Diagnosing Sulfite Intoxication Disorders Including MoCD Type A

The diagnosis of MoCD Type A can be challenging due to the overlap in presentation of symptoms with other disorders[1]

MoCD Type A is a disorder of sulfite intoxication that often presents early in the neonatal period with intractable **seizures** and **encephalopathy**.[2,3]

Most patients present with symptoms of MoCD in the first days of life. Other early symptoms that may present with MocD Type A include[5,6]:

- Feeding difficulties
- High-pitched cries
- Exaggerated startle response (hyperekplexia)
- Opisthotonos

Consideration of MoCD at symptom onset may lead to earlier diagnosis and the opportunity to intervene.[2]

MoCD may mimic other conditions such as hypoxic-ischemic encephalopathy (HIE)[1,6,7]

Inborn errors of metabolism (including MoCD Type A) account for 30% of intractable neonatal seizures and should be considered in the differential diagnosis.[8]

The following may suggest MoCD:

Clinical[9]

- Delivery history inconsistent with hypoxia/ischemia

Neuro-imaging[6,9]

- Mega cisterna magna/Dandy-Walker malformation
- Hypoplastic/atrophic corpus callosum
- Evidence of prenatal brain degeneration present at birth

Biochemical[5,6]

- Low, falling, or absent uric acid in the plasma or urine
- Increased sulfites in the urine

Sulfite intoxication can be ruled out with one urine test.[2,10]

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Differentiating disorders of sulfite intoxication

Disorders of sulfite intoxication can be distinguished both biochemically and with genetic testing[6,11]

Sulfite intoxication may be a result of isolated sulfite oxidase deficiency (ISOD) or MoCD.[2]

Although clinically indistinguishable from ISOD, MoCD and ISOD are biochemically distinct entities due to a loss of function of MoCo-dependent enzymes in MoCD, including xanthine dehydrogenase and aldehyde oxidase.[4,5]

- MoCD results in decreased, absent, or falling levels of uric acid, as well as increased sulfites, S-sulfocysteine (SSC), and xanthine.[5,6]
- SSC is a reliable biochemical marker of sulfite intoxication that can be assessed in either urine or plasma.[2,5]

Metabolic test	ISOD	MoCD Type A
Sulfites (U)	+++	+++
S-sulfocysteine (U/P)	+++	+++
Uric acid (U/P)	Normal	Decreased
Xanthine (U/P)	Normal	Increased

P, plasma; U, urine.

Upon suspicion of sulfite intoxication, an SSC test with rapid turnaround can be ordered from Duke Health or the Mayo Clinic Laboratories.*

Diagnostic confirmation of MoCD and differentiation of MoCD Types A, B, and C can be obtained with genetic testing[2,11]

MoCD	Affected Gene
Type A	*MOCS1*
Type B	*MOCS2*
Type C	*GPHN*

MoCD Types A, B, and C are caused by biallelic inactivation of *MOCS1*, *MOCS2*, or *GPHN*, respectively.[2]

- Rapid whole genome sequencing and whole exome sequencing offer the most comprehensive genetic testing available.[12,13]
- Single-gene and genetic panels that test for *MOCS1* may also be used to confirm a diagnosis of MoCD Type A.

*Expedited SSC testing, defined here to mean diagnostic results within 48 hours of when a sample is received, is available from certain laboratories, including Duke and Mayo Clinic. Other laboratories may offer expedited SSC testing services, and turnaround times may vary. The ultimate choice of laboratory is solely between the patient and the treating physician. Please contact your preferred laboratory to verify whether expedited testing is available and to confirm turnaround time.

If you are aware of another laboratory that provides expedited SSC testing or would like to have your laboratory included in this brochure, please email medical_affairs@sentynl.com. Sentynl does not subsidize any tests nor does it have any financial interests in the laboratories listed.

To find out where you can order a genetic test for *MOCS1*, visit aboutMoCDTypeA.com

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References: 1. Vijayakumar K, Gunny R, Grunewald S, et al. *Pediatric Neurology.* 2011;45:246-252. **2.** Spiegel R, Schwahn BC, Squires L, Confer N. *J Inherit Metab Dis.* 2022;45(3):456-469. **3.** Zaki MS, Selim L, El-Bassyouni HT, et al. *Eur J Paediatr Neurol.* 2016;20(5):714-722. **4.** Mechler K, Mountford W, Hoffmann G, et al. *Genet Med.* 2015;17: 965–970. **5.** Misko A, Liang Y, Kohl J, Eichler F. *Neurol Genet.* 2020;6(4):1-10. **6.** Johannes L, Fu CY, Schwarz G. *Molecules.* 2022;27(20):6896. **7.** Panayiotopoulos CP. *The Epilepsies: Seizures, Syndromes and Management.* Bladon Medical Publishing; 2005. **8.** Chan D, Tan E, Cleary M. *Proc Singap Healthc.* 2010;19(2):112-123. **9.** Misko A, Mahtani K, Abbott J, et al. In: Adam MP, Everman DB, Mirzaa GM, et al, eds. *GeneReviews.* Seattle, WA: University of Washington, Seattle; December 2, 2021. **10.** Veldman A, Santamaria-Araujo JA, Sollazzo S, et al. *Pediatrics.* 2010;125(5):e1249-e1254. **11.** Atwal PS, Scaglia F. *Mol Genet Metab.* 2016;117(1):1-4. **12.** Kingsmore SF, Ramchandar N, James K, et al. *Cold Spring Harb Mol Case Stud.* 2020;6(1):a004705. **13.** Wright CF, FitzPatrick DR, Firth HV. *Nat Rev Genet.* 2018;19(5):253-268.

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