

## Phenotypes

Motor neurone disease can be categorised on the basis of sites of involvement at presentation and the balance between lower motor neurone (LMN) and upper motor neurone (UMN) features.

The demarcation between the different MND clinical groups is frequently blurred. As the disease progresses there may be considerable overlap resulting in more generalised muscle wasting and weakness (MND Australia 2014).

## Turner and others 2013

...with profound clinical, prognostic, neuropathological, and now genetic heterogeneity, the concept of ALS as one disease appears increasingly untenable. This background calls for the development of a more sophisticated taxonomy, and an appreciation of ALS as the breakdown of a wider network rather than a discrete vulnerable population of specialised motor neurons.

## Ravits and others 2013

Amyotrophic lateral sclerosis (ALS) is characterized phenotypically by progressive weakness and neuropathologically by loss of motor neurons. Phenotypically, there is marked heterogeneity. Typical ALS has mixed upper motor neuron (UMN) and lower motor neuron (LMN) involvement. Primary lateral sclerosis has predominant UMN involvement. Progressive muscular atrophy has predominant LMN involvement. Bulbar and limb ALS have predominant regional involvement. Frontotemporal dementia has significant cognitive and behavioral involvement. These phenotypes can be so distinctive that they would seem to have differing biology. However, they cannot be distinguished, at least neuropathologically or genetically.

## Turner and Al-Chalabi 2007

Motor neurone disease comprises a number of clinical phenotypes united by the pathological feature of progressive motor neuronal loss. They can be distinguished on clinical and pathological features.

The most common form of MND is amyotrophic lateral sclerosis, where there is clinical evidence of both upper and lower motor neurone involvement.

Clinically 'pure' lower motor neurone MND is termed progressive muscular atrophy, and pure upper motor neurone MND is termed primary lateral sclerosis. The latter is particularly rare and associated with significantly slower progression.

## More Facts - MND Australia 2014

The disease can be classified into four main types depending on the pattern of motor neurone involvement and the part of the body where the symptoms begin.

### 1. Amyotrophic lateral sclerosis (ALS)

- both upper and lower motor neurones are affected
- limb muscle weakness and wasting

ALS is the most common type, characterised by muscle weakness and stiffness, over-active reflexes and, in some cases, rapidly changing emotions. Initially the limbs cease to work properly. The muscles of speech, swallowing and breathing are usually also later affected. ALS is the term commonly applied to MND in many parts of the world.

## 2. Progressive bulbar palsy (PBP)

- both upper and lower motor neurones are affected
- speech and swallowing muscle weakness and wasting

When ALS begins in the muscles of speech and swallowing it is designated PBP. PBP, mixed bulbar palsy and pseudo-bulbar palsy involve the muscles of speech and swallowing. The nerves that control these functions are located in the bulb (the lower part of the brain), hence the term bulbar palsy (paralysis). The limb muscles may also later be affected.

## 3. Progressive muscular atrophy (PMA)

- lower motor neurones are affected
- slower rates of progression and significantly longer survival compared to ALS and PBP

PMA is characterised initially by lower motor neurone signs resulting in more generalised muscle wasting and weakness, absent reflexes, loss of weight and muscle twitching. PMA can be the hardest form of MND to diagnose accurately. Recent studies indicate that many people diagnosed with PMA subsequently develop upper motor neurone signs. This would lead to a reclassification to ALS. PMA may begin in the arms (flailarm type) or the legs (flail leg type).

## 4. Primary lateral sclerosis (PLS)

- upper motor neurones are affected
- very rare and diagnosis is often provisional