



Module Three

How practitioners are testing
mitochondrial function
(Chapters 1-3)



Learning Objectives

- Understand the routine testing methods used in assessing mitochondrial function
- Differentiate biomarker, genetic and function testing
- Review the benefits and limitations of each type of testing
- Understand functional testing methods and the measures that can be reported



Current Consensus and Reality of

Testing for Mitochondria Function



The Mitochondrial Medicine Society has published consensus statements on the diagnosis, management, treatment, and care standards of mitochondrial disease. They recommend biopsying the affected tissue to assess mtDNA variants and OXPHOS function.



Although mitochondrial dysfunction is the known cause of primary mitochondrial disease and is secondary to many multifactorial chronic conditions, it is often difficult to measure and prove, especially when biopsies of affected tissue are not readily available.

Three classes of testing are available:



- Functional markers measured in blood cells and live cells
- Biochemical markers of serum/plasma
- DNA markers



While none of the reviewed single biomarkers may perfectly reveal all underlying mitochondrial dysfunction, combining biomarkers that cover different aspects of mitochondrial impairment is a good strategy.





Chapter 1: Genetic and Epigenetic Testing





Genetic Testing

Genetic tests examine your DNA to pinpoint changes, known as mutations or variants, which can significantly inform and alter your medical care.

This type of testing is foundational in identifying genetic conditions and tailoring healthcare to individual genetic profiles.

Genetic tests identify the *potential* of something that may or may not happen.



Types of Genetic Tests



Single gene testing

This method focuses on one gene to detect specific conditions. If symptoms of a known disorder like Duchenne muscular dystrophy are present, or there's a family history of a genetic mutation, this test is often recommended.



Panel testing

These tests evaluate multiple genes simultaneously, often related to specific medical concerns like epilepsy or developmental delays. Such tests can provide comprehensive insights into complex genetic influences on health.

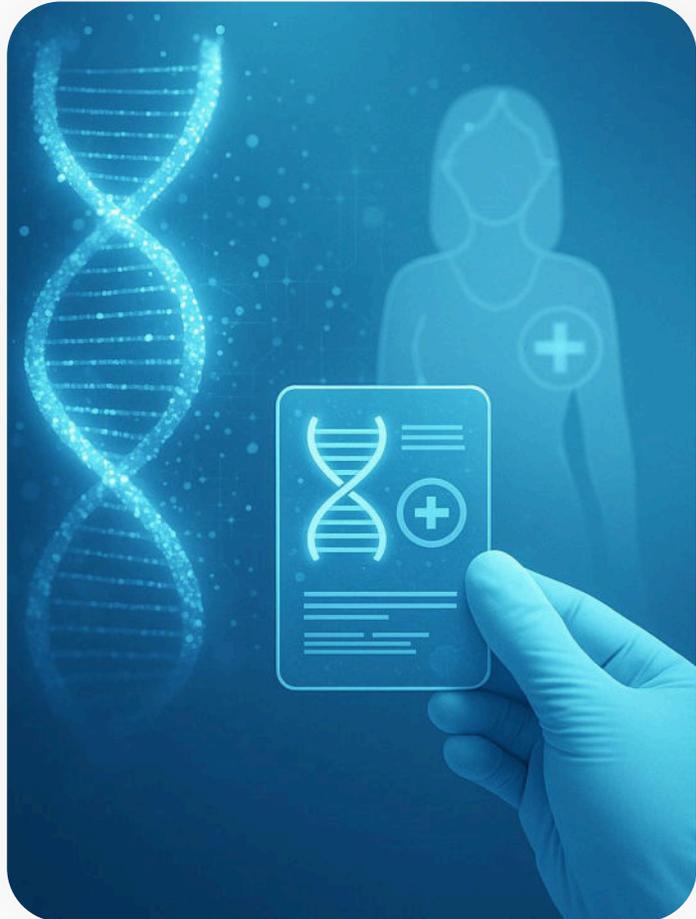


Large-scale genetic testing

Including exome sequencing, which examines all genes, and genome sequencing, which reviews the entire DNA. These tests are utilized for individuals with complex health issues, often uncovering the primary genetic information and secondary findings that might influence health management.



Application of Genetic Testing



Genetic testing serves multiple critical functions in healthcare. It is used to diagnose inherited conditions, assess risk levels for future health issues, and guide treatment plans.



By understanding a patient's genetic makeup, healthcare providers can predict potential health challenges and intervene early.



Genetic tests, which identify specific DNA mutations, are highly accurate in detecting those genetic variants they are designed to find.



The precision of these tests is largely dependent on the technology used, such as next-generation sequencing, which boasts a high degree of specificity and sensitivity.





Epigenetic Tests

Epigenetic tests explore how external factors like diet, lifestyle, and environment can alter the way genes express themselves without changing the underlying DNA sequence.

Unlike genetic mutations detected in standard genetic tests, epigenetic changes are typically reversible and can switch genes “on” or “off,” which can significantly influence health and disease potential.



Types of Epigenetics Tests



DNA methylation tests

These tests identify the addition or removal of chemical groups to DNA, which can inhibit or facilitate gene expression. Methylation patterns are crucial for understanding various conditions and how external factors may suppress or activate certain genes.



Histone modification tests

By examining changes to histones (proteins around which DNA is wrapped), these tests can reveal how tightly DNA is packaged. If DNA is tightly wrapped, gene expression is decreased; if loosely wrapped, expression is increased.



Non-coding RNA tests

These tests focus on RNA molecules that do not code for proteins but play a critical role in regulating gene expression. They help in understanding how genes are controlled at the transcriptional level.



Application of Epigenetic Testing

Epigenetic testing is utilized in various medical and scientific fields to understand better and treat conditions influenced by gene expression levels.



These tests are pivotal for researching developmental diseases, behavioral disorders, and other conditions where gene expression changes are significant.

For instance, alterations in epigenetic markers can indicate the presence of certain behavioral disorders, providing insights that are not apparent through genetic testing alone.

Under what conditions is epigenetic testing helpful?



Epigenetic testing shows promise in behavioral disorders. Certain epigenetic changes in gene expression related to neural activity might influence behaviors and susceptibilities to these disorders



Epigenetic modifications can also indicate responses to environmental stresses or dietary changes, which are essential in managing diabetes or cardiovascular diseases.



Epigenetic testing offers a dynamic perspective on how genes are regulated and interact with our environment, providing a deeper understanding of numerous diseases and conditions beyond what genetic tests can reveal.

This understanding aids clinicians in devising more targeted and effective interventions based on epigenetic profiles.



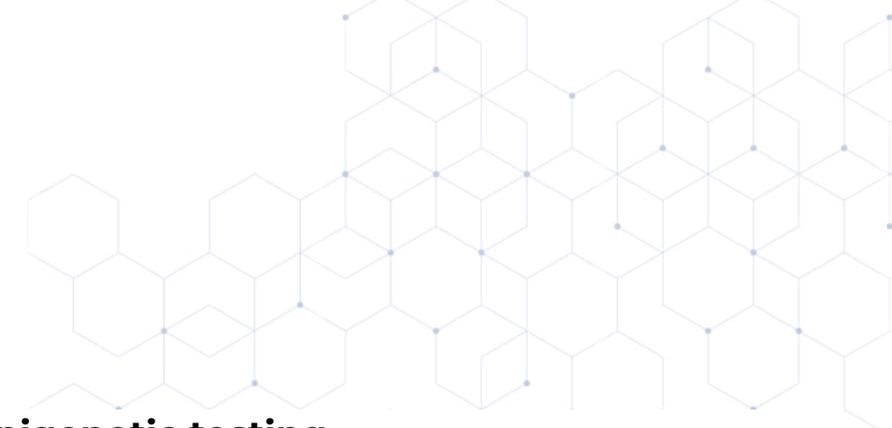
The accuracy of epigenetic tests can be more variable than genetic tests and is influenced by the individual's current state, which can fluctuate based on various external factors.

For example, changes in lifestyle or environment can alter epigenetic markers, which may complicate the interpretation of results.



Comparison of

Genetic & Epigenetic Testing



Aspect	Genetic testing	Epigenetic testing
What it measures	DNA sequence mutations and variations.	Modifications in gene expression (not the DNA sequence itself).
Focus	Identifying inherited risks and genetic mutations.	How environmental and lifestyle factors affect gene expression.
Technological methods	Polymerase Chain Reaction (PCR), microarrays, next-generation sequencing.	Bisulfite sequencing, Chromatin Immunoprecipitation followed by sequencing (ChIP-seq).
Information type	Static; provides a long-term view of genetic risks.	Dynamic; can change with lifestyle, environment, and over time.
Impact on disease understanding	Essential for diagnosing inherited diseases, carrier screening, and risk assessment.	Useful for understanding how non-genetic factors influence diseases, progression, and treatment response.
Clinical applications	Predictive risk assessment, carrier testing, prenatal screening.	Monitoring disease progression, evaluating treatment response, lifestyle impact assessment.

