Progressive myoclonic epilepsy

Progressive Myoclonic Epilepsy (PME)

Progressive Myoclonic Epilepsy (PME) refers to a **heterogeneous group of rare epileptic disorders** marked by the combination of:

- **Myoclonus**: Sudden, brief, shock-like muscle jerks.
- **Seizures**: Often generalized tonic-clonic.
- **Progressive neurological deterioration**: Cognitive decline, cerebellar ataxia, and sometimes behavioral changes.

Core Clinical Features

- Multifocal **myoclonus**, often **stimulus-sensitive**.
- **Seizures**: Generalized tonic-clonic (GTC) most common.
- **Progressive neurological dysfunction**, including:
  - Cognitive decline
  - Cerebellar signs (ataxia, dysarthria)
  - Pyramidal and extrapyramidal features in some cases
- Onset usually in **childhood or adolescence**, but adult-onset forms exist.

Etiologies

Common genetic and metabolic causes of PME include:

Disorder	Gene(s)	Notes
Unverricht-Lundborg (EPM1)	CSTB	Most common in some populations; relatively benign.
Lafora disease	EPM2A, NHLRC1	Severe, rapidly progressive; Lafora bodies in neurons.
Neuronal ceroid lipofuscinosis (NCLs)	Multiple	Visual loss, seizures, cognitive regression.
MERRF (Myoclonic Epilepsy with Ragged Red Fibers)	Mitochondrial DNA (MT-TK)	Myopathy, ataxia, hearing loss, lactic acidosis.
Sialidosis	NEU1	Myoclonus, cherry-red macula, coarse facial features.
DRPLA (Dentatorubral-pallidoluysian atrophy)	ATN1	Trinucleotide repeat disorder; ataxia, chorea, dementia.

Diagnosis

- **Clinical suspicion** based on triad: myoclonus + seizures + decline.

- **EEG**: Generalized polyspike-and-wave; background slowing.
- **MRI**: Often shows cerebellar or cortical atrophy.
- **Genetic testing**: Crucial for etiologic diagnosis.
- **Metabolic workup**: Especially in pediatric or atypical cases.

Treatment

Antiepileptic Therapy

- Often **resistant** to standard drugs.
- Useful agents:
  - `Levetiracetam`
  - `Valproate`
  - `Clonazepam`
  - `Zonisamide`
  - `Piracetam`
- **Avoid**: `Phenytoin`, `Carbamazepine` → can worsen myoclonus.

Supportive and Adjunctive Care

- **Neurorehabilitation**
- **Cognitive support and education**
- **Nutritional care**
- **Speech and physical therapy**

Experimental and Palliative Options

- Targeted therapy for specific mutations (still in development).
- **Corpus callosotomy** may help in **refractory disabling myoclonus** (e.g., in adult DRPLA).

Prognosis

- Variable and depends on cause.
  - EPM1: slower decline.
  - Lafora, NCLs: rapidly fatal.
- Most patients eventually suffer **severe disability**.

Summary for Clinicians

- PME should be suspected in young patients with myoclonus, seizures, and cognitive/neurological regression.
- Early **genetic confirmation** is crucial for prognosis and family counseling.
- Multidisciplinary care is essential.