What Parents Need To Understand About Fragile X Testing

1. Fragile X Syndrome is a mutation on the Fragile X Mental Retardation 1 (FMR1) gene on the X chromosome. This gene produces the Fragile X Mental Retardation Protein (FMRP) when the gene is turned off it produces no protein, or not enough protein, which results in Fragile X Syndrome.
2. Males have an X and Y chromosome, and females have two X chromosomes.
    - Males have only one X chromosome when the gene is turned off it will result in Fragile X Syndrome.
    - Females have two X chromosomes and their X chromosome in which the gene is normal may or may not produce enough protein, they may or may not be affected.
3. Any doctor – including your pediatrician, neurologist or psychiatrist - can order the blood test.
4. Karotyping or chromosome analysis CANNOT accurately diagnose Fragile X.
    - Used for diagnosis prior to the discovery of the gene in 1991, with the passage of time they have found karotyping and chromosome analysis unreliable in diagnosing fragile X, producing false negatives.
    - Anyone previously tested for fragile X by karotyping or chromosome analysis alone should be retested.
5. The Southern Blot DNA test with PCR analysis is 99%+ accurate in diagnosing Fragile X. The only problem with these tests is that they may not pick up a deletion of the gene, which can occur but is a rare. Southern Blot DNA test with PCR analysis is less expensive than the older karotyping/chromosome analysis tests.
6. Southern Blot and PCR can identify changes in the DNA code represented as CGG repeats in the FMR1 gene. Special note: The type of tube used for drawing the blood is important. They need to use the right tube or the preservatives inside the tube could destroy the blood sample for DNA testing, the tube should have a purple top.
7. CGG repeats in the FMR1 gene signify the absence or presence of Fragile X.
    - CGG repeats less than 50 indicates the gene is normal
    - CGG repeats greater than 50 but less than 200 indicates a premutation, the gene is unstable and can expand in future generations
    - CGG repeats greater than 200 indicate a full-mutation, the gene is turned off, produces no protein, or not enough protein
8. CGG repeat numbers, other than identifying individuals as normal, premutation (carrier) or full-mutation, cannot be used to identify how affected an individual with Fragile X will be. Fragile X is a spectrum disorder causing anything from mild learning disabilities to severe cognitive impairment (mental retardation).
9. How can you tell if the right test was ordered:
    - Test results should provide the CGG repeat count on the allele, with males there should be one allele, with females there should be two alleles.
    - If no CGG repeat count is provided this is a strong indication that they may have performed the older, unreliable tests and testing should be redone using Southern Blot DNA test with PCR analysis.
10. Where to learn more:
    - Fragile X Syndrome: Diagnostic and Carrier Testing, http://www.acmg.net/StaticContent/StaticPages/FragileX.pdf
    - FRAXA Research Foundation, www.FRAXA.org
    - National Fragile X Foundation, www.fragilex.org