CT Genomics Forum

Danielle Bonadies, MS, CGC
Co-Founder and Director of Genetics
My Gene Counsel
Danielle@MyGeneCounsel.com
Overview

1. Genetics in Medicine
2. What Tests Are Available?
3. How Does It Work?
4. Avenues of Testing
5. Who is Involved?
6. Regulation and Protections
7. Opportunities
Rare to Common
What Tests Are Available?
Prenatal
Newborn Screening

- Heel stick
- Most states screen for at least 35 genetic conditions
- CT screens for 65+ genetic conditions
- Early treatment
## Pediatrics

### Age-Appropriate Skills to Look For

<table>
<thead>
<tr>
<th></th>
<th>4 - 5 months</th>
<th>9 - 12 months</th>
<th>18 - 23 months</th>
<th>3 years</th>
<th>4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Movement</strong></td>
<td>Does Baby do push-ups or bring hands and toys to his or her mouth?</td>
<td>Does child sit independently, crawl, creep or scoot forward?</td>
<td>Does child climb into chairs, walk forward, turn pages in a book?</td>
<td>Does child run easily, telling rarely, or kick a ball forward?</td>
<td>Does child run easily, or copy a circle and a square?</td>
</tr>
<tr>
<td>(physical growth)</td>
<td><strong>Thinking and Learning</strong></td>
<td><strong>Communication</strong></td>
<td></td>
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<tr>
<td></td>
<td>Does Baby listen to conversations or follow conversations with eyes?</td>
<td>Does Baby initiate some sounds you make (like a cough)?</td>
<td>Does Baby respond to own name (for example, look up when called)?</td>
<td>Does child use words that describe things like “it’s icy” or “I’m hungry”?</td>
<td></td>
</tr>
<tr>
<td>(cognitive</td>
<td></td>
<td></td>
<td>Does child point to objects or people to express a need?</td>
<td></td>
<td><strong>The Senses: Vision, Hearing and Touch</strong></td>
</tr>
<tr>
<td>development)</td>
<td></td>
<td></td>
<td>Does child use words that describe things like “it’s icy” or “I’m hungry”?!</td>
<td></td>
<td><strong>Sensory development</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Relating to Self and Others</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Social and emotional development</strong></td>
</tr>
<tr>
<td><strong>Self Care</strong></td>
<td>Does Baby sleep regularly for three to four hours at a time?</td>
<td>Does child feed soft with fingers?</td>
<td>Does child put off simple clothes (such as socks)?</td>
<td>Does child wash his teeth by self or with help?</td>
<td></td>
</tr>
<tr>
<td>(daily living</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>skills)</td>
<td></td>
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</tr>
</tbody>
</table>
Hereditary Cancer

Smith Sisters
Ancestry: Italian
Cardiovascular

• Familial Hypercholesterolemia
  – Markedly elevated LDL cholesterol levels beginning at birth
  – In males, heart attacks often occur in 40s-50s
  – 85% of men have an MI by age 60
  – In females, onset of heart attacks generally occur a decade later
Polygenic: Coronary Artery Disease

Clinical risk

Polygenic risk

Combined risk

Cholesterol: per 40 mg/dl increase
Smoking: per 50 cigarettes/day
Systolic blood pressure: per 20 mmHg increase

CAD relative risk

PRS percentile

0th
20th
50th
80th
100th

Low polygenic risk
Intermediate polygenic risk
High polygenic risk

Combined risk

Clinical risk and high polygenic risk
Clinical risk and intermediate polygenic risk
Clinical risk and low polygenic risk
Clinical risk and unmeasured polygenic risk

CAD absolute risk
Pharmacogenetics

Same Diagnosis = Same Treatment
Genetic Testing Is NOT Precision Medicine
Genetic Testing Is NOT Precision Medicine
Treatment of Cancer

Tumor Biopsy
Tumor Biopsy

Treatment of Cancer
Person to Protein

NORMAL GENE

DNA

Gene

Protein

Healthy Protein

GENE WITH A MUTATION

Altered Protein
How Does It Work?

Whole genome  Exome  Targeted genes or hotspots
How Does It Work?

**DNA Sequencing**
Full gene analysis for many different types of mutations

**Genotyping**
Focuses on specific areas; may miss known genetic markers
## Avenues of Testing

<table>
<thead>
<tr>
<th>Provider Initiated</th>
<th>Patient Initiated</th>
<th>Direct-to-Consumer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional medical test</td>
<td>Patient initiated, but...</td>
<td>Initiated by consumer</td>
</tr>
<tr>
<td>Most comprehensive</td>
<td>Doctor “approved”</td>
<td>No MD/clinician involved</td>
</tr>
<tr>
<td>Provider recommends and coordinates testing</td>
<td>Typically full genetic analysis/sequencing</td>
<td>Often ordered online</td>
</tr>
<tr>
<td>Diagnostic tests</td>
<td>Generally self-pay</td>
<td>Genotyping for particular variants/SNPs</td>
</tr>
<tr>
<td>Often covered by health insurance when certain criteria are met</td>
<td></td>
<td>Patient self-pay</td>
</tr>
</tbody>
</table>
# BRCA1/2: Breast and Ovarian Cancer Syndrome

<table>
<thead>
<tr>
<th>CANCER</th>
<th>AVG RISK</th>
<th>BRCA1+ RISK</th>
<th>BRCA2+ RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Breast</td>
<td>12-13%</td>
<td>50-85%</td>
<td>40-70%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1-2%</td>
<td>25-60%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Prostate</td>
<td>11%</td>
<td>increased</td>
<td>20-30%</td>
</tr>
<tr>
<td>Male Breast</td>
<td>&lt;1%</td>
<td>1-2%</td>
<td>7%</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>&lt;1%</td>
<td>2-3%</td>
<td>2-5%</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1-2%</td>
<td>increased</td>
<td>3-5%</td>
</tr>
</tbody>
</table>
Entertainment vs. Health
Who Is Involved?

• Genetic counselors
  – Specialized graduate degrees and experience in the areas of medical genetics and counseling
  – Certified by the American Board of Genetic Counseling
  – Licensure by state
  – Several insurers now only pay for testing after being seen for genetic counseling
  – Adoption of H.R. 3235, the “Access to Genetic Counselor Services Act of 2019” needed for field growth

• Medical genetics

• Other health care providers

• The patient/consumer
Testing Without Guidance = Misinterpretation

**ORIGINAL ARTICLE**

**Errors in Genetic Testing: The Fourth Case Series**

Meagan B. Farmer, MS, CGC, MBA,** Danielle C. Bonadies, MS, CGC,* Suzanne M. Mahon, DNSc, RN, AOCN, AGN-BC;† Maria J. Baker, PhD, FACMG, MS, LCGB,* Samedha M. Ghathe, MS, CGC;‡ Christine Munro, MS, MPH, LCGB,§ Chimmayee B. Nagaraj, MS, LCGB,‡ Andria G. Beser, MS, CGC,** Kara Bai, MS, CGC,‡ Christen M. Cisny, MS, CGC,** Brianne Kirkpatrick, MS, LCGB,** Andrew J. McCarthy, MS, LCGB,** Shelly Weiss McGaughy, MS, CGC,** Jessica Sebastian, MS, LCGB,** Dave L. Sterns, MS, LCGB,** and Ellen T. Matloff, MS, CGC*

**Purpose:** In this ongoing national case series, we document 25 new genetic testing cases in which tests were recommended, ordered, interpreted, or used incorrectly.

**Methods:** An invitation to submit cases of adverse events in genetic testing was issued to the general National Society of Genetic Counselors Listers; the National Society of Genetic Counselors Cancer Special Interest Group members, private genetic counselor laboratory groups, and via social media platforms (i.e., Facebook, Twitter, LinkedIn). Examples highlighted in the invitation included errors in ordering, counseling, and/or interpretation of genetic testing and did not limit submissions to cases involving genetic testing for hereditary cancer predisposition. Clinical documentation, including pedigrees, was requested. Twenty-five cases were accepted, and a thematic analysis was performed. Submitters were asked to approve the representation of their cases before manuscript submission.

**Results:** All submitted cases took place in the United States and were from cancer, obstetric, preconception, and general adult settings and involved both medical-grade and direct-to-consumer genetic testing with raw data analysis. In 8 cases, providers ordered the wrong genetic test. In 2 cases, multiple errors were made when genetic testing was ordered. In 3 cases, patients received incorrect information from providers because genetic test results were misinterpreted or because of limitations in the provider's knowledge of genetics. In 3 cases, pathogenic genetic variants identified were incorrectly assumed to correlate with the maximum genetic counseling delivery models, expanding the genetic counseling workforce, improving genetics and genomics education of non-genetics health care professionals, addressing health care policy barriers, and more. Genetic counselors have also positioned themselves in new roles to help patients and consumers as well as health care providers, systems, and payers adapt to new genetic testing technologies and models. The work to be done is significant, but so are the consequences of errors in genetic testing.

**Key Words:** Cancer genetic testing, direct-to-consumer screening and testing, genetic counseling, genetic counseling delivery models, genetic services, genetic testing, genetic testing adverse events, genetic test misinterpretation, genomics, multigene panel testing

(Cancer J 2019;25: 231–236)

**ERRORS IN GENETIC TESTING: THE FOURTH CASE SERIES**

The availability of genetic testing is growing at an exponential rate. In a 2018 study providing an overview of the current genetic testing landscape, authors estimated that there were approximately 75,000 genetic tests on the market, with 10 new tests being introduced daily. Four out of five of these tests, and 2 to 3 of the new tests introduced per day, were panel tests, a category that includes
Volume & Complexity of Genetics Is Exploding

Demand for Results Exceeds Capacity to Process

- Direct-to-consumer testing going to 100 million people by 2021
- Global genetic testing market to exceed $22 billion by 2024
- Large population genome studies planned globally
- Gene panels more complex, requiring more interpretation
- Genetic research evolving at a rapid pace

Limited supply of experts who can provide proper guidance:

<5,000 genetic counselors in US
Regulation

**Laboratory Performing Test**
- CMS pursuant to Clinical Laboratory Improvement Amendments (CLIA)
- New York State Clinical Laboratory Evaluation Program (CLEP)
- College of American Pathologists (CAP)

**Laboratory Tools** *(instruments, reagents)*
- FDA pursuant to the medical device authority under the Federal Food, Drug, and Cosmetic Act
- Safety and effectiveness for intended use

**Laboratory Developed Test**
- CLIA
- NYS
- College of American Pathologists (CAP)

**Advertising**
- Federal Trade Commission
- Prohibits unfair trade practices, including false or misleading advertising
Protections

1996
HIPAA
The Health Insurance Portability and Accountability Act
This law prohibits insurers from using genetic information as a preexisting condition.

2008
GINA
The Genetic Information Nondiscrimination Act
This law protects individuals from discrimination by health insurance companies and employers based on genetic information.

2010
ACA
Affordable Care Act
This law forbids group health plans from denying insurance or adjusting premiums based on any preexisting conditions.
Opportunities

• Genetic testing will be in every specialty, every disease
• Responsible testing and interpretation
• Access to genetics professionals
  – CT workforce studies
  – Grow the genetic counseling workforce
  – Support the UConn program
  – Support H.R. 3235, the “Access to Genetic Counselor Services Act of 2019”
• Tools for providers and patients
• Long-term follow-up
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