Classification by Aetiology

I. PHYSIOLOGICAL MYOCLONUS
   Hypnic jerks
   Hiccoughs
   Physiologic startle

II. ESSENTIAL MYOCLONUS (+/– DYSTONIA)
   Myoclonic dystonia (DYT11)
   Myoclonic dystonia (DYT15)
   Familial, no gene identified
   Sporadic

III. EPILEPTIC MYOCLONUS
   IIIA- Fragments of epilepsy
      Isolated epileptic myoclonic jerks
      Epilepsia partialis continua
      BADFME
      Photosensitive myoclonus

   III-B Childhood myoclonic epilepsy
      Infantile spasms
      Lennox–Gastaut syndrome
      Severe myoclonic epilepsy of infancy (Dravet syndrome)
      Myoclonic astatic epilepsy (Doose syndrome)
      Cryptogenic myoclonus epilepsy (Aicardi)

   III-C Idiopathic generalised myoclonic epilepsies
      Myoclonic absence seizures
      Juvenile myoclonic epilepsy

   III-D Progressive myoclonus epilepsy:
      Baltic myoclonus (Unverricht–Lundborg)
      MERRF (myoclonic epilepsy with ragged red fibres)

IV. SYMPTOMATIC MYOCLONUS

   IVA-Storage diseases
      Neuronal ceroid lipofuscinosis*
      Sialidosis *
Lafora body disease *
GM2 gangliosidosis (Tay–Sachs disease)
Gaucher's disease type III
Krabbe's disease

**IVB- Spinocerebellar ataxias**
Rumsay–Hunt syndrome
Friedreich's ataxia
Ataxia–telangiectasia
SCA (2,3,17)

**IVC- Other neurodegenerative diseases**
Wilson's disease
Pantothenate kinase associated neurodegeneration (PKAN)
Progressive supranuclear palsy (PSP)
Dentatorubropallidoluysian atrophy (DRPLA)
Multiple system atrophy (MSA)
Huntington's disease (HD)
Alexander's disease

**IVD-Dementias**
Prion disease
Corticobasal syndrome, including corticobasal degeneration
Dementia with Lewy bodies
Parkinson's disease dementia
Alzheimer's disease
Frontotemporal dementia linked to chromosome 17

**IV-E Infectious or postinfectious**
Arbovirus encephalitis
Herpes simplex encephalitis
Human T-lymphotropic virus I (HTLV-I)
HIV
Malaria
Syphilis
Cryptococcus
Lyme disease
Progressive multifocal leukoencephalopathy (PML)
Whipple's disease
Subacute sclerosing panencephalitis
Postinfectious encephalitis
Encephalitis lethargic
IV-F Autoimmune Limbic encephalitis
  Hashimoto encephalopathy
  Coeliac disease
  Eosinophilic encephalopathy

IV-G Metabolic
  Hyperthyroidism
  Hepatic failure
  Renal failure
  Dialysis syndrome
  Hyponatraemia
  Hypocalcaemia
  Hypomagnesaemia
  Hypoglycemia
  Non-ketotic hyperglycemia
  Biotin deficiency
  Mitochondrial dysfunction
  Hypoxia
  Metabolic alkalosis
  Vitamin E deficiency

IVH-Toxic and drug-induced syndromes

IVI- Posthypoxic action myoclonus (Lance-Adams)

IVJ-Paraneoplastic

IVL-Focal nervous system lesion
  Poststroke
  Postthalamotomy
  Tumour
  Trauma
  Inflammation

V. PSYCHOGENIC MYOCLONUS
Physiological Myoclonus

Physiological myoclonus occurs in healthy people. Jerks on falling asleep (hypnagogic myoclonus), hiccups and physiological startle response are common examples.

Essential Myoclonus (Myoclonus Dystonia)

In essential myoclonus, myoclonus is isolated or the most prominent finding from which the patient experiences some, even if mild disability. It may be sporadic or hereditary.

Hereditary essential myoclonus is synonymous with myoclonus dystonia (DYT11), an autosomal dominant disease with variable penetrance. Approximately 50% of clinically definitive cases are due to mutations of the epsilon-sarcoglycan gene on chromosome 7q21. Myoclonus dystonia is typically inherited from the father due to maternal genomic imprinting. It typically starts in childhood, with myoclonic, 'lightning' jerks in combination with usually mild dystonia, while other neurological deficits are absent. In a proportion of cases, psychiatric features such as anxiety, depression and OCD are part of the clinical picture. Myoclonus and dystonia affect mainly the head, neck and arms, but occasionally falls caused by myoclonic jerks in the legs may be the main feature. Typically, there is quite a dramatic response of myoclonic jerks to alcohol. Stimulus sensitivity is not an important characteristic of this condition. Pathophysiology of myoclonus dystonia is not clear. Cortical somatosensory evoked potentials are normal and back-averaging of EEG activity preceding jerks reveals no cortical correlate.

Epileptic Myoclonus

This term is used to denote conditions where myoclonus occurs in the setting of epilepsy. Epileptic myoclonus may be positive or negative (lapses of postural tone). Epileptic myoclonus is accompanied by generalized epileptiform discharges on EEG, but the myoclonus itself may be focal, segmental or generalized. Generalized myoclonus can occur in the syndromes of primary (idiopathic) generalized epilepsy (e.g. juvenile myoclonic epilepsy) or in the secondary (symptomatic) generalized epilepsies (e.g. PME). Focal myoclonus can occur in symptomatic epilepsy, in the setting of infection, inflammation, vascular disease, trauma or tumours.

Familial cortical tremor, also known as benign autosomal dominant familial myoclonic epilepsy (BADFME), is a rare, although interesting disorder, because it clinically resembles essential tremor. It is a benign condition characterized by fine, shivering-like tremor, which usually starts in the third or fourth decade. Generalized seizures are infrequent and there is no significant clinical progression. The condition has been mapped to chromosome 8q and to chromosome 2p.

Secondary Myoclonus

This type of myoclonus occurs in the context of an underlying neurological or nonneurological disorder and is the most common form of myoclonus. The aetiology includes posthypoxic myoclonus, drug-induced myoclonus, toxic–metabolic causes, myoclonus due to focal nervous system damage, neurodegenerative diseases and hereditary metabolic diseases. Myoclonus due to toxic–metabolic causes is usually accompanied by encephalopathy and additional neurological
findings, such as ataxia or seizures. Borg has given an exhaustive review of symptomatic myoclonus.

It is important to recognize that the following metabolic derangements may cause symptomatic myoclonus: renal failure, hepatic failure, respiratory failure, glycaemic disturbances, electrolytic disturbances, hyperthyroidism, metabolic alkalosis or acidosis, vitamin E deficiency, Hashimoto encephalopathy and hypoxia. Symptomatic myoclonus is usually cortical, focal or multifocal and sensitive to stimuli. However, NM (asterixis) and brainstem reticular myoclonus may also be seen.

Toxic causes of myoclonus include chronic abuse of alcohol and withdrawal, the dialysis syndrome due to aluminium toxicity, chronic toluene abuse, methyl bromide and gasoline sniffing.

Drugs that may cause myoclonus include levodopa, antidiarrhoeal bismuth subsalicylate, benzodiazepines, antidepressants (cyclic antidepressants, selective serotonin uptake inhibitors, monoamine oxidase inhibitors), lithium, antiinfectious agents (quinolone antibiotics, cephalosporines), clozapine, opioids, anticonvulsants (particularly gabapentin, pregabalin, lamotrigine, phenytoin, phenobarbital), anaesthetic propofol, cardiac medications (calcium channel blockers, antiarrhythmics) and contrast media.

Postanoxic myoclonus (Lance–Adams syndrome) is a distinct condition that may follow severe cerebral hypoxia, usually after respiratory rather than cardiac arrest. Myoclonus is mainly cortical and multifocal and there is a combination of positive myoclonus and NM, but reticular reflex myoclonus and exaggerated startle may also occur. Action myoclonus is the main disabling feature of this condition, although a variable degree of cognitive impairment and seizures may be present in a proportion of patients. NM in proximal leg muscles ('bouncy legs') is very resistant to the treatment and may leave the patient wheelchair-bound. Some patients may show late improvement and eventually be able to walk unaided and to discontinue antmyoclonic drugs.

The progressive myoclonic epilepsy syndromes are a group of rare disorders, characterized by myoclonic epilepsy, generalized tonic clonic seizures, progressive ataxia and dementia. Six main categories are recognized: Unverricht–Lundborg disease, myoclonic epilepsy with ragged red fibres (MERRF), Lafora body disease, neuronal ceroid lipofuscinosis, sialidosis and dentato-rubo-paladal-Lysian atrophy (DRPLA). Myoclonus in PME is multifocal, typically involving the distal limbs and face and is provoked by posture or action. It is sensitive to touch, noise and light. Patients are typically severely disabled by their action myoclonus.

Action myoclonus–renal failure syndrome is a distinct type of PME that is associated with renal impairment. Mutation of the LIMP-2 gene has been recently identified as a cause and the condition is inherited in autosomal recessive fashion. It usually starts with the tremor (age 17–26), followed by action myoclonus, infrequent generalized seizures and cerebellar signs. Proteinuria is invariably present in the course of the disease and the condition progresses to renal failure.
Progressive myoclonic ataxias, also known as Rumsey–Hunt syndrome, include conditions with prominent myoclonus and ataxia, but little in the way of epilepsy or progressive dementia. PMA include coeliac disease, some cases of mitochondrial diseases, vitamin E deficiency and some cases of Unverricht–Lundborg disease.

Myoclonus is often linked to neurodegenerative disorders.

Cortical myoclonus is present in about 15% of patients with dementia with Lewy bodies or Parkinson's disease dementia, but is rare in Parkinson's disease without dementia.

Patients with MSA often display irregular, small-amplitude myoclonic movements (polyminimyoclonus) of the hands and/or fingers on keeping outstretched posture (jerky postural tremor). Polyminimyoclonus is stimulus-sensitive and accentuated during voluntary movements. A cortical origin can be demonstrated by back-averaging techniques, and SSEPs are sometimes 'giant'.

Myoclonus occurs in 50% patients with CBD. It appears focally in the affected arm, together with apraxia, rigidity, dystonia and alien limb phenomenon. At the beginning of the illness, it occurs in repetitive rhythmic fashion (jerky tremor) on an attempt to activate the arm or following somatosensory stimulation (reflex myoclonus). As the disease progresses, spontaneous myoclonus adjoins. A cortical origin has been postulated, even though an additional subcortical origin is possible.

In contrast to CBD, myoclonus is rare in progressive supranuclear palsy.

In relation to Huntington's disease, myoclonus may be seen in individuals with a juvenile onset and longer CAG repeats.

In Alzheimer's disease, myoclonus may appear in the middle or late stages of disease, is usually multifocal, occurring both at rest and during action. In patients with early onset AD and in familial cases, it may be present early in the disease.

Myoclonus is typical finding in sporadic, familial and new variant CJD. Jerks, often limited and sporadic at the disease onset, become diffuse, generalized and relatively rhythmic (0.6–1.5 Hz) as the disease progresses.

**Psychogenic Myoclonus**

Psychogenic myoclonus may occur spontaneously or following an external trauma. It may be focal (restricted to a few muscles) or generalized. Jerks are commonly distractible and inconsistent over time, with sudden onset and offset and day-to-day variability. Usually, there is exaggerated stimulus sensitivity. Despite these characteristics, it may be difficult to distinguish psychogenic from organic myoclonus and electrophysiology may be helpful.