to collect the following information: growth, frequency and duration of hospitalizations, intellectual outcomes, the incidence, prevalence, and severity of metabolic, cardiac, immune, blood, gastrointestinal, kidney, skeletal, neurological, and other organ manifestations of DPPMs.

Participants may be seen at the NIH Clinical Center for a period of 1-7 days with periodic follow-up if the study team finds it necessary. Participants with DPPMs may be asked to participate in medical studies. Here is a list of some of the most common tests doctors may recommend:

- Medical and dietary history, physical examination;
- Expert health professionals and doctors of the heart, hearing loss, nervous system, behavior, development, nutrition, physical medicine and rehabilitation or other areas of medicine as needed (such as digestive tract, endocrine or growth glands, kidney, blood cells and immune system, sedation) may need to be consulted during the study. These doctors may recommend additional tests and/or evaluations, and we will discuss these with you.
- We may use your blood for sequencing of your DNA and to link it to your medical and/or family history.
- Blood tests to assess liver and thyroid function, purine and pyrimidine levels, blood counts and blood chemistries, for genetic tests and basic research studies;
- Urine collection to examine purines, pyrimidines, electrolytes, organic chemicals, sugar, and proteins for measuring kidney function;
- A stool sample to study how gut microbes affect the fate of chemicals, purines and pyrimidines, in your body;
- Collect dietary history to help us understand how food impacts chemicals, purines and pyrimidines, in your body;
- Dental exams to check your teeth;
- An eye doctor may give you a full eye exam;
- We may check your hearing
- Photographs of the face and body (wearing underwear) to help track growth and appearance;
- Brain or abdomen magnetic resonance imaging (MRI);
- Ultrasound and computed tomography (CT) to check your abdomen and other organs;
- Electrocardiogram and echocardiogram of the heart;

- Hand X-ray to determine bone age;
- Dual energy X-ray absorptiometry (DEXA) scan to evaluate bone density;
- We may do an EEG of your brain.
- Nerve conduction and electromyogram (EMG). Not all participants will need this testing;
- Skin biopsy for cell culture (cells to grow in the laboratory for future testing) if not yet performed or unavailable. Not all participants will need this testing;
- Direct measurements of the glomerular filtration rate. Not all participants will need this testing;
- Neurocognitive tests to measure leaning abilities and behaviors;
- Other medical tests or procedures recommended by consulting doctors, if indicated.

There are three types of participants that will be included in this study:

1. Participants with known DPPMs
2. Family members of the above participants
3. Unrelated healthy volunteers

| **Inclusion Criteria** | | |
|---|---|---|
| 1. Participants with known, suspected, or uncharacterized DPPMs | 2. Family members of participants with known DPPMs | 3. Unrelated healthy volunteers |
| • At least one month of age;<br>• A medical history that, in the expert opinion of the study team, is consistent with the DPPM;<br>• Have a primary metabolic or genetic physician, or primary care provider<br>• Willingness of participant or legally authorized representative to sign informed consent. | • At least one month of age; andnot pregnant;<br>• Relationship either by blood or marriage, to an individual enrolled or about to be enrolled in the study with known or suspected DPPM;<br>• Willingness of participant or legally authorized representative to sign informed consent. | • No personal or family history of DPPMs;<br>• Regardless of gender, at least one month old, and not pregnant;<br>• No symptoms of DPPMs;<br>• Ability to sign informed consent |
| **Exclusion Criteria for all three types** | | |
| 1. Intercurrent or chronic conditions which in the opinion of the investigators, can then interfere with the interpretation of research studies (e.g. ongoing cancer treatment resulting in bone marrow suppression in a study participant with a suspected DPPM also presenting with bone marrow suppression). | | |

## Contact Information

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# Invitation to Participate in a Research Study for Early Disease Diagnosis

We are working to develop a **newborn screening** assay panel for **10 biomarkers** covering **nearly 21 disorders**. We are seeking dried blood spots from individuals diagnosed with the following disorders:

1. Adenylosuccinase deficiency (*ADSL*)
2. AICA-ribosiduria due to ATIC deficiency (ATIC)
3. Aromatic L-amino acid decarboxylase deficiency (*DDC*)
4. GABA-transaminase deficiency (*ABAT*)
5. Molybdenum cofactor deficiency A (*MOCS1*)
6. Molybdenum cofactor deficiency B (*MOCS2*)
7. Molybdenum cofactor deficiency C (*GPHN*)
8. Sulfite oxidase deficiency (*SUOX*)
9. Ornithine transcarbamylase deficiency (*OTC*)
10. Hereditary orotic aciduria (*UMPS*)
11. Transaldolase deficiency (*TALDO1*)
12. Transketolase deficiency (*TKT*)
13. Ribose 5-phosphate isomerase deficiency (*RPIA*)
14. Sedoheptulokinase deficiency (*SHPK*)
15. Bachmann-Bupp syndrome (*ODC1*)
16. Synder-Robinson syndrome (*SMS*)
17. Pyridoxine-dependent epilepsy (*ALDH7A1*)
18. Zellweger syndrome and peroxisome biogenesis disorders
19. Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), thymidine phosphorylase deficiency (*TYMP*)
20. Cerebrotendinous xanthomatosis, CTX (*CYP27A1*)

Key points about the study:

- We need volunteer participants to provide samples for validating the assay for disease screening.
- Your involvement would entail a simple finger prick procedure to obtain a dried blood spot sample.
- Conveniently, we can send you a home collection kit.

Families could also request that newborn blood spots for family members diagnosed with these disorders from the state labs be sent to us. We can provide the forms required to do this.

We are also interested in obtaining samples from parents or siblings of those diagnosed with the disorders to strengthen the assay further.

If you are open to participating, please contact **Abbhi Rajagopal** at **abbhirami.rajagopal@bcm.edu**. We will connect with you to answer any potential questions and obtain your informed consent for this study.

***Your contribution will significantly enhance our understanding and potentially expedite the diagnosis of these disorders.***

*This study is approved by the Baylor College of Medicine Institutional Review Board*

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# Variant of Uncertain Significance

## Does your child really have ADSL Deficiency?

Some people receive a confusing genetic test result called a “Variant of Uncertain Significance” or VUS. If you or your loved one has received this result, a bit more testing may be useful in being certain the disorder is really present.

### BE CERTAIN WITH ADDITIONAL TESTING

Families can get a “Purine and Pyrimidine Panel” test. This test measures metabolites in either blood or urine. People with ADSLD will have elevated levels of a compound called succinyladenosine, or S-Ado. If you choose to get this test, not only will you be certain the deficiency is present, but others with the same variant in the future will be certain as well.

### IMPROVE THE PICTURE OF YOUR CHILD’S GENETICS

If you’ve been diagnosed with ADSLD through genetic testing, every few years those results may be eligible for a review at no cost to the family. This would not require collecting a new sample, instead, the testing company will re-interpret the genetic data. Genetic information is a bit like pixels on a digital camera. Over time, the resolution improves and the complete genetic picture becomes sharper. Your doctor will still need to place an order for this review, even though it will be free to you.

| Laboratory | Contact | Order Code |
|---|---|---|
| **GeneDx** | Whole Exome Reanalysis | Test Code 660 |
| **GeneDx** | Whole Genome Reanalysis | Test Code TG73 |

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# Crisis Checklist

COMPILED FROM FAMILIES – FOR INFORMATIONAL PURPOSES ONLY

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**IN THE EVENT A PATIENT IS EXPERIENCING AN UNIDENTIFIED MEDICAL CRISIS, PLEASE CONSIDER THE FOLLOWING:**

- Hydration Levels
- Constipation
- Draw Labs for -
  - Seizure Medication Levels
  - Liver, Kidney Function
  - Toxicology for Ammonia
- Test for Streptococcus, E. Coli, Staph Infection
- Test for UTI, Ear Infection, Virus
- Broken Bones
- lood Sugar Levels
- Sodium Levels
- Low Protein Level in Blood (hypoproteinemia)
- Mouth Ulcer/Abscess
- Subclinical Seizures
- Sleep Study for Apnea
- Metabolic Stroke

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