

First-Tier Metabolic Testing: Evidence-Based Practice Change Recommendation

In 2012, a standardized first-tier metabolic test panel (TIDE panel) was introduced in BC as a pilot project providing a protocol for the investigation of children with global developmental delay/intellectual disability (GDD/ID).

A recent review of the diagnostic yield from the TIDE panel¹ over the years found that:

- Specific neurological features or other red flag signs commonly found in Inborn errors of metabolism (IEM) were present in children who received a diagnosis.
- Disorders of amino acids, organic acidurias, homocysteine and creatine deficiency disorders were the most frequently established diagnoses.
- No diagnoses were established through acylcarnitine, copper, and ceruloplasmin testing.
- No diagnoses were established through lactate or ammonia levels without other abnormalities detected from plasma amino acids or urine organic acids.
- Despite a dramatic increase in first-tier TIDE test volume, there was no concomitant increase in diagnoses in patients.
- The urine purine / pyrimidine panel is no longer necessary as the only treatable condition detected by this panel (GAMT deficiency) is now part of newborn screening.

Based on these findings, the following TIDE first-tier screenings tests are:

Newly recommended:

Plasma amino acids Draw specimen prior to feeding for infants <1 year; 3-4 hours after a meal for older children
Plasma homocysteine Fasting as above
Urine organic acids

No longer recommended for routine screening in GDD/ID:

Acylcarnitines
Copper
Ceruloplasmin
Lactate
Ammonia
Purine/Pyrimidine

Please make these modifications to your lab ordering requisitions in your EMR.

Note: *TIDE panel* is not an orderable test in B.C. Tests must be ordered individually.

Patient Selection Criteria when ordering a TIDE first-tier panel

Recommended for children with GDD/ID with additional neurological and/or metabolic features. Red flags include²:

Severe hypotonia, hypertonia (spasticity), dystonia, ataxia
Intractable seizures
Regression in developmental milestones
Neuroimaging abnormalities
Recurrent episodes of vomiting, ataxia, lethargy
Head circumference >2SD above or below mean
Unexplained failure to thrive
Consanguinity, family history of an IEM or unexplained infant death
History of being severely symptomatic and needing longer to recover from inter-current viral illness
Immigrant from country with limited or no newborn screening (add blood spot acylcarnitine profile)

No longer recommended for children with GDD/ID without clear neurological signs or other red flags.

Also, not recommended for:

Non-syndromic autism ³

If you have questions regarding the information given in this letter,

please contact us at
BGLOnService@phsa.ca

For other investigations such as chromosomal microarray refer to
www.genebc.ca

For information about all treatable intellectual disabilities, visit the updated *Treatable ID* app:
www.treatable-id.org

If you have questions regarding a patient,

please consult with our on-call team:

- Laboratory | (604) 875-2307 or BGLOnService@phsa.ca
- Clinical | (604) 875-2000
Ask for the Biochemical Diseases Physician on-call

If your patient screens negative but you still want to rule out treatable GDD/ID,

please refer your patient to the Division of Biochemical Diseases for further evaluation via:

- Mailing Address:
4480 Oak Street (Room K3-200)
Vancouver, BC V5Z 4H4
- Fax Number: (604) 875-2349

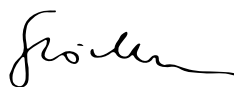
¹Vallance H et al. Diagnostic yield from routine metabolic screening tests in evaluation of global developmental delay and intellectual disability. Paediatr Child Health 2020;1-5 doi:10.1093

²Belanger et al. Evaluation of the child with global developmental delay and intellectual disability. Paediatr Child Health 2018 Sep;23(6):403-19

³Campistol et al. Inborn errors of metabolism screening in individual with nonsyndromic ASD. Dev Med and Child Neur;2016;58(8):842-7



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