YES-ILAE Graphical summary

Current practice in diagnostic genetic testing of the epilepsies

An update by the ILAE Genetics Commission on clinical genetic testing practice, including current techniques, indications, yield of genetic testing, recommendations for pre- and post-test counseling, and follow-up after genetic testing is completed.

Designed by Matheus Gallas-Lopes

Current practice in diagnostic genetic testing of the epilepsies

YOUNG EPILEPSY SECTION

Genetic testing aims

- Uncovering specific genetic causes
- Guiding precision treatments
- Understanding the condition's origin, reducing uncertainty and psychological strain;
- Improving long-term care planning by prognostication and explaining potential comorbidities.

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Pre-test considerations

- ☑ Discuss reasons for testing
- ☑ Explain potential outcomes; including social and psychological implications of results (e.g., family dynamics, health insurance);
- ☑ Thorough phenotyping of the patient to guide test selection
- ☑ Informed consent

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Which genetic test is indicated first?

Exome sequencing — Analyzes all coding regions of the genome

Genome Sequencing — Analyzes entire genome (coding & non coding regions)

these are the Next-generation sequencing methods.

Preferred for diagnostic testing as a First-line approach

Gene Panels — Targets a curated set of known genes.
limited than ES or GS,
cost-effective
recommended if ES/GS are unavailable

Chromosomal Microarrays — Detects larger structural changes, such as duplications or deletions

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Diagnostic yield in epilepsy:

Genome Sequencing (GS): **up tp 48%**

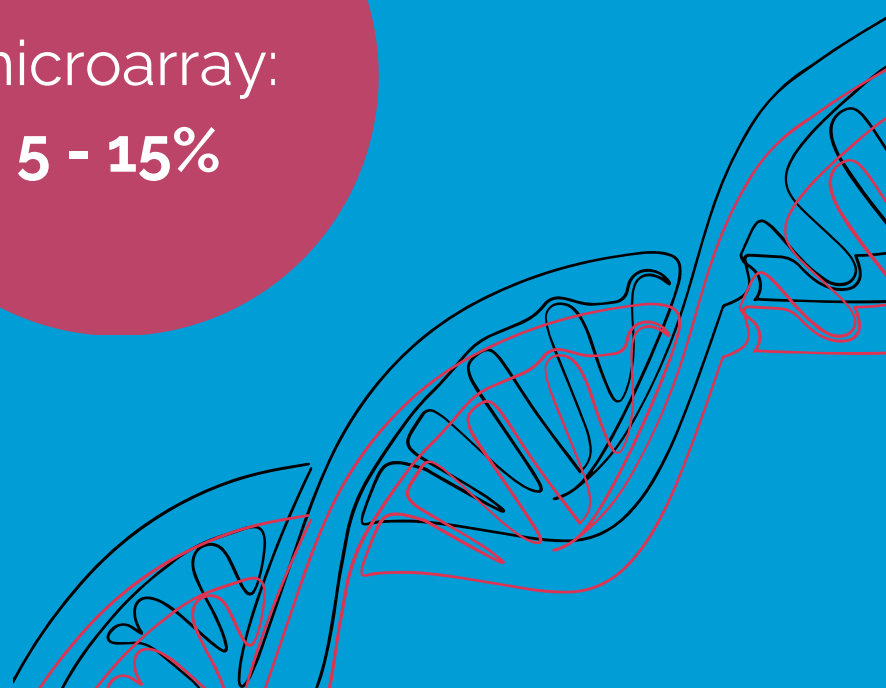
Exome Sequencing (ES): **up tp 45%**

Epilepsy gene panels: **up tp 25%**

Chromosomal microarray: **5 - 15%**

Sanger sequencing: **very low**

Chromosome analysis: **very low**



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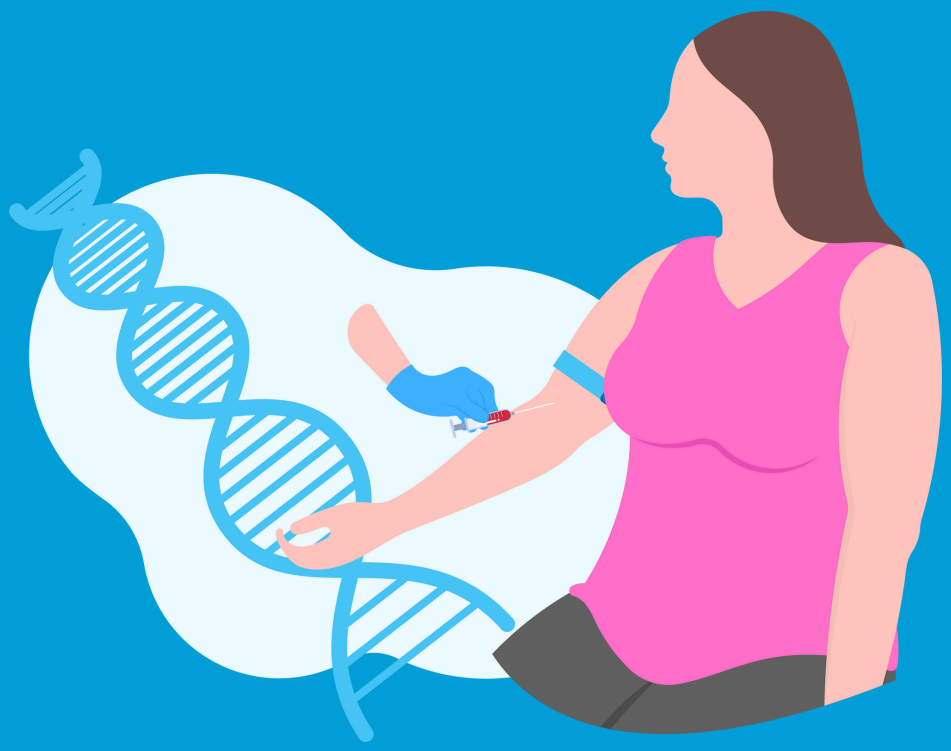
Post-test considerations:

1. If a causative genetic variant is found, offer genetic counseling to explain the diagnosis and discuss therapeutic implications;
2. For uncertain results, further deep phenotyping or family testing may be needed;
3. Even 'negative' results should be revisited periodically as new genes are discovered.



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Limitations of genetic testing:
Results may be inconclusive, especially for variants of uncertain significance (VUS).

Testing access can vary by region, affecting availability.
Interpretation of results is complex, requiring expertise in genetics.

Results may not lead to immediate treatment changes in all cases.

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Summary:

- Genetic testing, as well as genetic counseling before and after testing should be performed by appropriately qualified and trained professionals;
- In most cases, next-generation sequencing is currently recommended as first-line testing;
- Periodical genetic re-evaluation should be undertaken for individuals with suspected genetic epilepsy without a molecular genetic diagnosis.

Workflow of genetic testing:

Patient with indication for genetic testing

Sample collection

Genetic testing, human phenotype ontology, and genetic report

Re-evaluation on re-visit of patient, genetic couselling recurrence risk and prognosis, and precision therapy

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