INDICATIONS FOR TESTING
Developmental delay (DD), intellectual disability (ID), and/or autism spectrum disorder (ASD)
AND/OR
One or more comorbidity (eg, dysmorphic features, seizures, congenital defects, psychiatric disorders, family history of recurrent miscarriages)

Down syndrome, trisomy 13, or trisomy 18 suspected

ORDER
Chromosome Analysis, Peripheral Blood, with Reflex to Genomic Microarray

Conduct comprehensive medical history, family history, physical examination, and neurologic examination

Specific disorder suspected

ORDER
Disorder-specific testing

First-Tier Testing

ORDER
Cytogenomic SNP Microarray or Cytogenomic SNP Microarray Buccal Swab

AND
Fragile X (FMR1) with Reflex to Methylation Analysis

CONSIDER
Testing for metabolic and/or mitochondrial disorders (if clinical indicators present)

ORDER
Autism and Intellectual Disability Comprehensive Panel

Panel includes cytogenomic microarray, fragile X, and metabolic disorders testing (plasma acylcarnitine and amino acids; serum or plasma creatine; and urine mucopolysaccharides, organic acids, and creatine disorders panel)

AND
Medical genetics/genetic counseling referral

Second-Tier Testing

Consider additional specific molecular studies:
- Rett Syndrome (MECP2) Sequencing and Deletion/Duplication if patient is female
- PTEN-Related Disorders Sequencing and Deletion/Duplication if patient has ASD and macrocephaly (head circumference >2.5 standard deviations)
- X-linked disorder testing if indicated by clinical and family history
- Whole exome sequencing
- Brain imaging studies

*The American College of Medical Genetics and Genomics suggests fragile X syndrome screening for males and females with compatible clinical features and family history. The American Academy of Pediatrics and American Academy of Neurology recommend screening in all cases.

Consider metabolic testing (eg, acylcarnitine, amino acids, creatine, mucopolysaccharides, organic acids; creatine disorders panel, very long-chain and branched-chain fatty acids profile, uric acid, pyridoxine-dependent epilepsy panel [includes p-aminobenzoic acid and total AAS-A-P6C]) and review of newborn screening results even if low incidence/suspicion because intervention may be possible. Clinical indicators may include poor feeding, vomiting, dehydration, lethargy, hypotonia, and seizures in the newborn period. Clinical indicators outside of the newborn period exhibit marked variability and may be episodic and/or progressive.

References