

# Testing for Genetic Syndromes Related to Developmental Delay (DD) and Intellectual Disability (ID)

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**INDICATIONS FOR TESTING**  
DD and/or ID  
**WITH OR WITHOUT**  
One or more comorbidities (eg, dysmorphic features, seizures, congenital defects, psychiatric disorders, family history of recurrent miscarriages)

**PERFORM**  
Comprehensive medical history, family history, physical examination, and neurologic examination

Down syndrome, trisomy 13, or trisomy 18 suspected

Etiology unknown; no specific disorder suspected

Specific disorder (other than aneuploidy) suspected

**ORDER**  
Chromosome analysis

**ORDER DISORDER-SPECIFIC TESTING**  
(depending on clinical indications):

- Testing for Rett syndrome
- Testing for *PTEN*-related disorders
- Testing for Angelman syndrome/Prader-Willi syndrome
- X-linked disorder testing
- Other nonlaboratory assessments

Etiology identified

Etiology not identified

Etiology not identified

Etiology consistent with patient phenotype identified

No further testing

**First-Tier Testing**

**ORDER**  
CMA with fragile X testing  
**OR**  
WGS or WES with fragile X testing and consideration of microarray  
**OR**  
A panel test that includes genetic, fragile X, and metabolic testing  
**AND**  
Refer to medical genetics/genetic counseling  
**AND CONSIDER**  
Testing for metabolic and/or mitochondrial disorders

Etiology not identified

Etiology consistent with patient phenotype identified

**Second-Tier Testing**

**ORDER**  
WGS/WES (if not already performed)  
**AND**  
Refer to medical genetics/genetic counseling

No further testing

**Abbreviations**

CMA	Chromosomal microarray
DD	Developmental delay
ID	Intellectual disability
WES	Whole exome sequencing
WGS	Whole genome sequencing

**References**

- Manickam K, McClain MR, Demmer LA, et al. [Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics \(ACMG\)](#). *Genet Med*. 2021;23(11):2029-2037.
- Michelson DJ, Shevell MI, Sherr EH, et al. [Evidence report: Genetic and metabolic testing on children with global developmental delay: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society](#). *Neurology*. 2011;77(17):1629-1635.
- Moeschler JB, Shevell M, Committee on Genetics. [Comprehensive evaluation of the child with intellectual disability or global developmental delays](#). *Pediatrics*. 2014;134(3):e903-e918.
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