Classification by Underlying Physiology

Cortical Myoclonus

Cortical myoclonus is the most common form of myoclonus, seen in both outpatient and inpatient clinical settings.

Cortical myoclonus mainly affects the distal upper limbs and face, which reflects the largest cortical representations of these body areas. It is often focal, but may be multifocal, bilateral or generalized, as a consequence of intracortical and transcallosal spreading of abnormal activity.

It typically occurs on voluntary action and may affect speech and gait.

Cortical myoclonic jerks are stimulus sensitive, typically to touch, but sensitivity to visual stimuli is also described. Most patients with cortical myoclonus have both positive myoclonus and NM, occurring either independently or together as a complex of the two kinds of myoclonus.

If cortical myoclonus is prolonged and lasts for hours, days or weeks, it is called epilepsy partials continua and is considered to be a rare form of focal epileptic status.

Focal cortical myoclonus almost always points to an underlining lesion of the sensori-motor cortex, which produces hyperexcitability (e.g. vascular, inflammatory or neoplastic). Recently, Alvarez and Caviness reported a case series of 7 patients aged over 65 with progressive cortical myoclonus, but no cause was identified after detailed investigations and they termed the condition as 'primary progressive myoclonus of aging'.

Examples of multifocal cortical myoclonus include posthypoxic myoclonus (Lance–Adams syndrome), progressive myoclonic epilepsies (PMEs), progressive myoclonic ataxias (PMAs) and neurodegenerative diseases.

Negative Myoclonus

NM occurs when there is sudden interruption of ongoing muscle contraction. Clinically, it appears as a shock like involuntary jerk that causes postural lapses. When trunk or lower limbs are involved, as for example in Lance–Adams syndrome, NM will cause a person to fall.

NM may be of cortical or subcortical origin. NM of an epileptic nature, or epileptic negative myoclonus (ENM), is defined as an interruption of tonic muscle activity, which is time-locked to an epileptic EEG abnormality, without evidence of an antecedent positive myoclonus.

ENM can be observed in idiopathic, cryptogenic and symptomatic epilepsy, i.e. in PME. ENM is never an isolated sign, but occurs in association with other types of seizures, such as partial motor seizures (often of the rolandic type), absences or atonic seizures.
NM may also be of subcortical origin. For example, asterixis is a type of subcortical NM that occurs in toxic–metabolic encephalopathies. It is usually bilateral and rhythmic (6–11 Hz). Unilateral asterixis may be seen in thalamic lesions.

**Subcortical Myoclonus**

Subcortical myoclonus has its origin between the cortex and the spinal cord. It may be divided into the nonsegmental and the segmental types.

**Nonsegmental Subcortical Myoclonus**

Startle/hyperekplexia and reticular reflex myoclonus are considered to be classical examples of brainstem myoclonus. In addition, myoclonus dystonia and drug-induced myoclonus are also believed to be of subcortical origin, due to the absence of cortical correlates of myoclonic jerks.

Brainstem myoclonus is manifested by generalized jerks and its most striking clinical feature is sensitivity to auditory stimuli.

Two main types are (i) startle response, which may be physiologic or pathologic (hyperekplexia), and (ii) reticular reflex myoclonus.

Physiologic startle is an example of physiological brainstem reflex, which places the body in a defensive posture, following an unexpected stimulus such as sudden noise. Sensitivity to somatosensory stimuli delivered to the mantle area (e.g. touching head, face and or upper chest) and visual stimuli may also be present. In startle response, EMG activity starts in sternocleidomastoid muscles and is followed by face, trunk and limb involvement in an orderly fashion, as myoclonic activity spreads up the brainstem and down the spinal cord. Startle involves proximal and distal muscles, bilaterally and synchronously, and produces brief, shock-like movement comprising grimacing, arm abduction and flexion of the neck, trunk, elbows, hips and knees. Hyperekplexia is pathological exaggeration of the normal startle response, which does not habituate on repeated stimuli. Hyperekplexia may be familial as a result of mutation in the alpha1 subunit of the glycine receptor, idiopathic or symptomatic of brainstem encephalitis, vascular lesions or multiple sclerosis.

Brainstem reticular myoclonus is another rare form of generalized myoclonus. Clinically it may be distinguished from hyperekplexia by the frequent occurrence of spontaneous myoclonus and sensitivity to somatosensory stimuli delivered to distal limbs rather than to the mantle area. It may occur in posthypoxic encephalopathy, brainstem encephalitis and uraemia.

**Segmental Subcortical Myoclonus–Palatal Myoclonus.**

Palatal myoclonus is a type of segmental brainstem myoclonus, although it is considered by some authors as a form of tremor. It consists of rhythmic (1–2 Hz) contractions of the soft palate, presumably due to a dysfunction (essential palatal myoclonus [EPM]) or a lesion (symptomatic palatal myoclonus [SPM]) in the Guillain–Mollaret triangle (GMT).
The GMT comprises connections between dentate nucleus, red nucleus and inferior olivary nucleus.

EPM is a result of rhythmic contractions of the tensor veli palatini muscle, which arises from the lateral wall of the Eustachian tube. Repetitive opening and closing of the tube, as the result of its contraction, produce an audible 'click', typical for EPM. EPM disappears in sleep. In SPM, the main muscle involved is the levator veli palatini. SPM is usually not accompanied by clicking and tends to persist in sleep. SPM is more common than EPM.

Important causes of SPM include vascular lesions, multiple sclerosis and brainstem tumours. Another well-recognized cause of SPT is progressive ataxia palatal tremor syndrome (PAPT).

PAPT may be sporadic or familial. Familial PAPT is associated with marked brainstem and spinal cord atrophy and no evidence of olivary hypertrophy. Some familial cases of PAPT are due to a GFAP mutation and represent adult onset of Alexander disease. A rare cause of SPT is autosomal dominant neuroferritinopathy due to ferritin light chain (NFL) gene mutation. Clinically, palatal myoclonus may sometimes be confused with palatal tics.

**Spinal Myoclonus**

Spinal myoclonus may be segmental or propriospinal, reflecting spinal segmental organization and the presence of propriospinal pathways which connect different spinal segments. It is generally resistant to supraspinal influences such as sleep (therefore it may persist in sleep) or voluntary action (therefore it is present at rest, independently of activation) and may or may not be stimulus sensitive.

Spinal segmental myoclonus is usually symptomatic of an underlying structural lesion such as syringomyelia, myelitis, spinal cord trauma, vascular lesion or malignancy. It is confined to one or few contiguous myotomes and may occur irregularly or quasi-rhythmically, with the frequency as low as 1–2 per minute or as high as 100–200 per minute. EMG myoclonic bursts are prolonged up to 1000 ms.

Propriospinal myoclonus is a form of spinal myoclonus where the spinal generator recruits axial muscles up and down the spinal cord via long propriospinal pathways. Typically, there are axial flexion jerks involving the neck, trunk and hips with a frequency of 1–6 Hz. EMG bursts are long, lasting several hundred milliseconds. Clinically, it can be distinguished from brainstem myoclonus, which is also axial in distribution, by sparing of the face and insensitivity to auditory stimuli. It typically occurs spontaneously, especially in recumbent position or may be provoked by tapping of the abdomen or by eliciting tendon reflexes. As opposed to segmental myoclonus, most patients with propriospinal myoclonus have no clear aetiology. Symptomatic forms are reported in cervical trauma, tumour or viral myelitis. Psychogenic forms of propriospinal myoclonus are now increasingly recognized. One recent study on a large cohort of patients with idiopathic spinal myoclonus, showed that at least 30% of patients had a definite premovement (Bereitschaftspotential) potential, indicating that the aetiology was psychogenic. In another large series, a psychogenic cause was suggested in 34 out of 35 patients with axial jerks, who were initially thought to have propriospinal myoclonus.
Peripheral Myoclonus

Peripheral myoclonus is characterized by rhythmic or semirhythmic jerks secondary to plexus, nerve, root lesion or rarely anterior horn cell disease. Hemifacial spasm is the most common example of peripheral myoclonus, while other causes are relatively rare.