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Isolated Sulfite Oxidase Deficiency

Synonym: Sulfocysteinuria

Parayil Sankaran Bindu, MD, DM,[1] Madhu Nagappa, MD, DM,[1] Rose Dawn Bharath, DM,[2] and Arun B Taly, MD, DM[2]

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Summary

Clinical characteristics

The spectrum of isolated sulfite oxidase deficiency ranges from classic early-onset (severe) disease to late-onset (mild) disease.

- *Classic ISOD* is characterized in the first few hours to days of life by intractable seizures, feeding difficulties, and rapidly progressive encephalopathy manifest as abnormal tone (especially opisthotonus, spastic quadriplegia, and pyramidal signs) followed by progressive microcephaly and profound intellectual disability. Lens subluxation or dislocation, another characteristic finding, may be evident after the newborn period. Children usually die during the first few months of life.
- *Late-onset ISOD* manifests between ages six and 18 months and is characterized by ectopia lentis (variably present), developmental delay/regression, movement disorder characterized by dystonia and choreoathetosis, ataxia, and (rarely) acute hemiplegia as a result of metabolic stroke. The clinical course may be progressive or episodic. In the episodic form encephalopathy, dystonia, choreoathetosis, and/or ataxia are intermittent.

Diagnosis/testing

Laboratory findings that suggest the diagnosis of ISOD are dipstick positive for urinary sulfite, elevated urinary thiosulfate and S-sulfocysteine, low urinary organic sulfate, and markedly reduced plasma levels of total homocysteine. The diagnosis is confirmed by identification of biallelic pathogenic variants in *SUOX* by molecular genetic testing.

Author Affiliations: 1 Department of Neurology, National Institute of Mental Health and Neurosciences, Bangalore, India; Email: drpsbindu@yahoo.co.in; Email: madhu_nagappa@yahoo.co.in. 2 Department of Neuroimaging and Interventional Neuroradiology, National Institute of Mental Health and Neurosciences, Bangalore, India; Email: drrosedawn@yahoo.com; Email: abtaly@yahoo.com.

Management

Treatment of manifestations: No treatment exists for the underlying metabolic defect. Symptomatic treatment can include: anti-seizure medication (ASM) for seizures; medications to reduce spasticity; and early consideration of gastrostomy tube placement to manage difficulties with swallowing, assure adequate caloric intake, and reduce risk of aspiration. Other measures can include vigorous chest physiotherapy to prevent respiratory complications. Treatment of vomiting, gastroesophageal reflux, and aspiration pneumonia are per routine.

Surveillance: Periodic assessment by a multidisciplinary team with particular attention to nutritional status, neurologic status (to evaluate dosages of ASMs and their side effects), and degree of spasticity and related complications.

Genetic counseling

ISOD is inherited in an autosomal recessive manner. The parents of an affected child are asymptomatic obligate heterozygotes (i.e., carriers of one *SUOX* pathogenic variant) and are not at risk of developing the disorder. Each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Once the *SUOX* pathogenic variants have been identified in an affected family member, carrier testing for at-risk relatives, prenatal testing for a pregnancy at increased risk, and preimplantation genetic testing are possible.

Diagnosis

Suggestive Findings

Classic early-onset (severe) and late-onset (mild) isolated sulfite oxidase deficiency (ISOD) should be suspected in infants with the following clinical, neuroimaging, and supportive laboratory findings.

Clinical Features

Classic ISOD

- Intractable seizures and feeding difficulties in the first few hours to days of life
- Progressive encephalopathy manifest as abnormal tone (especially opisthotonus, spastic quadriplegia, and pyramidal signs)
- Progressive microcephaly
- Profound intellectual disability
- Dysmorphic facial features: long face, narrow bifrontal diameter, deep and widely set eyes, elongated palpebral fissures, puffy cheeks, small nose, long philtrum, and thick lips (Figure 1) [Salih et al 2013, Bosley et al 2014]
- Lens subluxation or dislocation (ectopia lentis) after the newborn period
- Family history consistent with autosomal recessive inheritance

Late-onset ISOD

- Onset usually between age six and 18 months, often precipitated by febrile illness
- Ectopia lentis (variably present)
- Developmental regression
- Episodic encephalopathy, ataxia, choreoathetosis, and dystonia
- Acute hemiparesis as a result of metabolic stroke

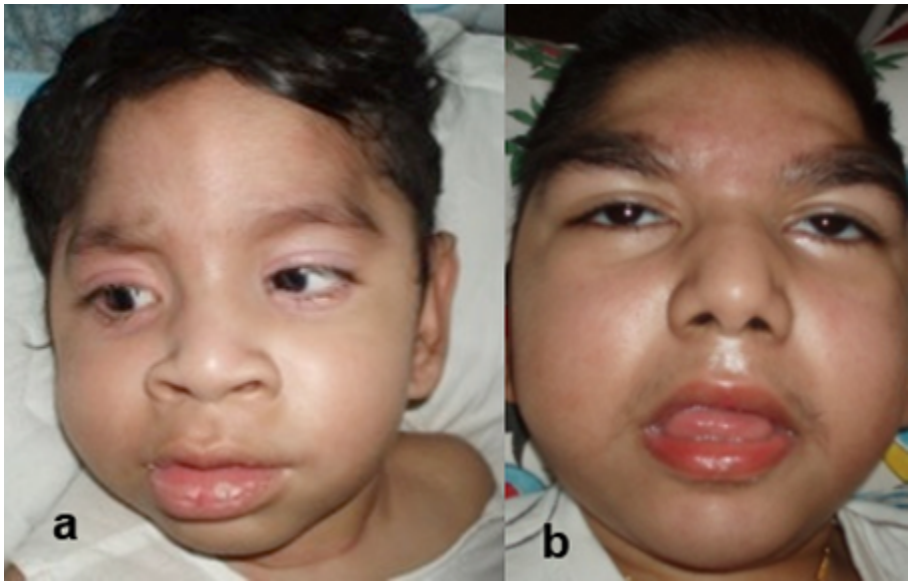

Figure 1. Two males of Indian origin with classic isolated sulfite oxidase deficiency

a. Male child age 14 months (head circumference 43 cm; <5th centile for age); note long philtrum and thick lips.

b. Male child age eight years with severe microcephaly (head circumference 45 cm; <5th centile for age); note puffy cheeks, narrow bifrontal diameter, elongated palpebral fissures, and long philtrum.

Neuroimaging Findings

Classic ISOD

- **Cranial MRI** resembles that of hypoxic-ischemic encephalopathy (Figure 2) in the following manner [Rupar et al 1996, Tan et al 2005, Basheer et al 2007, Sass et al 2010, Bindu et al 2011, Salih et al 2013, Bosley et al 2014]:
  - During the first week, loss of gray-white matter differentiation and edema in the cerebral cortex and basal ganglia
  - During the ensuing weeks, development of the following:
    - Cystic encephalomalacia in the subcortical white matter, external capsules, and basal ganglia
    - Ventriculomegaly and diffuse cerebral atrophy, which may be consistent with ulegyria
    - Thinning of the corpus callosum
- **CT** shows calcifications in thalami and/or basal ganglia [Salih et al 2013, Bosley et al 2014, Zaki et al 2016].

  Of note: Marked cerebellar hypoplasia and the progressive cystic and atrophic changes seen ISOD help differentiate it from mild-to-moderate hypoxic ischemic encephalopathy, in which the cerebellum, brain stem, and deep gray matter structures are usually spared [Volpe 2008].
- **Diffusion-weighted imaging** shows diffuse and symmetric cytotoxic edema involving the basal ganglia, cerebral cortex, and subcortical white matter suggesting an acute metabolic derangement [Eichler et al 2006, Bosley et al 2014].
- **Magnetic resonance spectroscopy** shows reduced N-acetylaspartate/total creatine ratio and abnormal elevation of lactate, glutamine, and glutamate peaks [Hoffmann et al 2007].

- **Single-photon emission tomography** using 99mTc-ethyl cysteinate dimer in one individual showed decreased uptake bilaterally in the frontal lobes [Huang et al 2012].

Late-onset ISOD

- **Cranial MRI** shows T_2-weighted hyperintensities in the globus pallidi at presentation; thin corpus callosum is the other finding [Del Rizzo et al 2013, Rocha et al 2014].

Laboratory Findings

Both classic and late-onset ISOD exhibit a characteristic metabolic profile that includes the following:

- **Urinary sulfite identified on a dipstick screening test**

  Note: (1) Urinary sulfite is very unstable and disappears rapidly from urine either at room temperature or even when urine is stored at 40° C; therefore, testing immediately after voiding is recommended [Johnson & Duran 2001, Tan et al 2005]. (2) False positive urinary sulfite results may be caused by:

  - Drugs containing free aliphatic sulfhydryl group such as N-acetyl cysteine, mercaptamine, dimercaprol, and mucolite drug 2-mercaptoethane sulfonate;
  - Certain antibiotics such as cefotaxime, cefuroxime, ampicillin, and benzylpenicillin [Tan et al 2005]; and
  - Bacterial degradation of urine samples as reflected by increased levels of compounds such as succinic acid, benzoic acid, 2-hydroxyglutaric acid, and uracil [Sass et al 2010].

- **Elevated urinary thiosulfate and S-sulfocysteine and low urinary organic sulfate.** Urinary thiosulfate, a stable compound, is measured by a spectrophotometric method. S-sulfocysteine is measured by tandem mass spectrometry [Rashed et al 2005, Salih et al 2013]. (Note that serum uric acid levels are normal – as are urine xanthine and hypoxanthine levels.)

- **Markedly reduced plasma level of total homocysteine,** a sensitive and specific indicator of sulfite oxidase deficiency [Basheer et al 2007, Sass et al 2010]

Establishing the Diagnosis

The diagnosis of ISOD **is established** in a proband by the identification of biallelic pathogenic (or likely pathogenic) variants in *SUOX* by molecular genetic testing (see Table 1).

Note: (1) Per ACMG/AMP variant interpretation guidelines, the terms "pathogenic variants" and "likely pathogenic variants" are synonymous in a clinical setting, meaning that both are considered diagnostic and both can be used for clinical decision making [Richards et al 2015]. Reference to "pathogenic variants" in this section is understood to include any likely pathogenic variants. (2) Identification of biallelic *SUOX* variants of uncertain significance (or of one known *SUOX* pathogenic variant and one *SUOX* variant of uncertain significance) does not establish or rule out the diagnosis.

Molecular genetic testing approaches can include a combination of **gene-targeted testing** (single-gene testing, multigene panel) and **genomic testing** (comprehensive genomic sequencing) depending on the phenotype.

Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Because the phenotype of isolated sulfite oxidase deficiency is broad, children with the distinctive findings of classic ISOD described in Suggestive Findings are likely to be diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from many other inherited neonatal seizures or those with late-onset (milder) ISOD are more likely to be diagnosed using genomic testing (see Option 2).

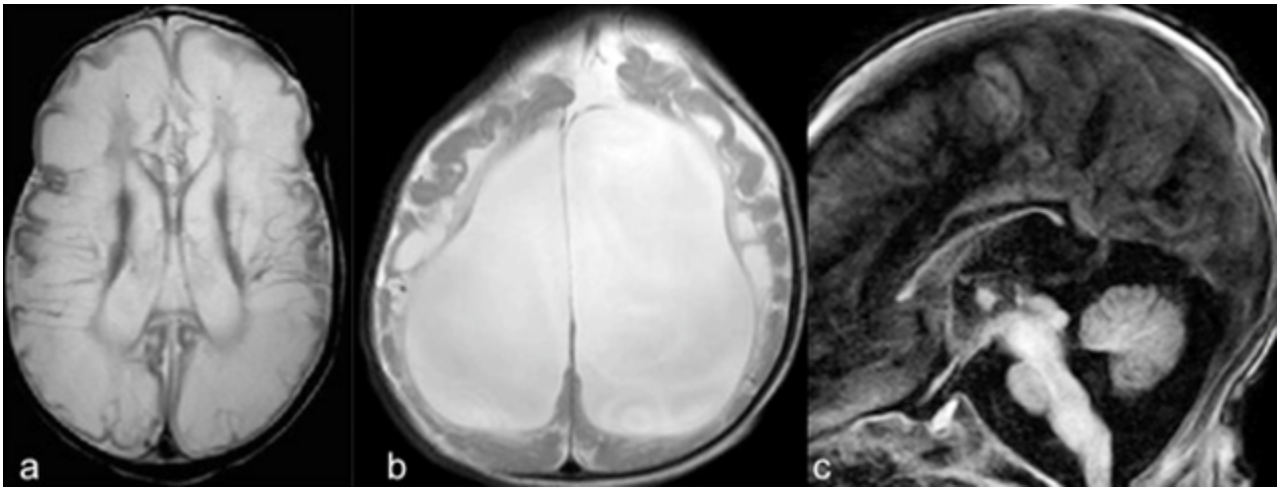

Figure 2. Brain MRI in a child with classic isolated sulfite oxidase deficiency

a. T_2-weighted axial view demonstrates cystic leukomalacia at age 29 days.

b. Follow-up MRI at age eight months shows ventricular dilatation and diffuse ulegyria.

c. T_1-weighted sagittal view shows cerebellar hypoplasia and thin corpus callosum.

Option 1

When the phenotypic and laboratory findings suggest the diagnosis of ISOD, molecular genetic testing approaches can include **single-gene testing** or use of a **multigene panel**:

- **Single-gene testing.** Sequence analysis of *SUOX* is performed first. If only one pathogenic variant is found, gene-targeted deletion/duplication analysis could be considered; however, to date no exon or whole-gene deletions have been reported.
- **A multigene panel** that includes *SUOX* and other genes of interest (see Differential Diagnosis) may also be considered. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*; thus, clinicians need to determine which multigene panel is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

  For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Option 2

When the phenotype is indistinguishable from many other inherited neonatal seizures, molecular genetic testing approaches can include **genomic testing** and/or **gene-targeted testing**:

- **Comprehensive genomic testing** (when clinically available) includes exome sequencing and genome sequencing.

  For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

- **A neonatal epileptic encephalopathy multigene panel** may be considered.

Table 1. Molecular Genetic Testing Used in Isolated Sulfite Oxidase Deficiency

Gene [1]	Method	Proportion of Probands with Pathogenic Variants [2] Detectable by Method
SUOX	Sequence analysis [3]	All variants reported to date have been identified by sequence analysis.
	Gene-targeted deletion/duplication analysis [4]	Unknown [5]

1. See Table A. Genes and Databases for chromosome locus and protein.
2. See Molecular Genetics for information on variants detected in this gene.
3. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
4. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.
5. No data on detection rate of gene-targeted deletion/duplication analysis are available.

Clinical Characteristics

Clinical Description

Isolated sulfite oxidase deficiency (ISOD), a rare inborn error of metabolism of sulfur-containing amino acids, comprises a spectrum ranging from classic early-onset (severe) disease to late-onset (mild) disease [Johnson & Duran 2001].

Classic ISOD

Classic ISOD typically manifests within few hours to days of life with intractable seizures, feeding difficulties, and rapidly progressive encephalopathy [Sass et al 2010, Salih et al 2013, Bosley et al 2014]. The clinical features resemble that of neonatal hypoxic ischemic encephalopathy.

Almost all affected infants are born after uncomplicated pregnancy. Of note, sustained abdominal trembling resembling vibration of mobile phones (interpreted as fetal seizures) has been reported in the third trimester in one instance [Chen et al 2014]. Delivery is usually uncomplicated, although Apgar scores may be depressed.

Multiple types of seizures including tonic-clonic and multifocal myoclonic seizures not responding to treatment are the main feature [Sass et al 2010, Bindu et al 2011, Salih et al 2013, Bosley et al 2014]. Rarely, infantile spasms and hypsarrhythmia, exaggerated startle response, or hyperekplexia also have been reported [Bosley et al 2014, Holder et al 2014]. Electroencephalography (EEG) shows low-amplitude or disorganized background [Sass et al 2010, Holder et al 2014], multifocal epileptiform discharges [Holder et al 2014], or a burst suppression pattern [Relinque et al 2015].

Neurologic examination reveals abnormalities in tone including opisthotonus, spastic quadriplegia, and pyramidal signs.

All affected children develop profound psychomotor retardation: neurologic development is halted at the level of brain stem reflexes and children lack any response to environmental stimulation except for exaggerated startle and intermittent seizures [Bosley et al 2014].

Although head circumference is normal at birth, severe progressive postnatal microcephaly develops [Bosley et al 2014]. Progressive facial dysmorphism is an additional feature.

Systemic manifestations are rare and can include such findings as severe asthma and pyloric stenosis [Bindu et al 2011, Bosley et al 2014].

Prognosis is poor and children usually die during the first few months of life.

A significant proportion of infants who survive the newborn period develop ectopia lentis (lens dislocation or subluxation) [Johnson & Duran 2001, Bosley et al 2014]. The natural history of ectopia lentis is not known: it may not be present (or at least not obvious) during the first few months and may only become evident (and detectable by ophthalmologic examination) during the first year. Subtle lens dislocation may be obvious only after dilation of the pupil and slit lamp examination (over time) [Lueder & Steiner 1995].

Late-Onset ISOD

Late-onset ISOD differs from the classic form in that onset is between ages six and 18 months and some suggestive findings (e.g., intractable seizures, ectopia lentis) may be absent.

The main clinical features are developmental delay/regression, movement disorder characterized by dystonia and choreoathetosis, ataxia, and (rarely) acute hemiplegia as a result of metabolic stroke. The clinical course may be progressive or episodic. In the episodic form encephalopathy, dystonia, choreoathetosis, and/or ataxia are intermittent [Van der Knaap &Valk 2005, Del Rizzo et al 2013, Rocha et al 2014].

Ectopia lentis (lens dislocation or subluxation) may or may not be present at the time of presentation.

Genotype-Phenotype Correlations

The number of individuals with confirmed pathogenic variants in *SUOX* is too small to make any conclusive genotype-phenotype correlations.

Prevalence

Prevalence of ISOD is unknown. Approximately 50 affected individuals have been reported to date. The disorder is probably underdiagnosed. The incidence may be higher in populations with a high rate of consanguinity.

Genetically Related (Allelic) Disorders

No phenotypes other than those discussed in this *GeneReview* are known to be associated with pathogenic variants in *SUOX*.

Differential Diagnosis

Table 2. Disorders to Consider in the Differential Diagnosis of Isolated Sulfite Oxidase Deficiency (ISOD)

DiffDx Disorder	Gene(s)	MOI	Features of DiffDx Disorder	
			Overlapping w/ISOD	Distinguishing from ISOD
Molybdenum cofactor deficiency	*MOCS1* *MOCS2* *MOCS3* *GPHN*	AR	Intractable seizures & feeding difficulties in 1st few hrs to days of life; subsequent severe ID, spasticity, & seizures refractory to ASM	↓ serum uric acid levels; ↑ urinary xanthine & hypoxanthine levels due to loss of function of xanthine dehydrogenase

Table 2. continued from previous page.

DiffDx Disorder	Gene(s)	MOI	Features of DiffDx Disorder	
			Overlapping w/ISOD	Distinguishing from ISOD
Glycine encephalopathy	*GLDC* *AMT* *GCSH*	AR	Progressive lethargy, hypotonia, & myoclonic jerks in 1st few hrs to days of life; subsequent profound ID & seizures refractory to ASM	↑ glycine levels in plasma & CSF; on MRI: diffusion restriction of areas that are myelinating at birth (e.g., posterior limb of internal capsule & pericentral area)
Pyridoxine-dependent epilepsy	*ALDH7A1*	AR	Soon after birth: seizures refractory to ASM	Seizures respond to large supplements of pyridoxine.
Pyridox(am)ine 5'-phosphate oxidase deficiency	*PNPO*	AR	Soon after birth: seizures refractory to ASM & pyridoxine	Seizures respond to pyridoxal-5' phosphate.

ASM = anti-seizure medication; AR = autosomal recessive; DiffDx = differential diagnosis; ID = intellectual disability; MOI = mode of inheritance

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease and/or needs in an individual with a diagnosis of isolated sulfite oxidase deficiency (ISOD), the following evaluations are recommended:

- Complete neurologic assessment by a pediatric neurologist
- Formal developmental assessment
- Ophthalmologic evaluation
- EEG/video EEG to monitor seizures
- Assessment of feeding and nutrition and appropriate intervention
- Consultation with a clinical geneticist and/or genetic counselor

Treatment of Manifestations

To date, no definitive treatment for ISOD has been identified. Symptomatic management by a multidisciplinary team consisting of specialists in neurology, nutrition, gastroenterology, pulmonary medicine, physiotherapy, and orthopedics is recommended. Management includes the following:

- Appropriate medications for management of seizures and spasticity
- Early consideration of gastrostomy tube placement to manage difficulties with swallowing to assure adequate caloric intake and reduce the risk of aspiration.
- Appropriate management of vomiting, gastroesophageal reflux disease, and aspiration pneumonia
- Chest physiotherapy to prevent respiratory complications
- Sleep studies to assess nocturnal hypoventilation and institute appropriate interventions
- Assessment for scoliosis

The following treatment modalities have been tried with minimal success:

- **Dietary.** A low-protein diet restricted in cysteine and methionine has been tried in a few individuals with ISOD. Clinical and biochemical improvement were reported in two individuals with late-onset ISOD [Del Rizzo et al 2013]. No clinical benefit has been noted in those with classic ISOD. The value of these diets in presymptomatic individuals has yet to be established.

- **Medical.** No medical treatment that improves the neurologic outcome or prevents the development of neurologic manifestations in individuals with ISOD has been identified. The following agents have been tried on an experimental basis with minimal clinical effect:
  - Betaine has been used to increase the remethylation of homocysteine back to methionine, which reduces cysteine and leads to reduction in sulfite levels.
  - Thiamine replacement has been attempted (given that the accumulation of sulfite leads to depletion of thiamine).
  - Use of cysteamine and penicillamine (chelating agents used to chelate sulfite) resulted in no beneficial clinical effects.

Surveillance

Periodic assessment by the multidisciplinary team with particular attention to the following:

- Nutritional status
- Neurologic status including evaluation of dosages of anti-seizure medication and their side effects
- Degree of spasticity and related complications, including scoliosis
- Periodic sleep studies

Evaluation of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Isolated sulfite oxidase deficiency (ISOD) is inherited in an autosomal recessive manner.

Risk to Family Members

Parents of a proband

- The parents of an affected child are obligate heterozygotes (i.e., carriers of one *SUOX* pathogenic variant).
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Sibs of a proband

- At conception, each sib of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Offspring of a proband. The offspring of an individual with isolated ISOD would be obligate heterozygotes (carriers) for a pathogenic variant in *SUOX*. To date, no affected individuals have reproduced.

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of a *SUOX* pathogenic variant.

Carrier Detection

Carrier testing for at-risk relatives requires prior identification of the *SUOX* pathogenic variants in the family.

Related Genetic Counseling Issues

Family planning

- The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected, are carriers, or are at risk of being carriers.

DNA banking. Because it is likely that testing methodology and our understanding of genes, pathogenic mechanisms, and diseases will improve in the future, consideration should be given to banking DNA from probands in whom a molecular diagnosis has not been confirmed (i.e., the causative pathogenic mechanism is unknown). For more information, see Huang et al [2022].

Prenatal Testing and Preimplantation Genetic Testing

Once the *SUOX* pathogenic variants have been identified in an affected family member, prenatal and preimplantation genetic testing are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **Metabolic Support UK**
  United Kingdom
  Phone: 0845 241 2173
  metabolicsupportuk.org

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Isolated Sulfite Oxidase Deficiency: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar

Table A. continued from previous page.

SUOX	12q13.2	Sulfite oxidase, mitochondrial	SUOX database	SUOX	SUOX

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Isolated Sulfite Oxidase Deficiency (View All in OMIM)

272300	SULFITE OXIDASE DEFICIENCY, ISOLATED; ISOD
606887	SULFITE OXIDASE; SUOX

Gene structure. The longest *SUOX* transcript (NM_000456.2) comprises eight exons distributed over 2.5 kb. This is the sequence typically analyzed by standard screening.

See Table A, **Gene** for a detailed summary of gene and protein information.

Pathogenic variants. The variants identified in *SUOX* include deletions, insertions, and missense variants.

An individual with uniparental disomy 12 (UPD12) with a paternal p.Tyr400Ter reduced to homozygosity has been reported [Cho et al 2013].

Table 3. Selected *SUOX* Pathogenic Variants

DNA Nucleotide Change	Predicted Protein Change	Reference Sequence
See footnote 1.	p.Ser427Tyr	NM_000456.2
c.520delG [2]	Premature termination	
c.650G>A	p.Arg217Gln	
c.794C>A	p.Ala265Asp	
c.1400C>G	p.Tyr400Ter	
c.1589G>A	p.Gly530Asp	

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.
1. The original publication does not use current naming conventions and the c. nomenclature could not be determined [Edwards et al 1999].
2. The original publication does not use current naming conventions and names this variant c.1244delG [Seidahmed et al 2005].

Normal gene product. Sulfite oxidase is a molybdohemoprotein comprising 466 amino acids localized to the intermembrane space of mitochondria. The enzyme is a dimer of identical units consisting of three domains: an N-terminal heme domain, a central molybdenum domain, and a C-terminal domain. Sulfite oxidase catalyzes the oxidation of sulfite to sulfate, the terminal reaction in the pathway of degradation of the sulfur amino acids cysteine and methionine. The electrons derived from this reaction are transferred to cytochrome *c* on the mitochondrial inner membrane.

Abnormal gene product. The effects of pathogenic variants on sulfite oxidase structure that have been characterized in a few instances include: (1) conformational changes around the active site leading to perturbation of substrate binding and/or oxidation; (2) global effects on the stability and alteration of the sulfite oxidase dimer; and (3) defective molybdenum cofactor binding [Karakas & Kisker 2005].

Chapter Notes

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- 21 September 2017 (bp) Review posted live
- 27 March 2017 (psb) Original submission

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