

Clinical considerations for PURA SYNDROME



purasyndrome.org

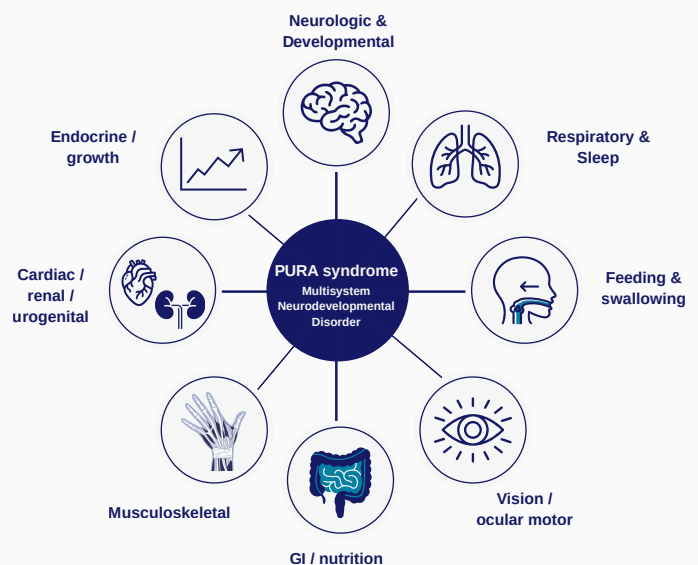
Current clinical understanding, care considerations, and the evolving PURA research ecosystem

Prepared by the PURA Syndrome Foundation from Foundation resources and the GeneReviews chapter · Last updated October 2026

What Is PURA Syndrome?

PURA syndrome (OMIM #616158) is caused by pathogenic or likely pathogenic variants in the **PURA gene**, although classification as a variant of uncertain significance (VUS) does not rule out clinical relevance. Inheritance is **autosomal dominant**, and the great majority of diagnosed cases arise **de novo**. First described in the medical literature in **October 2014**, PURA syndrome is a neurodevelopmental disorder—but its clinical footprint extends well beyond developmental delay alone, with recognized involvement across multiple organ systems. Clinical expression varies considerably from person to person.

Recognized involvement may extend across multiple systems



How to Think About PURA Clinically

Principle 1

Think multisystem, not only developmental delay.

Recognized clinical involvement may include neurologic, respiratory, feeding/swallowing, sleep, ophthalmologic, musculoskeletal, gastrointestinal, urogenital, cardiac, and endocrine features.

Prevalence varies widely across systems.

Principle 2

Characterize neurologic events carefully.

Epilepsy is common in PURA syndrome and can arise at any time into adolescence, but nonepileptic movements and paroxysmal phenomena are also well described. Formal neurologic assessment, including EEG or video-EEG when indicated, is recommended before assuming either category.

Principle 3

Think longitudinally.

The genetic diagnosis is the beginning of clinical characterization — not the end. Manifestations, needs, and complications can change with age, and no formal guidelines yet define the full lifespan course.

No matter the severity in symptom presentation, longitudinal surveillance is essential.

Principle 4

Expect heterogeneity.

Communication and intellectual ability, mobility, seizure burden, respiratory involvement, and feeding needs vary substantially between individuals, including between people with the same genetic variant. The medical literature has not yet caught up to the vast variability in severity and symptoms observed in the PURA community. *There is no single PURA phenotype.*

Recognized Clinical Considerations

Neurologic & Developmental

- **Hypotonia** (very common, often from birth)
- **Global developmental delay/intellectual disability** (nearly universal but varies in severity)
- **Epilepsy** (about half, high lifetime risk)
- **Nonepileptic movements** (startle, dystonia, dyskinesia)
- **Communication impairment** (many non-speaking; AAC early)
- Tone/motor phenotype can shift over time

Respiratory & Sleep

- **Neonatal/infant apnea** and hypoventilation common, sometimes needing temporary respiratory support.
 - Usually improves after year one but can recur with illness
- **Hypersomnolence** and sleep-disordered breathing frequently reported

Feeding & Gastrointestinal

- **Feeding difficulties** very common in infancy.
- **Dysphagia** often persists.
- Aspiration risk from hypotonia and swallowing dysfunction.
- **GERD and constipation** frequently reported.

Vision / Ophthalmology

- **Strabismus** and refractive errors common
- **Nystagmus** and other abnormal eye movements occur
- **Cerebral visual impairment** in a meaningful minority.

Musculoskeletal

- **Motor impairment** from hypotonia
- **Scoliosis** (often adolescent-onset, can progress quickly)
- **Hip dysplasia or subluxation** (may develop later, not always present at birth)
- **Low bone density** is likely underassessed.

Other Systems

- **Renal/urinary anomalies** uncommon
- **Male genital anomalies**, most often cryptorchidism
- **Structural cardiac anomalies** (a minority, often mild)
- **Endocrine** findings including thyroid, pubertal timing, and cortisol-axis differences.

Acute Care & Hospital Considerations

Respiratory decline with illness

Apnea and hypoventilation can recur with infection, even after infancy. Monitor breathing closely.

Sedation & anesthesia

Hypotonia and hypoventilation may increase sensitivity to sedatives and opioids; monitor breathing after procedures.

Temperature regulation

Hypothermia and temperature instability are reported; check core temperature in acutely unwell patients.

Aspiration

Dysphagia and hypotonia raise aspiration risk; consider aspiration pneumonia in any respiratory decline.

Seizure vs. nonepileptic events

Paroxysmal movements are common and can mimic seizures; confirm with EEG before escalating antiseizure therapy.

Caregivers know baseline

Many patients are non-speaking. Caregivers are the best source of baseline and early signs of illness.



NOTE: This resource does not replace individualized medical care. No formal consensus clinical practice guidelines for PURA-related neurodevelopmental disorders currently exist; recommendations above reflect the current published literature and expert clinical experience.

Clinical Surveillance — What to Reassess Over Time

At Diagnosis — Baseline Evaluation

	Area	Recommended evaluation
☐	Development	Formal developmental assessment, if not already done
☐	Seizures	EEG if seizures are suspected; differentiate from seizure-like movements and exaggerated startle
☐	Brain imaging	MRI, especially with confirmed or suspected seizures, apneas, or visual problems
☐	Vision	Formal eye exam, which may include electrodiagnostic testing
☐	Sleep and breathing	Sleep study, especially if central or obstructive apneas are suspected
☐	Feeding and GI	Formal swallow assessment for safety and aspiration risk; evaluate for constipation
☐	Heart and kidneys	Baseline ultrasound to exclude congenital malformations (these appear uncommon)
☐	Orthopedics	Assess for hip dysplasia and scoliosis
☐	Bone health	Vitamin D level; bone density if older and nonambulatory, on long-term antiseizure medication, or after a low-energy fracture

Ongoing — Long-Term Follow-Up

	Area	Recommended evaluation
☐	Development	Regular follow-up with a developmental pediatrician
☐	Seizures	New or changing events; EEG if seizures are suspected. Refractory epilepsy is common.
☐	Sleep and breathing	Apneas, hypersomnolence, sleep disturbance
☐	Feeding and GI	Swallowing problems, aspiration risk, constipation
☐	Growth and nutrition	Weight and growth trajectory
☐	Vision	Regular eye exams
☐	Communication	Speech and language support; review AAC needs (receptive language often exceeds expressive)
☐	Motor function	Physical and occupational therapy as needed
☐	Orthopedics	Hip dysplasia and scoliosis, at least annually
☐	Bone health	Vitamin D; bone age; bone density if risk factors develop
☐	Puberty and endocrine	Early (precocious) or delayed puberty
☐	Behavior and sensory	Anxiety, self-injury, sensory sensitivities
	Temperature regulation	Hypothermia or temperature instability

Genetic Counseling — After a PURA Diagnosis

Most PURA syndrome cases are *de novo*. Recurrence risk for future pregnancies is not zero, because of the possibility of parental gonadal (germline) mosaicism—and this risk may be somewhat elevated compared with typical *de novo* conditions, since PURA loss-of-function variants appear to have a selective growth advantage in germline cells. *It is important to note that while this is a low possibility, it has not been a common observation in the population.* Parental testing may help refine this risk for a given family.

PURA syndrome (an intragenic PURA variant) should be distinguished from the related, generally more severe, 5q31.3 microdeletion syndrome (a larger chromosomal deletion involving PURA and often neighboring genes). The two require different counseling. There is currently no defined genotype-phenotype relationship.

A genetic diagnosis alone does not predict an individual child's developmental ceiling; connection to multidisciplinary care, genetics professionals, the PURA parent support group, and Foundation resources is recommended for every family.

Important Questions Remain

PURA syndrome was recognized only in the last decade, and complete longitudinal natural-history data are still being gathered.

Open questions include:

- What does the phenotype look like across the full lifespan, including adulthood?
- How do manifestations change with age?
- Which features track with specific variant types?
- What clinical measures or biomarkers are sensitive enough to detect meaningful change?
- What screening intervals are most appropriate for each system?
- Which interventions most effectively improve function and quality of life?
- What outcomes would be meaningful in a future clinical trial?



NOTE: Detailed, structured documentation in the EHR does more than support this patient's own care. PURA syndrome is so rare that every well-documented visit becomes a data point the field can draw on, so thorough clinical notes today directly feed the natural-history research, registries, and eventual treatment development that patients and families are counting on tomorrow.

Where the Field Has Come From

2014 — PURA syndrome is described as a distinct genetic disorder in the medical literature.

2015 — Families begin connecting internationally; a parent-led online community forms.

2016 — The PURA Syndrome Foundation is formally established as a 501(c)(3) nonprofit, governed by volunteer international board members.

2017–present — Clinical and molecular literature expands rapidly; GeneReviews publishes and periodically updates a dedicated clinical reference chapter.

Today — As of October 2026, fewer than 900 individuals are known to the global PURA community. The field now has a relaunched Global Patient Registry, an active biobank network across the United States, Germany, and Australia, and a Disease Concept Model in development — all aimed at improving care and preparing for future therapeutic development.

The PURA Syndrome Foundation's mission is to support and drive research, raise public awareness, and connect, educate, serve, and empower families impacted by PURA syndrome worldwide.

Building the PURA Medical and Research Ecosystem

Individuals and families contribute to the **Global Patient Registry**, run in partnership with COMBINEDBrain on the Matrix platform. Clinical Research ID (CRID), a free, de-identified identifier links patient data across studies, so information shared once can support many research efforts. The registry works alongside an **international Biobank network**, now live in the United States, Germany, and Australia.

Separately, a **Disease Concept Model** is in development with COMBINEDBrain. It will connect PURA biology to the outcomes that matter most to patients and families, and publication is expected in late 2027.

The long-term goals of these efforts are a better-defined natural history, clinically meaningful outcome measures and biomarkers, improved clinical guidance, and readiness for future clinical trials.

How clinicians can help

- Encourage caregivers to enroll in the patient registry. Your recommendation carries weight with families, and every new participant strengthens the data.
- Document thoroughly in the medical record, recording the diagnosis as PURA syndrome (OMIM #616158); a dedicated ICD code is still being pursued. The registry currently holds caregiver-reported data only. To fill that gap, an upcoming collaboration with Citizen Health will conduct a natural history study based on electronic health records. Your clinical notes will be a core data source for that study, so detailed documentation of symptoms, findings, and changes over time directly shapes what we learn about PURA syndrome.

No PURA-specific therapy is currently available, and management remains supportive.

Know a resource we should share? If you know of country-specific resources that would help PURA families, such as specialty clinics, support organizations, or local services that we could add to our website, please contact us at science@pura-syndrome.org.

Connect & Contribute

GLOBAL CLINICIAN DIRECTORY

Are you a clinician with experience caring for individuals with PURA syndrome?

Help families and other clinicians connect with knowledgeable providers.

To suggest a clinician for inclusion, contact info@pura-syndrome.org.

The Clinician Directory is provided for informational purposes and does not constitute endorsement by the PURA Syndrome Foundation.



PATIENT REGISTRY

Join the PURA Syndrome Patient Registry.

Participation supports natural-history research, biomarker discovery, trial readiness, and future treatment-development efforts.

Ask about upcoming COMBINEDBrain Roadshow events for in-person enrollment help and biosample donation across the US.

Questions? science@pura-syndrome.org



PURA PARENTS & CAREGIVERS COMMUNITY

Parents and caregivers can connect with the international PURA community for peer support, shared experiences, and updates.

facebook.com/groups/PURA.Tribe

Email families@pura-syndrome.org for help joining.

PURA Syndrome Foundation — purasyndrome.org — Learn more about PURA syndrome.

Key References

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3. Lalani SR, Zhang J, Schaaf CP, Brown CW, Magoulas P, Tsai ACH, et al. Mutations in PURA cause profound neonatal hypotonia, seizures, and encephalopathy in 5q31.3 microdeletion syndrome. Am J Hum Genet. 2014;95(5):579-583.
4. Taniguchi N, Watanuki K, Nakato D, Takenouchi T, Kosaki K, Koga H. PURA-related neurodevelopmental disorders: a systematic review on genotype-phenotype correlations. J Med Genet. 2025;62(3):191-198.

Medical Disclaimer

This resource is educational and is not a substitute for individualized medical advice. Clinical care should be guided by qualified healthcare professionals and the needs of the individual.