Chromosomal microarray (array CGH) testing is recommended as the first-tier genetic test for the evaluation of postnatal patients with multiple congenital anomalies, developmental/intellectual disabilities, and autism spectrum disorders.

In December 2013, the American College of Obstetricians and Gynecologists (ACOG) released a committee opinion addressing the use of chromosomal microarray in prenatal diagnosis1.

ACOG now recommends chromosomal microarray testing be performed in the following instances:

- In patients with a fetus with ≥1 major structural abnormality identified on ultrasound, and who are undergoing invasive prenatal diagnosis.
- In cases of intrauterine fetal demise or stillbirth when further cytogenetic analysis is desired.

Prenatal chromosome microarray analysis may also be offered to any woman undergoing an invasive procedure regardless of maternal age or absence of fetal anomalies.

Chromosomal microarray testing is currently not recommended for the evaluation of first- and second-trimester pregnancy losses due to the limited data available regarding its clinical utility in these circumstances.

Chromosomal microarray will not routinely detect balanced alterations (reciprocal translocations, Robertsonian translocations, and inversions) or imbalances less than 200 kb in size.

Detection Rates2:
Detection rates vary based on reason for referral. Overall detection rate, given normal karyotype, is estimated at 2.5%. Prenatal microarray is most beneficial in cases where fetal anomalies have been noted by ultrasound examination, detecting clinically relevant findings in 6% of cases with ultrasound anomalies and a normal karyotype. Detection rate in cases where women are undergoing testing due to maternal age is estimated at 1.7%.

Array vs. Karyotype
Chromosomal microarray is equally effective as standard chromosome analysis in the detection of common autosomal and sex chromosomal aneuploidies. With a higher resolution, chromosome microarray also has the ability to detect less common, but clinically significant microdeletion/duplications that may be missed by standard karyotype. Another advantage of chromosomal microarray is that analysis does not require dividing cells, which is especially useful in cases of fetal demise or stillbirth. The use of SNP probe analysis also allows for the detection of triploidy and loss of heterozygosity.

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Phenotype Information & Interpreting Microarray Results
In order to continue to provide accurate and timely microarray result interpretation, UW Cytogenetic Services-WSLH is requesting phenotype data collection forms be completed and submitted along with both prenatal and postnatal patient samples. Forms can be found on our website at http://www.slh.wisc.edu/cytogenetics. Completed forms should be returned to WSLH directly with patient sample or via fax (608-265-7818).

CPT code update: We are now using CPT code 81229 for chromosomal microarray testing

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New Probe Added to Multiple Myeloma FISH Panel

Multiple Myeloma is a malignant B-cell process characterized by M-protein in serum or urine and a significant monoclonal population of plasma cells in the bone marrow. Certain genetic findings are associated with favorable [hyperdiploidy, t(11;14), and t(6;14)] and unfavorable prognosis [deletion 13, t(4;14), t(14;16), t(14;20), deletion 17p13 (p53), gain of 1q, and hypodiploidy].

In an effort to provide the most comprehensive evaluation, we have updated our diagnostic fluorescence in situ hybridization (FISH) panel to include probes for gain of 1q effective December 1, 2013.

Spotlight: Fragile X Syndrome

Fragile X syndrome (FXS) is the most common known inherited cause of intellectual disability. Features include:
- Mild-moderate intellectual disability
- Autism
- Seizures
- Macroorchidism
- Characteristic facies: macrocephaly, long face, large forehead, and prominent ears.

Cause of FXS
FXS is caused by mutations in the FMR1 gene, located on the X chromosome. Most mutations are due to an expanded CGG trinucleotide repeat. Individuals with >200 CGG repeats are considered to have a full mutation; individuals with 55-200 repeats have a premutation (normal range is 5-44 repeats). Nearly all males with a full mutation will have FXS; however, females with a full mutation tend to have milder features (mild intellectual disability or learning disability) or may show no signs of FXS due to skewed X-inactivation.

FMR1 related disorders
Premutation carriers may show some mild features of fragile X syndrome, including autism. They are also at risk for developing fragile X-associated tremor/ataxia syndrome (FXTAS) and approximately 20% of female permutation carriers can experience primary ovarian insufficiency (POI).

Testing
Testing for FMR1 related disorders (fragile X syndrome, FXTAS, and FMR1-related POI) is typically done using PCR analysis and/or Southern blot hybridization. Testing should be considered in individuals with:
- Developmental delay or intellectual disability of unknown etiology
- Autism
- A family history of Fragile X syndrome
- A personal or family history of progressive cerebellar ataxia and intention tremor
- Females with primary ovarian insufficiency