Testing for Genetic Syndromes Related to Developmental Delay (DD), Intellectual Disability (ID), and Autism Spectrum Disorder (ASD)

ARUP Consult

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INDICATIONS FOR TESTING
Developmental delays (DD), intellectual disabilities (ID), and/or autism spectrum disorders (ASD)
AND/OR
One or more co-morbidity (eg, dysmorphic features, seizures, congenital defects, psychiatric disorders, recurrent miscarriages)[a]

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

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DD/ID/ASD of unknown etiology[b]

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First-Tier Testing

ORDER
Cytogenomic SNP Microarray (Peripheral Blood or Buccal Swab)
AND
Fragile X (*FMR1*) with Reflex to Methylation Analysis[c]
CONSIDER
Testing for metabolic disorders (if clinical indicators present)[d]

OR

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

Proceed to genetic counseling and/or referral to medical geneticist

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Second-Tier Testing

Depending on results of above tests, medical geneticist and/or genetic counselor may also recommend one or more of the following:

Brain imaging studies
Additional specific molecular studies
- *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)
- Angelman syndrome and Prader-Willi syndrome by methylation sensitive PCR – especially in cases of severe hypotonia

Targeted multi-gene panel (eg, X-linked intellectual disability panel if patient is male, epilepsy panel)
Whole exome sequencing
Chromosome analysis (standard karyotype) if chromosomal anomaly suspected
Metabolic disorders 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 pipecolic acid and total AASA-P6C})
Mitochondrial disorders testing

[a]Family history of DD, ID, or ASD with co-morbidities generally increases diagnostic yield of testing.
[b]If specific disorder(s) suspected, order disorder-specific testing and/or consult with medical geneticist.
[c]ACMG suggests fragile X syndrome screening for male patients.
[d]Consider metabolic testing 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
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