Myths about Genetics in Primary Care—Setting the Record Straight

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Beth Tarini, MD, MS, FAAP

Thursday, July 26
12:00 - 12:30pm Central

Time Out for Genetics Webinar Series
Presented by the Genetics in Primary Care Institute
American Academy of Pediatrics

Presenters

- **Beth Tarini, MD, MS, FAAP**
  - Co-Medical Director, GPCI
  - General practicing pediatrician and health services researcher at the University of Michigan

- **Wendy Chung, MD, PhD, FAAP, FACMG**
  - GPCI QI Expert Group Member
  - Clinical and molecular geneticist
  - Directs the clinical genetics program at Columbia University; researcher
Drs Chung and Tarini have no financial relationships or conflicts of interest to disclose relevant to this presentation.

Acknowledgments

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Learning Objectives

1. Identify and clarify commonly held myths about the use of genetics in primary care practice
2. Illustrate examples of how to improve genetic services delivered by primary care physicians

Myths: Where they come from and why?

- Were once true (in past)
- Based on individual experience
- More comforting than the truth
Myth

Genetics just deals with rare diseases

Truth: Rare Diseases

<table>
<thead>
<tr>
<th>“RARE” DISORDER</th>
<th>PREVALENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA 1/2 carrier</td>
<td>1:40 – 1:2,000</td>
</tr>
<tr>
<td>Sickle cell anemia</td>
<td>1:500 African-Americans</td>
</tr>
<tr>
<td>Familial hypercholesterolemia</td>
<td>1:500</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>1:500</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>1:500 (heterozygotes)</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>1:3,000</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1:3,000 (births)</td>
</tr>
</tbody>
</table>
Truth: Rare Diseases

<table>
<thead>
<tr>
<th>“RARE” GENETIC DISORDERS/CONDITIONS</th>
<th>INCIDENCE/PREVALENCE</th>
<th>“RARE” NON-GENETIC DISORDERS/CONDITIONS</th>
<th>INCIDENCE/PREVALENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA 1/2 carrier</td>
<td>1:40 – 1:2,000</td>
<td>Neonatal sepsis (culture-proven)</td>
<td>1:500</td>
</tr>
<tr>
<td>Sickle cell anemia</td>
<td>1:500 (African-Americans)</td>
<td>Pertussis epidemic 2011 (&lt;1 years old)</td>
<td>1:1,000</td>
</tr>
<tr>
<td>Familial Hypercholesterolemia</td>
<td>1:500</td>
<td>SIDS</td>
<td>1:1,850</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>1:500 (heterozygotes)</td>
<td>Melanoma (men)</td>
<td>1:3,700</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>1:3,000</td>
<td>Ovarian cancer</td>
<td>1:7,800</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1:3,000 (births)</td>
<td>Tuberculosis cases in U.S. (new)</td>
<td>1:29,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meningococcal disease (age 14-24)</td>
<td>1:200,000</td>
</tr>
</tbody>
</table>

Common Indications for Referrals to Genetics

- Fetal anomalies/birth defects in a child
- Multiple miscarriages/infertility
- Developmental Delay/Intellectual Disabilities/Autism Spectrum Disorder
- Short stature/failure to thrive
- Family history of a condition
  - Risk stratification
  - Risk of recurrence
- Early age of disease onset
- Unusual combination of clinical features suggesting a syndrome
Myth

Testing is too complicated and too expensive

Truth: Testing

• Some tests are expensive
  – Chromosome microarray ~ $2,000
• But there are other cheaper (and helpful) “genetic” tests that primary care doctors can order…
  – Karyotype/Routine chromosome analysis: $650-$800
  – Plasma amino acids: $270
• Specimen requirements are only blood (or urine) for most tests
Compare to other commonly used tests...

- Routine chromosome analysis: $650-$800
- Plasma amino acids: $270

<table>
<thead>
<tr>
<th>COMMON TEST</th>
<th>ESTIMATED COST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid function tests (TSH, FT4)</td>
<td>$250</td>
</tr>
<tr>
<td>Non-contrast CT Scan (head)</td>
<td>$1,000-1,500</td>
</tr>
<tr>
<td>MRI (head)</td>
<td>$1,500-2,000</td>
</tr>
</tbody>
</table>

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ARTICLE

Consensus Statement: Chromosomal Microarray Is a First-Tier Clinical Diagnostic Test for Individuals with Developmental Disabilities or Congenital Anomalies


Chromosomal microarray (CMA) is increasingly utilized for genetic testing of individuals with unexplained developmental delay/intellectual disability (DD/ID), autism spectrum disorders (ASD), or multiple congenital anomalies (MCA). Performing CMA and G-banded karyotyping on every patient substantially increases the cost of genetic testing. The International Standard Cytogenomic Array (IICA) Consortium held two international workshops and conducted a literature review of 33 studies, including 21,698 patients tested by CMA. We provide an evidence-based summary of clinical cytogenomic testing comparing CMA to G-banded karyotyping with respect to technical advantages and limitations, diagnostic yield for various types of chromosomal aberrations, and issues that affect test interpretation. CMA offers a much higher diagnostic yield (35%–40%) for genetic testing of individuals with unexplained DD/ID, ASD, or MCA than a G-banded karyotype (>9%, excluding Down syndrome and other recognizable chromosomal syndromes), primarily because of its higher sensitivity for submicroscopic deletions and duplications. Truly balanced rearrangements and low-level mosaicism are generally not detectable by CMA, but these are relatively infrequent causes of abnormal phenotypes in this population. Available evidence strongly supports the use of CMA in place of G-banded karyotyping as the first-tier cytogenetic diagnostic test for patients with DD/ID, ASD, or MCA. G-banded karyotype analysis should be reserved for patients with obvious chromosomal syndromes (e.g., Down syndrome), a family history of chromosomal rearrangement, or a history of multiple miscarriages.


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Available evidence strongly supports the use of chromosome microarray in place of G-banded karyotyping as the first-tier cytogenetic diagnostic test for patients with developmental delay/intellectual disability, autism spectrum disorder, or multiple congenital anomalies.

Access to Testing

- Cost of testing is increasingly covered by health insurance, including medicaid, for common tests
- Many genetic testing laboratories will assist with insurance pre-authorization (testing for common indications: seizures, mitochondrial disorders, cardiomyopathies, intellectual disabilities, whole exome sequencing)
Testing: You are not alone!

- Call a friend...
  - Genetics professionals can help you decide on the front end
  - This can get the testing process started before patient is seen by genetics professional

Myth

A genetic diagnosis is only a label, it doesn't help anyone
Why a Genetic Diagnosis Matters?

• Provides prognostic information and informs anticipatory guidance
• Provides information about associated conditions
• May provide information for treatment (but may not)
• Allows for risk stratification in family members
• Provides closure
• May absolve some parents of guilt
• Allows for informed reproductive planning

GINA and Health Insurance

• Health insurers (Group, Individual, Medicare, Medicaid) may not require individuals to provide their genetic information or the genetic information of family members to the insurer for eligibility, coverage, underwriting, or premium-setting decisions
• Health insurers may not use genetic information either collected with intent, or incidentally, to make enrollment or coverage decisions
• Health insurers may not request or require that an individual or an individual’s family member undergo a genetic test
• Genetic information cannot be used as a preexisting condition
GINA and Health Insurance

• GINA does not protect genetic discrimination in life insurance, disability insurance or long-term-care insurance

Reproductive Options

• Preimplantation Genetic Testing
• Prenatal testing
  – Chorionic villus sampling
  – Non-invasive prenatal testing
Preimplantation Genetic Diagnosis

Egg + Sperm

Using IVF techniques

Blastomere

Remove one or two cells for testing

Test DNA or chromosomes

Test result

Genetic disorder excluded

embryo implanted

Genetic disorder detected

embryo discarded
Myth

The geneticist doesn't need my help to manage the patient

Truth: Co-Management

Medical home is a critical partner in the care and management of patients with genetic disorders or potentially genetic-related disorders
Example: Neurofibromatosis

- Primary Care Helps with Surveillance
  - Tumors
  - Blood pressure (renal artery stenosis)
  - Neurological deficits
  - Musculoskeletal problems (scoliosis)
  - Growth (short stature)
  - Behavioral or cognitive impairment
  - Increased risk of breast cancer

Myth

Collecting family history takes too long and doesn't help anticipatory guidance
Truth: Time for Family History

- Study observing family practice docs*
  - 3 minutes for established patients
  - 6 min for new patients


Tips For a Quicker Family History

- Have patient complete at home
- Have patient complete in waiting room
- Checklist like in Bright Futures
- Integration into electronic health record
- Online tools
Truth: Sudden Cardiac Death

- Sudden cardiac death
  - Young athletes
  - Adults 30s-40s
- Some possible causes
  - Hypertrophic cardiomyopathy
  - Myocarditis
  - Coronary artery disease
  - Marfan's syndrome
  - Conduction system abnormalities
  - Aortic stenosis

Truth: Family History and Sudden Cardiac Death

- Family history is critical to screening process
  - Sudden unexplained death age <50
  - Early cardiac death
    - Men age <55
    - Women age <65
  - Recurrent syncope
  - Seizures
  - SIDS
**Sudden Cardiac Death**

![Family Tree Diagram]

**Troponin T Mutation Specific Prognosis**

![Survival Graph]

- Val606Met
- Arg92Gln
In Summary...

• Genetic diseases are all around you, just need to look
• Testing should not be considered an insurmountable barrier
• Primary care providers are crucial partners in delivering quality care for patients with genetic conditions
Questions?

Thank you for your participation!

For more information, please contact
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lwilson@aap.org
847/434-7612

www.medicalhomeinfo.org/GPCI.aspx
Time Out for Genetics

Registration is now open for

“Heard About Genetic Counseling? What Does it Mean for You, Patients, and Families?”

Thursday, August 30
12:00 - 12:30pm Central

https://www2.gotomeeting.com/register/333904226