Over the last 15 years, dramatic advances in genetic testing have occurred, but what exactly are all of the different genetic tests and what do they do? An overview of genetic tests was given during the webinar, “Ordering the Right Tests: Genetics in Primary Care,” held on May 31, 2012. The webinar was presented by Leah Burke, MD, FAAP, FACMG, as part of the Time Out for Genetics webinar series hosted by the Genetics in Primary Care Institute (GPCI).

**Genetic Testing**

There are two forms of genetic testing that are often confused with each other: screening and diagnostic testing. Screening is performed on a population that is asymptomatic to identify those who may require further testing, also known as diagnostic testing. Examples of genetic screening include family history, prenatal tests, newborn screening, and the Modified Checklist for Autism in Toddlers (M-CHAT), which is used to screen for autism spectrum disorders, increasingly thought to be genetic based.

Diagnostic Testing is conducted on individuals but may have implications for families. Diagnostic testing is performed on either a symptomatic patient or in response to a positive screening test. It can provide information for prognostics, treatment options and reproductive choices.

**Diagnostic Genetic Testing**

There are a variety of diagnostic genetic tests. Some have similar abilities, while others have more specific capabilities. Practice guidelines can help choose which test to order. Following is an overview of the various diagnostic genetic tests.

- **Karyotype**: a chromosome analysis in which chromosomes are counted by a trained technician using a microscope. Karyotyping can detect whole chromosomal differences, translocations and deletions or duplications only if they are large enough to be seen through a microscope.

- **Fluorescent In Situ Hybridization (FISH) Image**: sections of DNA known to be deleted in certain conditions can be tagged with fluorescent dye. Markers in one color indicate the chromosome being examined, while the other color indicates the section of DNA in question. FISH imaging examines only a specific area of a particular chromosome so it not only misses deletions or duplications in other chromosomes but deletions or duplications in some parts of the same chromosome as well.

- **Whole Genome Microarray, also known as Array Comparative Genomic Hybridization (aCGH)**: a type of microarray test that includes all of the chromosomes. It is similar to FISH Image testing but analyzes thousands of pieces of DNA from the whole genome. It can detect very small duplications or deletions in any of the chromosomes. Most commercial platforms include a Whole genome Oligonucleotide Array that spans the whole genome as well as a targeted array that includes even smaller probes in regions with genes that cause known conditions. Whole genome arrays can also include a single nucleotide polymorphisms (SNP) array that looks for regions that are identical in sequence. Occasionally, testing can lead to variants of unknown significance so providers should be prepared to discuss this with parents, who may subsequently undergo genetic testing so that family samples can be obtained and compared.

- **Next Generation Sequencing**: a massively parallel sequencing technology in which millions of overlapping “reads” of DNA sequences are done at the same time. It can detect a single mutation in a panel of many genes. This technique is currently being used to diagnose cardiovascular conditions, cancer and childhood syndromes.

- **Exome Sequencing**: now offered clinically, this is parallel sequencing of at least 98% of the coding sequences. It is recommended when all other testing has produced negative results but must be confirmed using a second method of testing. At $9,000, this test can be cost-prohibitive.
Ethics Issues Associated with Pediatric Genetic Testing

- Informed consent is required for genetic testing.
- Genetic testing results may affect family members.
- Primary care providers should be aware of direct-to-consumer genetic testing. According to the American College of Medical Genetics, direct-to-consumer testing should be ordered and interpreted by a knowledgeable professional, the scientific evidence should be understandable to the consumer and the test should be accredited by a suitable lab.
- The consensus opinion of the American Academy of Pediatrics (AAP) is to protect the autonomy of the child so carrier testing or testing for adult onset conditions in a child may not be the decision of the parents to make and should be avoided.

What To Do For a Genetics Referral

- Obtain a family history.
- Provide prenatal and birth information.
- Refer the patient for developmental testing. Results of developmental testing may help to guide the genetic testing.
- Record any recurrent illnesses.

About the Presenter

Dr Burke is a pediatrician and clinical geneticist with the Vermont Regional Genetics Center in Burlington, VT, a professor at the University of Vermont and chair of the AAP Section on Genetics and Birth Defects.

About GPCI

The GPCI was established to increase primary care providers’ knowledge and skills in the provision of genetic-based services. The GPCI is a cooperative agreement between the US Department of Health and Human Services, the Health Resources & Services Administration, the Maternal & Child Health Bureau and the American Academy of Pediatrics.

For additional information on the GPCI, contact Natalie Mikat-Stevens, MPH, Manager, Genetics in Primary Care Institute, Division of Children with Special Needs, AAP, at 847/434-4738.

April 2013