

# Genetic Testing in Pediatrics

## Introduction

Genetic testing in pediatrics is used to identify genetic causes of diseases in children. Many pediatric disorders arise due to mutations in genes or chromosomal abnormalities. Early diagnosis helps in better treatment, prognosis, and prevention. With advanced technologies like Next Generation Sequencing (NGS), even rare disorders can now be diagnosed accurately.

### 1. Indications for Genetic Testing

These are some clinical situations where genetic testing is recommended:

#### ◆ Developmental Delay / Intellectual Disability

- When a child is not achieving milestones (speech, motor, cognition)
- Often caused by chromosomal abnormalities or gene mutations  
↳ Example: Down syndrome, Fragile X

#### ◆ autism spectrum disorders

- Genetic testing helps identify syndromic autism or underlying mutations  
↳ Example: *MECP2*, *SHANK3* genes

#### ◆ Multiple Congenital Anomalies

- Child has congenital defects in multiple organs (heart, kidney, limbs etc)
- Suggests chromosomal or syndromic disorder

#### ◆ Dysmorphic Features

- Abnormal facial/body features (wide-set eyes, low-set ears etc)
- Often indicates genetic syndrome

#### ◆ Neuromuscular Disorders

- Muscle weakness, delayed walking  
↳ Example: DMD, SMA

#### ◆ Metabolic Disorders

- Errors in metabolism leading to toxic accumulation  
     ↳ Example: Phenylketonuria (PKU)

### ❖ **Recurrent/Unexplained Illness**

- Repeated hospitalizations without diagnosis  
     ↳ Could be genetic/immunological disorder

### ❖ **Family History of Genetic Disease**

- Important for inherited disorders (autosomal dominant/recessive)

### ❖ **Suspected Chromosomal Abnormalities**

- Based on clinical features or prenatal screening

🔑 **Summary:** These indications help decide *when genetic testing is necessary* for diagnosis.


## 2. Commonly used Genetic Tests:

### 🔬 A. Cytogenetic Testing (Chromosome Level)

- **Karyotyping:** Detects large chromosomal abnormalities (extra/missing chromosomes)
- **FISH (Fluorescence in Situ Hybridization):** Targets specific chromosomal regions
- **QF-PCR:** Rapid detection of aneuploidy (13, 18, 21, X, Y) ↳ Eg.: Down syndrome, Turner syndrome
- **Chromosomal Microarray (CMA):** Detects submicroscopic microdeletions/duplications.

### 🔬 B. Molecular Genetic Testing (Gene/Exon Level)

- **Sanger Sequencing:** Gold standard for detecting targeted genetic variations in specific genes like Beta Thalassemia
- **MLPA (Multiplex ligation-dependent probe amplification):** Detects deletions/duplications (copy number changes). Eg. DMD, SMA

 **C. Next Generation Sequencing (NGS):** High-throughput, massively parallel DNA/RNA sequencing technology, determines the sequences of millions of genetic fragments simultaneously.

- **Targeted Panels:** Group of genes for specific diseases (Eg- Skeletal dysplasia Panels, Primary immunodeficiency panel)
- **CES (Clinical Exome Sequencing):** Common disease-related genes (4000-5000 gene)
- **WES (Whole Exome Sequencing):** All coding regions and involves around 20000 gene (~1–2% genome). These regions harbour roughly 85% of known disease-causing mutations.
- **WGS (Whole Genome Sequencing):** It covers 95%-98% of the genome, identifying risks for diseases, carrier status, and personalized medicine insights. It can also identify variants in regulatory regions (promoters, enhancers) and deep intronic variants.

 **Summary:** Different techniques detect different types of genetic changes.

### 3. Genetic Test Panels in Pediatrics

Panels are designed for specific disease groups:

#### Neurodevelopmental Panel

- Autism, intellectual disability, Epileptic encephalopathy

#### Neuromuscular Panel

- DMD, SMA, Congenital Myopathies and Neuropathies.

#### Metabolic Panel

- Inborn errors of metabolism, Metabolic Liver disease panels

#### Haematological Panel

- Thalassemia, sickle cell disease, Genetic anemias

#### Syndromic/Dysmorphology Panel

- Rare genetic syndromes

### **Endocrine & Growth Panel**


- Growth hormone deficiency, CAH, Multiple Endocrine Neoplasia, VHL

### **Cardiac Panel**

- Congenital heart diseases, Cardiomyopathy gene panels

### **Nephrology Panel**

- Genetic kidney disorders like HUS, Congenital Nephrotic syndrome, CAKUT

 **Benefit:** Faster & cost-effective diagnosis with better depth using targeted gene panels.

## **4. Genetic testing facilities at Post Graduate Institute of Child Health, Noida:**

✓ **MLPA** (Multiplex ligation-dependent probe amplification)

✓ **Beta-Thalassemia gene Sequencing**

✓ **Sanger Sequencing:** Diagnostics and Research samples

✓ **Targeted sequencing for Achondroplasia**

✓ **Whole Exome and Genome sequencing analysis and genetic counselling**

✓ **QF-PCR (Fragment analysis) for rapid chromosomal aneuploidy detection.**

### **Carrier Screening**

- We also provide pre conception and pre-marital genetic counselling
- Identifies couples carrying significant genetic variations
- Preventive steps can be undertaken after appropriate post-test genetic counselling.

## **5. Benefits of Genetic Testing**

✓ **Early Diagnosis**

- Helps in early intervention and proper surveillance plan.

### ✓ **Personalized Treatment**

- Tailored precision therapy based on the identified genetic etiology.

### ✓ **Prognosis**

- Predict disease progression

### ✓ **Genetic Counselling**

- Helps families understand risk

### ✓ **Prevention**

- Avoid recurrence in future pregnancies through pre implantation genetic testing/pre-natal testing

✧ **Impact:** Improves clinical management and family planning.

## **6. Sample Requirements (Pediatric Genetics)**

### 💧 **Peripheral Blood (EDTA)**

- Most commonly employed sample for molecular genetic testing

### 🧬 **DNA Samples\***

- Extracted DNA for testing

✧ \*Proper handling is essential for accurate results.

\*Contact Medical Genetics department for more details.

## **7. Important Notes**

- Testing requires **informed consent** and proper pretest and post-test genetic counselling by qualified medical genetics professionals. .