Non-invasive prenatal testing (NIPT) is based on the analysis of cell-free DNA fragments derived from the placenta (Liao, 2014). These tests have been rapidly adopted for the detection of fetal aneuploidy because of the lower risk of complications compared to invasive testing and the higher sensitivity and specificity rates compared to maternal serum screening. NIPT is currently recommended by the American College of Obstetricians and Gynecologists for use in populations at high-risk for fetal aneuploidy.

WSLH has received 32 cases whose reason for referral included a positive NIPT result. The average age of the patient was 36.1 years (range 28-45). Ten of the 32 (31%) cases were classified as false positives based on a normal karyotype by chromosome analysis. An abnormal result was confirmed in 22 of 32 cases (69%). Karyotype analysis can also provide information about genomic composition that is not provided by an NIPT test such as aneuploidy of chromosomes other than 13, 18, 21, X, or Y, Robertsonian translocations versus trisomy, or mosaicism. Abnormal ultrasound findings or maternal serum screening results were included in the reason for referral in 7 of 22 (32%) cytogenetically abnormal cases and in 2 of 10 (20%) cases with a normal karyotype.

The false positive rate of samples received by WSLH is in line with what has been reported by other groups (Wang, 2014). Commercially available NIPT tests have reported >99% sensitivity and specificity values. However, following a positive result, the likelihood of the fetal karyotype being abnormal can be much lower and depends on the prevalence of the condition. Appropriate counseling is essential to convey the true risk of an affected pregnancy and the importance of diagnostic testing, such as CVS or amnio, for confirmation of results.

References:
Disease Spotlight: Rett Syndrome

Rett syndrome is a rare progressive neurodevelopmental disorder. This condition almost exclusively affects females and is usually lethal in males. Girls with Rett syndrome can have normal development for the first year or more of life, but typically starting between the ages of 1 to 4 years there is a rapid and noticeable regression in skills, particularly purposeful hand and language skills. They also can display stereotypic hand movements such as hand wringing, clapping, washing, and mouthing. Breathing abnormalities such as apnea or autistic-like symptoms can also be seen. Following this period of regression is a plateau stage, which can last for years. Children in this stage may improve in behavior although movement problems continue to occur. The final stage of Rett syndrome is characterized by reduced mobility, scoliosis, muscle weakness, and spasticity; however, there is typically no further loss of cognition, understanding, or hand skills. Females with Rett syndrome typically survive into adulthood, but require continuous care and assistance.

Causes of Rett syndrome

Rett syndrome is caused by mutations in the MECP2 gene, located on the X chromosome. It is possible to inherit a mutation from a parent who has germine mosaicism for a MECP2 mutation, or, more rarely, is an asymptomatic female carrier; however, more than 99% of mutations are de novo. This means that usually there is only one affected individual in a family and risk to other family members is typically low.

Testing for Rett syndrome

Rett syndrome is typically diagnosed clinically, after a careful examination by a medical geneticist or other qualified health care provider. A clinical diagnosis of Rett syndrome can be molecularly confirmed in a patient by sequencing the MECP2 gene to look for disease-causing mutations. Sequence analysis and deletion/duplication studies will find a causal mutation in 88% of children with Classic Rett syndrome.

MECP2 testing will soon be available through the UW Cytogenetics and Molecular Genetics lab. Please call us at 608-262-0402 with any questions.