



Genetic Testing in the US: The GeneTests Perspective

Roberta A. Pagon, MD
Principal Investigator, GeneTests
Professor, Pediatrics
University of Washington, Seattle

The logo for GeneTests features a stylized DNA double helix in shades of green and purple. The word "GENE" is written in a bold, purple, sans-serif font, and "Tests" is written in a black, serif font, both in a large size.

GENE Tests

- What GeneTests is
- What GeneTests is not
- International component
- Future directions



www.genetests.org

Information resource for healthcare providers to help integrate genetic services into patient care

Located at

University of Washington
Seattle, WA

Funded by

National Institutes of Health

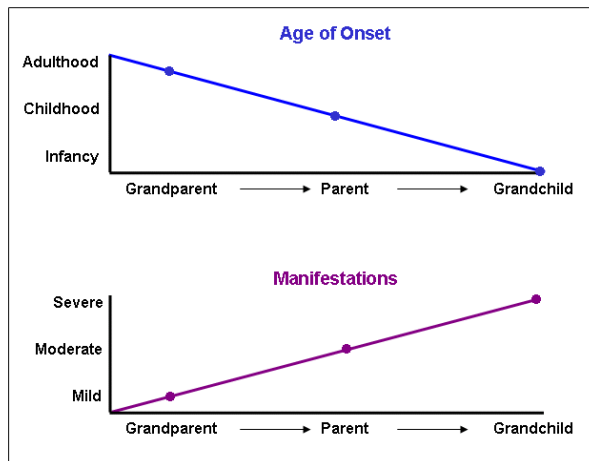
- **GeneReviews:** “User manual” for genetic testing for specific diseases
 - >400 *GeneReviews*
 - One new Review added each week
- **Laboratory Directory:** “Yellow Pages” of genetics labs
 - ~615 Clinical and research laboratories
 - ~1430 Inherited diseases

• Clinic

[Learn More](#)

• Illustrat

anticipation: The tendency in certain genetic disorders for individuals in successive generations to present at an earlier age and/or with more severe manifestations; often observed in disorders resulting from the expression of a **trinucleotide repeat mutation** that tends to increase in size and have a more significant effect when passed from one generation to the next



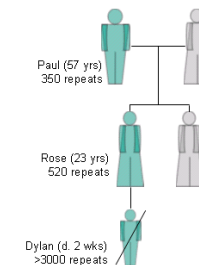
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Case Example

course

Case Example (anticipation): Myotonic dystrophy
 Paul is a 57-year-old man with myotonic dystrophy, a neuromuscular disorder caused by a trinucleotide repeat mutation inherited in an autosomal dominant manner. Paul noticed muscle weakness in his late 20s and now has difficulty opening jars and climbing stairs. His 23-year-old daughter, Rose, experienced onset of muscle cramping and weakness as a teenager. Her son, Dylan, born after a pregnancy complicated by polyhydramnios and poor fetal movement, was extremely hypotonic and expired at two weeks of age of respiratory failure. Trinucleotide repeat analysis of the *DMPK* gene reveals that Paul has 350 CTG repeats, Rose has 520 repeats and Dylan over 3000 repeats, consistent with the observed increase in severity of the disorder in subsequent generations.

Key
 ◆ = Myotonic dystrophy
 d. = death



	<i>DMPK</i> gene CTG Repeats	Onset	Clinical Findings
Paul	350	3 rd decade	Myotonia, weak facial muscles, general muscle weakness
Rose	520	2 nd decade	Myotonia, weak facial muscles, general muscle weakness
Dylan	>3000	Prenatal	Severe weakness, respiratory failure

Testing for Inherited Disorders From the Clinician's Perspective

- Molecular genetic testing
- Biochemical genetic testing
- Specialized cytogenetic testing (e.g., FISH, chromosomal breakage studies)

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GENE Tests Clinical Laboratories

- US: Must be certified by CLIA (US federal laboratory regulations)
- Non-US: Self-declared



- Helps clinicians with diagnosis, management and genetic counseling of patients and their families
- Allows non-expert clinicians to manage the first encounter with a patient with a given diagnosis
- Correlates information on uses of testing with test availability per GeneTests Laboratory Directory

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GeneTests Laboratory Listings

- Usually not recruited
- Occasionally recruited when a *GeneReview* author states that clinical testing is available, but no clinical laboratory is currently listed in GeneTests

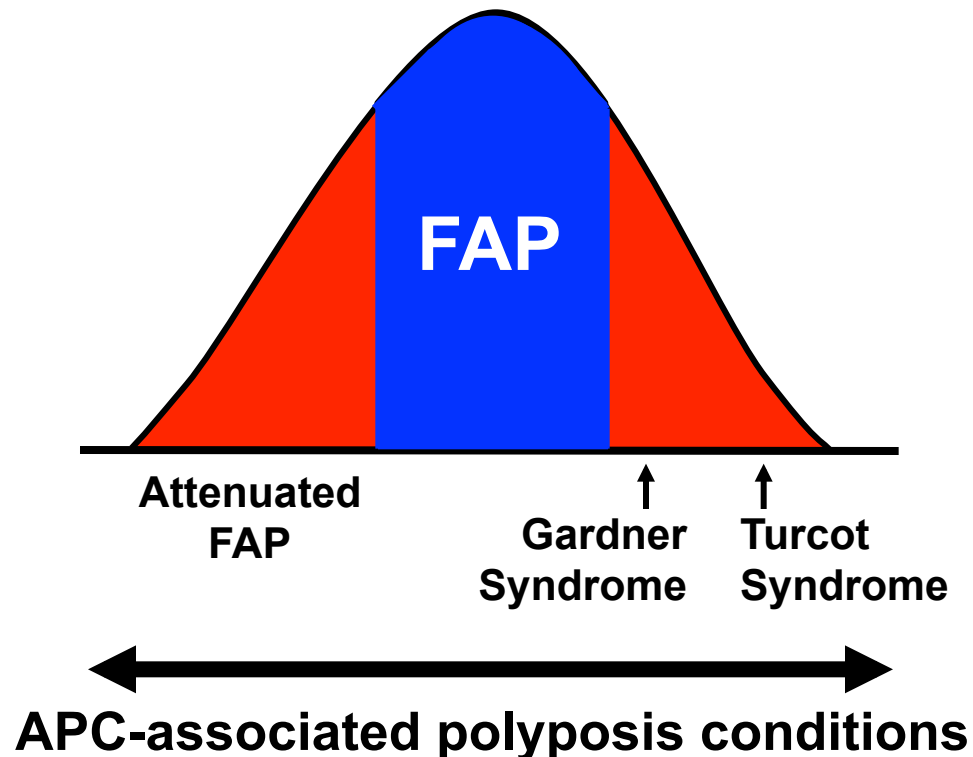


Tests Disease Naming System

- **Laboratory:** Testing detects alterations in a gene, not a phenotype
- **Clinician:** Patients present with altered phenotypes
- **Disease name:** Relate to genes for laboratories; relate to phenotypes for clinicians

Disease Naming

1. Pre-gene discovery: Phenotype is narrowly defined
- Essential to gene discovery
2. Post-gene discovery: Phenotypic spectrum expands
as patients are tested - Essential to patient care



Naming Hierarchy

Altered gene

APC-Associated Polyposis Conditions

Testing

Phenotypes

Attenuated FAP

Familial Adenomatous Polyposis

Gardner Syndrome

Turcot Syndrome

Naming Hierarchy

Altered gene

***FMR1*-related disorders** Testing

Phenotypes

- Fragile X syndrome
- FMR1*-related premature ovarian failure
- Fragile X-associated tremor/ataxia syndrome

Naming Hierarchy

Phenotype

Hereditary Hemorrhagic Telangiectasia

Altered gene

ACVRL1-Related HHT **Testing**
ENG-Related HHT **Testing**

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GENE Tests

- What GeneTests is
- What GeneTests is not
- International component
- Future directions

The logo for GENETests features the word "GENE" in a stylized, purple, blocky font, followed by "Tests" in a larger, black, sans-serif font. Above the text are three overlapping, wavy lines in shades of green, purple, and grey, resembling a DNA double helix or a signal waveform.

GENETests does NOT:

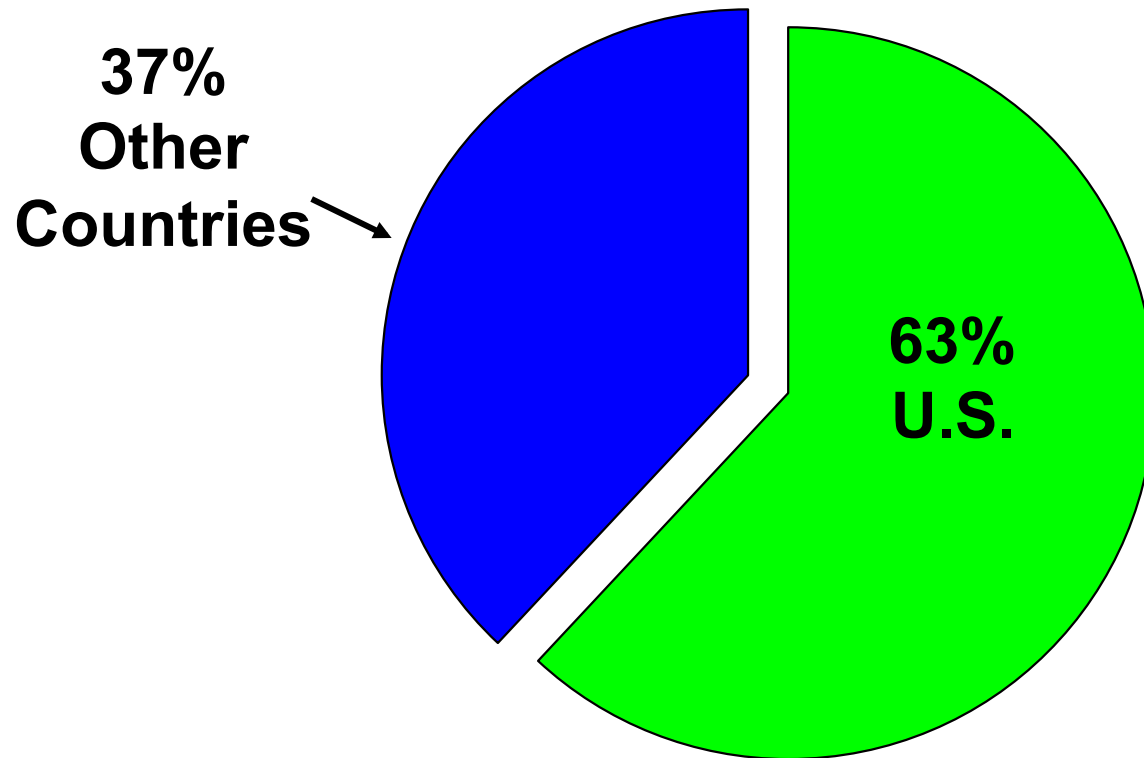
- Regulate
- Accredit
- Assess proficiency/quality

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GENE Tests

- What GeneTests is
- What GeneTests is not
- **International component**
- Future directions

913 International Expert Authors



Authors

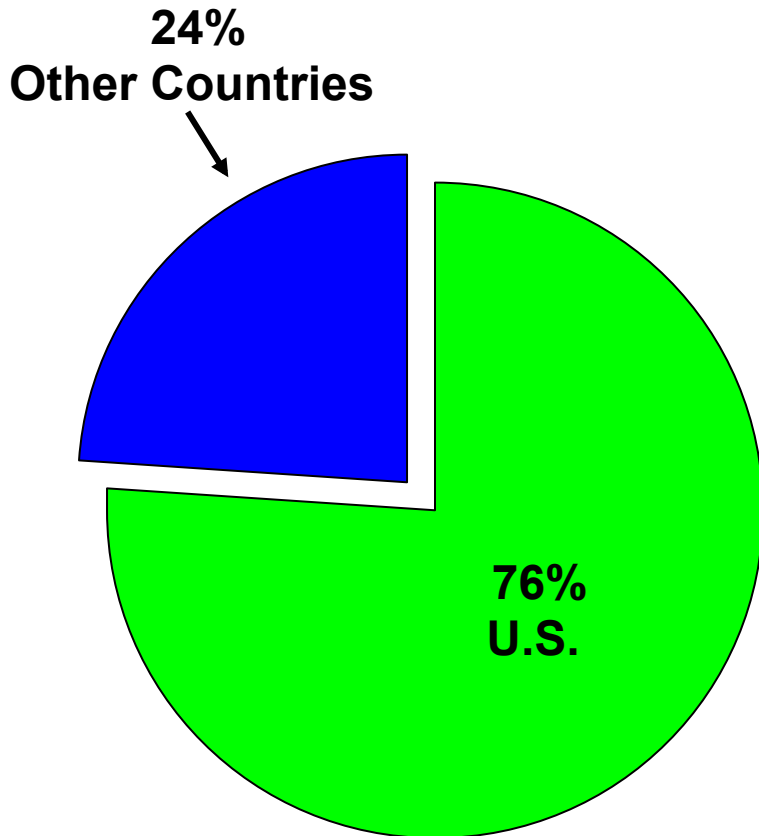
- **No financial compensation**
- **Must**
 - Adhere to *GeneReviews* format, style
 - Reflect clinical test availability as per GeneTests Laboratory Directory
 - Respond to internal and external peer review
- **Term of authorship**
 - Revise when test availability/methods change
 - Update every two to three years

Reviewers

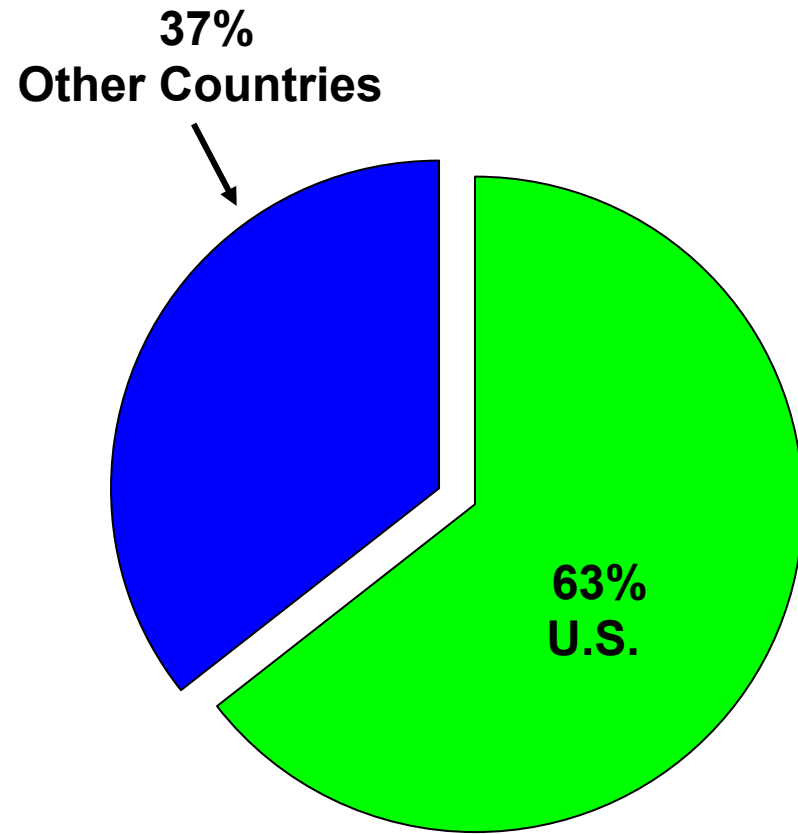
- **No financial compensation**
- **Review for:**
 - Accuracy
 - Currency
 - Suitability for healthcare providers

Laboratories

2001 (N = 498)



2007 (N = 616)



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GENE Tests Future Directions

- Use of standard mutation nomenclature with reference sequence to enable data sharing with mutation databases
- Collaboration with EuroGentest

Standard Mutation Nomenclature¹

[Gene Symbol] Allelic Variants Discussed in this *GeneReview*

Class of Variant Allele	DNA Nucleotide Change (Aliases ²)	Protein Amino Acid Change	Reference Sequence ³
Normal			
Pathologic			

¹per Human Genome Variation Society (www.hgvs.org).

²Variant designations that do not conform to current naming conventions

³Reference sequence (www.ncbi.nlm.nih.gov/Genbank/index.html)

The logo features three overlapping, wavy lines in shades of green, purple, and grey, resembling a DNA double helix or a stylized wave. The word "GENE" is written in a bold, purple, sans-serif font, partially overlapping the lines.

GENE Tests Future Directions

- Use of standard mutation nomenclature with reference sequences to enable data sharing with mutation databases
- **Collaboration with EuroGentest**



Collaboration

- **GeneTests:** Display information about testing for inherited diseases provided by clinical laboratories listed in EuroGentest
- **EuroGentest:** Display information about testing for inherited diseases provided by clinical laboratories in the US and Canada listed in GeneTests



Collaboration Benefits to GT/EGT Users and Labs

- Users: Improved access to worldwide information on clinical testing for rare inherited diseases
- Labs: Broader market for rare disease testing



Collaboration Benefits

Improved care for people with
inherited diseases and their families



www.eurogentest.org



www.genetests.org