Well-checks present an optimal opportunity to look for indicators of possible genetic conditions. Because identification of genetic conditions can have implications for medical, social, and educational interventions; monitoring and long-term care of conditions; and decisions about future pregnancies, it is important for pediatricians to understand what types of red flags to look for and how to talk to parents about genetic referrals.

This information was presented during the webinar, “Genetic Red Flags in Well-Checks,” held in November 2013. The webinar, which featured Beth A Pletcher, MD, FAAP, FACMG, was part of the Integrating Genetics into Your Practice webinar series hosted by the Genetics in Primary Care Institute (GPCI).

**Reasons for referral**
While the primary care clinicians should always use their own judgment, the following lists the types of indicators that could benefit from genetic evaluation.

### Neurological Issues
- Autism spectrum disorder
- Brain malformation
- Congenital deafness
- Hard to control seizures
- Hypertonia, hypopontonia, or spasticity
- Significant intellectual disabilities or developmental delays

### Congenital Abnormalities
- Diaphragmatic hernia
- Dysmorphic features
- Heart defect
- Limb or bone malformation
- Renal agenesis
- Tracheoesophageal fistula

### Growth Problems
- Disproportionate growth, overgrowth, hemihyperplasia, or marfanoid habitus
- Intrauterine growth retardation
- Failure to thrive
- Microcephaly or macrocephaly
- Short stature
- Small for gestational age

### Miscellaneous
- Abnormal skin findings - cafe-au-lait spots, multiple lipomas, ash-leaf spots
- Cardiomyopathy without viral cause
- Clotting abnormalities - thrombosis or excessive bleeding
- Multifocal or bilateral malignancies such as Wilms tumor or retinoblastoma
Benefits of a genetic referral

Parents and family members are sometimes resistant to genetic testing. For example, if there is no treatment, why make the diagnosis? Listed below are several benefits to discuss with families.

- Having a confirmed genetic diagnosis can
  - Highlight potential complications, allowing them to be monitored and addressed before they become serious
  - Guide diagnostic studies or surveillance strategies
  - Provide important prognostic information
  - Guide Individualized Education Program services

Genetic referrals through well-checks: Five case studies

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<tr>
<th>Case #1 – Referral for facial features reveals serious heart defect</th>
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<td>An infant was referred for genetic testing for dysmorphic facial features. A chromosome analysis demonstrated extra genetic material on chromosome 22, indicating renal and cardiac risks. Although no cardiac murmur had been identified, the child was referred for a renal sonogram and echocardiogram. He was found to have a single kidney and total anomalous pulmonary venous return, which required immediate surgery and prevented likely heart failure in the future.</td>
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<th>Case #2 – Referral for speech delays, streaky skin and poor handwriting reveals significant learning and physical issues</th>
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<td>A 5-year-old was referred for speech delays and streaky hyperpigmentation of the skin. Her teacher reports poor handwriting and that she didn't seem to be trying very hard. Testing revealed a mosaic marker chromosome associated with more significant learning issues and physical issues such as hypotonia, which caused weakness in her hands and accounted for her poor handwriting. School placement and support services such as occupational/physical therapy were re-evaluated.</td>
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<th>Case #3 – Referral for café-au-lait spots reveals impending vision loss</th>
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<td>A 2-year-old was referred for 6 café-au-lait spots but no other features of NF. Neurodevelopmental assessment was normal, however, a dilated eye exam and subsequent MRI demonstrated a left optic nerve glioma (ONG). Close follow-up showed decreased visual acuity, so he was referred for chemotherapy for the ONG. The treatment resulted in reduction in the size of the ONG.</td>
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<th>Case #4 – Referral for albinism avoids potential disaster</th>
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<td>A 12-year-old boy with albinism was referred for genetic evaluation because his mother was pregnant. When asked about bruising, they confirmed that he bruised easily. Based on that, it was suspected and confirmed that he had Hermansky-Pudlak syndrome instead of simple albinism, which put him at risk for excessive bleeding with surgical procedures, pulmonary fibrosis and granulomatous colitis. Knowing this, he could be better monitored and prepared for future surgeries.</td>
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<th>Case #5 – Referral of mom with disabled children demonstrates risk for sister’s pregnancy</th>
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<td>A woman was referred for genetic counseling because she had two children with severe intellectual disabilities and minor birth defects and her sister was pregnant and wanted to know if she could be a carrier of the condition. Family history was otherwise unremarkable and prior genetic testing was negative. A microarray was ordered on her children that revealed an unbalanced translocation. Specialized cytogenetic studies were performed to determine if prenatal testing was indicated.</td>
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Talking to parents about a genetic referral

Some parents may be anxious about proceeding with a genetic referral. They may want to know:

- What are the benefits of genetic testing and what are the risks?
- Can having a genetic diagnosis help us with educational planning?
- Can having a genetic diagnosis help us with family planning?
- Will having this information potentially impact other family members? If so, how do I go about telling others in the family?

The following are examples of ways to frame recommendations in a discussion reticent or anxious parents:

- “On my exam today, I see X finding. I want to be sure there isn’t a genetic condition and in order to be thorough, I am recommending that we seek the advice of a geneticist.”
- “Your child has been diagnosed with X and I would like to see if we can identify a possible cause for these difficulties. Therefore I am suggesting that he/she be seen by a geneticist.”
- “In order to address your question, I would like to refer you to medical genetics.”
- “In order to provide the best care for your child, I would like medical genetics to help me with the following question…”
- “I understand you are not concerned, but in order to provide the best care, I need X from medical genetics.”

Preparing patients for their genetic visit

To make the most of the genetic referral and ease the process for everyone, consider the following in order to prepare patients for their genetic visit:

- Provide reports from imaging studies if possible
- Provide lab results (especially any prior genetic tests) as well as recent routine blood work – CBC, CMP, TFTs, etc.
- Ask parents to bring copies of the school or program evaluations – physical therapy, occupational therapy, speech therapy, and other testing
- Provide reports from other subspecialists
- Encourage parents to gather and bring family history, including ages and causes of death, major medical diagnoses such as birth defects, and physical and intellectual disabilities
- Discuss with parents the likelihood that the genetic evaluation may not yield a specific diagnosis and that some children may benefit from a revisit with the genetic team in the future to see what new tests are available or as clinical findings change over time

About the Presenter

Dr. Pletcher is an Associate Professor of Pediatrics at the Rutgers New Jersey Medical School. She served on the Board of Directors of the American College of Medical Genetics for six years and is the immediate past Chair of the American Academy of Pediatrics (AAP) Committee on Pediatric Workforce. She was the first Chair of the AAP Section on Genetics and Birth Defects and is a past liaison to the AAP Committee on Genetics. Dr. Pletcher also serves on the University Hospital Bioethics Committee and is the Co-Director of The Neurofibromatosis Center of New Jersey. Her clinical and research interests include:

neurofibromatosis, autism, Fragile X syndrome, craniofacial disorders, cancer genetics, public policy on genetic screening, genetic education for primary care providers, as well as pediatric workforce issues.

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.

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