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Adolescence is a period of considerable change in a young person’s physical and emotional needs. It is a time when they are gaining independence and making choices about education, driving and future careers. When a young person presents with new onset neurological symptoms or signs it impinges on this independence. Epilepsy and neurodegenerative disorders may well be a lifelong diagnosis, with many disease processes having evolving signs and symptoms and thus posing a significant diagnostic challenge. Adult neurologists may be presented with a teenager with myoclonus and this article describes a practical approach to its diagnosis.

**Myoclonus**

Myoclonus is characterised by sudden, brief, shock like movements which are caused by involuntary muscle contraction with brief electromyographic bursts (positive myoclonus) or sudden cessation of muscle contraction associated with a silent period in the EMG discharge (negative myoclonus). It may occur as an epileptic or a non-epileptic event. It can be an isolated finding or occur as a symptom of many diseases. Myoclonus needs to be differentiated from tics, tremors, exaggerated startle (hyperekplexia) and chorea.

**Tics**

- Involuntary repetitive movements of skeletal or oropharyngeal muscles
- Brief or prolonged
- Variable pattern and site
- More complex movements
- Can be suppressed

**Tremor**

- Rhythmic oscillation of part of body (usually limb)
- Can be worse with action (cerebellar dysfunction) or be present at rest

**Chorea**

- Sudden, irregularly timed spontaneous movements that tend to affect proximal limbs, trunk and facial muscles.
- Exacerbated by mental concentration or stress

**Epileptic syndromes with myoclonic seizures**

Adolescents presenting with myoclonus may have one of a number of epileptic syndromes or neurological conditions with poor prognosis. They generally fall into two categories:

1. Idiopathic generalised epilepsies (IGE) –
   - Juvenile myoclonic epilepsy (JME)
   - Juvenile absence epilepsy (JAE)

2. Progressive myoclonic epilepsies (PME)

**Idiopathic generalised epilepsies**

Myoclonic (cortical) seizures are just one of many seizure types seen in IGE. In JME myoclonic jerks may occur in variable frequency with minimal absences – unlike JAE where absences are the predominant seizure type. Generalised tonic – clonic seizures can occur in both JME and JAE. The majority of adolescents respond well to treatment though there is a high relapse rate on stopping medications, hence the need for prolonged treatment.

**Table 1: Causes of non epileptic myoclonus**

<table>
<thead>
<tr>
<th>Non epileptic (subcortical myoclonus)</th>
<th>Non epileptic, non myoclonic phenomenon</th>
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</thead>
<tbody>
<tr>
<td>Benign neonatal sleep myoclonus</td>
<td>Tremor</td>
</tr>
<tr>
<td>Opsoclonus myoclonus syndrome</td>
<td>Tic</td>
</tr>
<tr>
<td>Psychogenic (worsens with stress)</td>
<td>Chorea</td>
</tr>
<tr>
<td>Drug induced myoclonus</td>
<td></td>
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</tbody>
</table>
Juvenile myoclonic epilepsy

The age of onset of the myoclonic jerks is usually 14-15 years. Jerks occurring after awakening are a prominent feature and should be directly asked about. There may be a history of clumsiness or frequently dropping things due to jerks affecting the upper limbs. The absences are atypical and often associated with impairment of cognition and eyelid flickering. The EEG shows 3-6 Hz generalised spike wave discharge associated with photosensitivity. A third of patients may also show focal EEG abnormalities. Response to valproate is good. Carbamazepine and lamotrigine may worsen the myoclonic jerks. Clonazepam at night is the most effective treatment for the absences.

Juvenile absence epilepsy (JAE)

JAE usually presents between 9-13 years (age range 5-20 years). The absence seizure is more prominent than the myoclonic jerks. The absences occur from 1-10 per day and are associated with mild impairment of consciousness and automatisms. They last between 4-30 seconds (average 16 seconds). The myoclonic jerks do not have the same circadian rhythm as JME, tending to occur more in the afternoon. The EEG shows 3-4 Hz generalised spike wave discharge and may show focal features. Sodium valproate and lamotrigine are the two main drugs of choice in this condition.

Progressive myoclonic epilepsies

Progressive myoclonic epilepsies are rare genetic disorders, usually autosomal recessive, characterised by myoclonic jerks, tonic clonic seizures and progressive neurological deterioration especially cerebellar signs and dementia. The myoclonus is exacerbated by stimuli (action myoclonus) such as light, sound, touch and emotional strain and is multifocal, involving the face, distal limbs and sometimes the proximal muscles causing recurrent falls. Each of the different neurological disorders may have additional clues to aid in diagnosis. The clinical characteristics and EEG of the five most common PME are highlighted in Table 2.

Rarer causes of PME include dento-rubral – pallidolusian atrophy, non-infantile neuronopathic Gaucher's disease, atypical inclusion body disease, neuroaxonal dystrophy, late infantile or juvenile forms of GM2 – gangliosidosis, Panthaotenate kinase associated neurodegeneration, and the childhood form of Huntington's chorea. SSPE can also rarely have myoclonus as a clinical feature.

The investigation of progressive myoclonic epilepsy can be extensive. A step wise approach to the diagnosis is outlined below:

**Initial investigations**

1. Biochemical – electrolytes, liver function tests, lactate and pyruvate (plasma and CSF)
2. Blood – light microscopy shows vacuolated lymphocytes and electron microscopy shows finger print inclusion bodies (Figure 1) in juvenile NCL
3. Fundoscopy may show a pigmentary retinopathy
4. EEG – normal initially later becoming abnormal, with many conditions associated with photosensitivity
5. ERG/VEP – becomes smaller while the SSEP may increase in amplitude in juvenile NCL
6. Brain imaging – initially the MRI can be normal or nonspecific. Later cerebral or cerebellar

**Table 2 PME – Clinical features and EEG changes in PME**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age of onset</th>
<th>Seizure pattern</th>
<th>Neurological signs</th>
<th>EEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unverricht disease</td>
<td>6-15 years</td>
<td>Myoclonus and GTCS absences can occur</td>
<td>Initially normal examination. Later mild progressive ataxia, inco-ordination, intention tremor, dysarthria and usually mild dementia</td>
<td>Initially normal or mimics IGE later abnormal and highly photosensitive</td>
</tr>
<tr>
<td>Lafora disease</td>
<td>6-19 years, can begin in early adulthood</td>
<td>Myoclonic and occipital seizures, occasionally GTCS, atypical absences, atonic seizures</td>
<td>Cognitive signs may present early progresses to spastic quadripleasia and constant myoclonus</td>
<td>Initially normal later generalised or focal predominately in the posterior regions, with photosensitivity</td>
</tr>
<tr>
<td>Juvenile NCL (NCL Type 3), Batten's disease</td>
<td>4-10 years</td>
<td>Myoclonus is mild. GTCS can occur</td>
<td>Starts with visual failure, gradually develop dementia and extrapyramidal signs, psychoses and hallucinations. Pigmentary retinopathy occurs</td>
<td>Slow background with generalised spike and wave, accentuated during sleep but not with photic stimulation</td>
</tr>
<tr>
<td>Sialidoses Type 1 and Type 2</td>
<td>Adolescence</td>
<td>Facial especially perioral myoclonus, persisting in sleep, GTCS</td>
<td>Type 1 – gradual visual failure, ataxia, cherry red spot on fundoscopy Type 2 – coarse facial features, corneal clouding, hepatomegaly, skeletal dysplasia, learning difficulties</td>
<td>Background shows low voltage fast activity with slowing with dementia</td>
</tr>
<tr>
<td>MERRF</td>
<td>Early childhood to late adulthood</td>
<td>Myoclonus, focal seizures may occur</td>
<td>Ataxia, mild myopathy, cognitive impairment, pigmentary retinopathy</td>
<td>Slow background activity with generalised or focal polyspike waves</td>
</tr>
</tbody>
</table>

Figure 1: Electron microscopy – Buffy coat preparation (lymphocytes) showing various inclusion bodies in NCL. (A) Granular osmiophilic deposits in infantile NCL, (B) Curvilinear inclusions in classical late infantile NCL, (C) Finger print inclusions in Juvenile NCL, (D) Mixed granular, curvilinear and finger print inclusions in juvenile NCL.
atrophy occurs in juvenile NCL and sialidosis. Brain atrophy and basal ganglia calcification has been reported in MERRF.

Second line investigations
1. Skin biopsy (Figure 2) – for Lafora disease the biopsy should be deep enough to include entire sweat gland ducts. The axilla should be avoided as a site for biopsy, because PAS-positive bodies may normally occur there. Electron microscopy of the biopsy reveals lipopigments in the case of NCL.
2. Muscle biopsy (Figure 2) – to look for ragged red fibres in MERRF.
3. Enzyme analysis – neuraminidase deficiency in leucocytes or fibroblasts in sialidosis. Enzyme analysis for PTT1 or TPP-1 in juvenile NCL may need to be done if the vacuolated lymphocytes are negative and awaiting gene testing.
4. Molecular genetic analysis – definitive diagnosis by mutation analysis is available for all the progressive myoclonic epilepsies (Table 3).

Summary
Myoclonic seizures in a teenager should be carefully evaluated in the form of history and clinical examination with observation or video of the seizures. It is important to look for any evidence of cognitive decline. Poor seizure control can be a clue to the progressive myoclonic epilepsies. New neurological signs that may develop are visual failure, pyramidal signs and extrapyramidal features such as chorea. Specific genetic testing is available but may need to be done after preliminary extensive investigations. Making the correct diagnosis and taking time to discuss the implications of this is of the utmost importance for a young person at a sensitive period of transition.

### Table 3 – Definitive diagnosis of PME

<table>
<thead>
<tr>
<th>Inheritance</th>
<th>Chromosome locus</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unverricht disease</td>
<td>AR</td>
<td>Ch 21q23.3</td>
</tr>
<tr>
<td>Lafora disease</td>
<td>AR</td>
<td>Ch 6q24</td>
</tr>
<tr>
<td>Juvenile NCL</td>
<td>AR</td>
<td>Ch 6p</td>
</tr>
<tr>
<td>Sialidosis Type 1</td>
<td>AR</td>
<td>Ch 6p21.3</td>
</tr>
<tr>
<td>Sialidosis Type 2</td>
<td>AR</td>
<td>Ch 20</td>
</tr>
<tr>
<td>MERRF</td>
<td>Maternal</td>
<td>Mitochondrial DNA</td>
</tr>
</tbody>
</table>

### REFERENCES