# Part ii – Neurological Disorders

# CHAPTER 14
# MOVEMENT DISORDERS AND MOTOR NEURONE DISEASE

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# *CHAPTER 14*

## MOVEMENT DISORDERS AND MOTOR NEURONE DISEASE

Movement disorders occur mainly because of disease of the basal ganglia and its central connections. Drugs may also cause them. They are characterized as those with too little movement or hypokinetic disorders as occurs in Parkinson's disease or with too much movement or hyperkinetic disorders as occur in tremor, dystonia and chorea. The most common overall movement disorder is tremor and the most common major movement disorder is Parkinson's disease (PD). This chapter outlines the main movement disorders and also motor neurone disease. The student should aim to be familiar with their main clinical features and management.

## PARKINSON'S DISEASE (PD)

Parkinson's disease is a progressive neurodegenerative disorder characterized by four key clinical features: tremor, rigidity, poverty of movement also known as bradykinesia or akinesia, and loss of normal posture with a tendency for falls (Figs. 14.1 & 2). PD occurs all over the world affecting >1% of the population >65 years in high income countries. PD also occurs in Africa but may be less frequent there with lower reported age adjusted prevalence rates of 40-67/100,000. Males and females are both equally affected. PD typically begins in the age group 50-60 years and then occurs with increasing frequency in older age groups. PD may also affect a younger age group <40 yrs (5-10%). Juvenile onset PD (<20 yrs) is usually hereditary and may have more dystonic features than the adult onset disorder.

### Causes

The underlying cause of most cases of PD is not known and the term idiopathic PD is used to describe the disease. Many of the clinical features of PD can result from a variety of other conditions including vascular disease, drugs, neurodegeneration and rarely encephalitis. When this happens the condition is called parkinsonism rather than PD.

### Pathophysiology

The classic features of PD are a result of degeneration of dopamine secreting substantia nigra neurones which project from the brainstem via the striatal neurones to the basal ganglia. This leads to a loss of the characteristic black pigment and the remaining dopamine secreting cells may show Lewy inclusion bodies. Clinical disease starts when the substantia nigra cell loss is >50% and striatal dopamine levels are reduced by >80%. Recent studies have shown however that the pathology in PD is more widespread and occurring much earlier than originally believed.

## Clinical Diagnosis

The initial presentation of PD is often mild with up to two thirds of patients presenting at onset with an asymmetrical rest tremor, affecting one limb or difficulty with fine repetitive motor movements e.g. doing buttons or tying shoelaces. If the dominant hand is involved then writing as it crosses the page becomes noticeably smaller. The **tremor** is characteristically coarse, regular, occurs at rest and disappears initially on intent such as holding a cup. The tremor becomes more noticeable when the person is distracted or whilst walking. It mostly affects the limbs but can affect any part of the body including the head, chin and tongue. The typical resting tremor is a rhythmical movement of the thumb on the hand called pill rolling. This is usually accompanied by increasing **bradykinesia** or slowing down of movements e.g. carrying out the activities of daily living (ADL) or walking. There may be a lack of spontaneous movement and facial animation **(expressionless face)**, (Fig. 14.1 & 2) and the blink rate is decreased.

On neurological examination, there is **rigidity** or stiffness of the limbs which results in increased tone throughout the full range of passive movement. This is called lead pipe rigidity or cog wheel rigidity if a tremor intrudes. **Gait disturbances** are usually mild in the first few years. Then posture becomes stooped and the gait is semi-flexed and shuffling with reduced arm swing and difficulty starting or stopping walking and turning (Fig. 14.1). There is a loss of postural righting reflexes which may lead to falls. The patient's voice may become quiet and muffled or hypophonic. Smell has recently been shown to be decreased or absent, sometimes for years before the onset of the other main symptoms.

**Table 14.1**  Main parkinsonian disorders

| Extrapyramidal disorder | Clinical characteristics | Main Causes |
|---|---|---|
| **Parkinson's disease** | rest tremor<br>rigidity<br>akinesia<br>loss of posture | idiopathic<br>neurodegeneration<br>genetic |
| **Parkinsonism** | akinesia & rigidity | neuroleptics antiemetics<br>vascular<br>head injury |

## Diagnosis

The diagnosis of PD is made clinically and laboratory investigations and standard CT/MRI neuroimaging are usually not helpful. The diagnosis is made if there are at least two of the four major clinical features present (Table 14.1) and is supported if there is a rapid clinical response to treatment with dopaminergic drugs.

bradykinesia

rigidity

tremor at rest

postural
instability
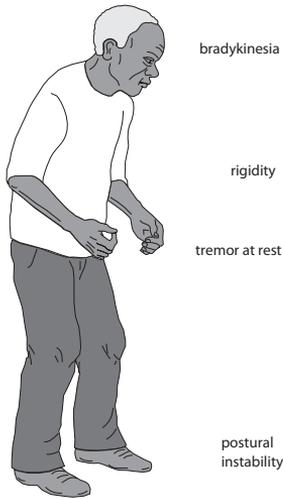
Patient with Parkinson's disease

**Figure 14.1** Parkinson's disease



Akinesia & semi flexed posture

**Figure 14.2** Parkinson's disease

## Key points

- PD is caused by a progressive loss of dopamine secreting cells in substantia nigra
- key features are rest tremor, rigidity, poverty of movement & postural instability
- tremor at rest in one hand /arm is often the earliest clinical sign
- diagnosis is supported by a good response to dopamine treatment

### Treatment

### Levodopa

Early Parkinson's disease does not require any drug treatment. The main aim of treatment of PD (Table 14.2) is to reduce motor disability. Levodopa (L-dopa) does this by replacing the missing dopamine which helps to relieve the symptoms but does not prevent disease progression. L-dopa is given orally and this is later converted into dopamine in the brain by the enzyme dopa decarboxylase which comes from the remaining substantia nigra neurones. In order to prevent conversion of the inactive L-dopa to dopamine in the peripheral circulation L-dopa is given in combination with a dopa decarboxylase inhibitor, either carbidopa or benserazide. Because the dopa decarboxylase inhibitors do not cross the blood brain barrier, this will result in increased dopamine levels in the brain without similar increases in the peripheral blood. This also reduces the nausea that results from peripheral dopamine. The overall aim is to keep the daily maintenance dose of L-dopa as low as possible in order to maintain good motor function and yet reduce any long term motor complications.

Generic preparations of these are available as carbidopa/levodopa and benserazide/levodopa. Treatment is started slowly with gradual increases in dosages. The usual starting dose is in **25/100 mg tabs,** either **½ or 1 tab taken three times daily** taken initially with meals. The main acute side effects are nausea, vomiting, hypotension, confusion and hallucinations. These often resolve spontaneously or with concurrent administration of an antiemetic e.g. domperidone

10-20 mg tds for the first 4 weeks of treatment. If the initial response is inadequate, then the L-dopa dose can be increased slowly every **4-6 weeks** by **½ tab tds** to a usual maintenance dose of **25/250 mg tabs 1 tds**. However, any necessary increases in dosage (½ tab tds) can be brought forward to **weekly** if it is clinically indicated and the patient tolerates it. Later, usually after years L-dopa may have to be given more frequently (changing from 8 to 6 to 4 to 3 hourly as necessary). A controlled release (CR) preparation may be helpful to be taken at night because of a longer duration of effect. Most patients respond very well initially but larger doses are required as the disease progresses.

In the later stages, the duration of response to each dose may shorten (the wearing off effect) and motor fluctuations may occur (the on–off phenomenon) and involuntary motor movements or dyskinesia are likely. The response to treatment may then become unpredictable and any sudden reduction or withdrawal of L-dopa is associated with deterioration.

**Table 14.2**  Levodopa treatment of Parkinson's disease

| Medication | Class | Initial dose | Maintenance dose | When to use | Main side effects |
|---|---|---|---|---|---|
| **carbidopa/levodopa** *or* **benserazide/levodopa** | levodopa | (25/100 mg tab) ½-1 tab tds | (25/250 mg tab) 1 tab tds | early and throughout illness (effect good) | nausea, vomiting, hypotension, confusion, hallucinations, dyskinesia |

## Other drug treatments

The L-dopa/decarboxylase inhibitor combinations are the most effective symptomatic treatment for PD. Other treatments include dopamine agonists, catechol-O-methyltransferase inhibitors (COMT), NMDA antagonists, monoamine oxidase B inhibitors (MOB) and anticholinergics (Table 14.3). In general, these treatments are added on when the response to L-dopa preparations has decreased or failed. The dopamine agonists may be used early on either as first line treatment alone or in combination with L-dopa especially in younger onset PD patients. The use of dopamine agonists is associated with less dyskinesia after 3-5 years of therapy. They act postsynaptically and therefore mimic the effects of dopamine in the basal ganglia. The dopamine agonists fall into two main groups: the ergot derived group which includes bromocriptine and cabergoline and the non ergot derived group which includes ropinirole among others.

The side effect profiles are similar to dopamine except that ergotism may occur in the first group. Ergotism is a serious limitation to their long-term use as up to 3% of treated patients develop pulmonary or less frequently retroperitoneal fibrosis. The newer non-ergot agonists have been associated with hypersomnolence and impulse control disorders, including, overeating, excessive shopping, gambling and hypersexuality. Their use is contraindicated in pre-existing vascular, heart and lung disease. Amantadine is considered a useful drug to start treatment for the first 6-12 months. It has relatively few side effects but only a modest effect on motor symptoms and a limited duration of action. It is effective however, for the dyskinesia seen as a side effect of levodopa. Other useful add on drugs include the COMT inhibitor entacapone and the MOB inhibitor selegiline. These inhibit the breakdown of dopamine and prolong its activity. Their use is mainly indicated in late disease for motor fluctuations and decreasing response to L-dopa. The side effects are largely similar to levodopa. The use of anticholinergics (benzhexol) may be helpful mainly in tremor dominant disease in younger patients. The drug treatment of PD is summarised in the table below.

**Table 14.3** Other drug treatments of Parkinson's disease

| Medication | Class | Initial dose | Maintenance dose | When to use | Main side effects |
|---|---|---|---|---|---|
| amantadine | NMDA antagonist | 100 mg/day | 100 mg/bid/tds | *early* (effect modest), dyskinesia | restlessness, confusion |
| bromocriptine | dopamine agonists (ergot) | 2.5 mg/day | 5-10 mg/tds | *early* delays need for L-dopa | as in levodopa *ergotism |
| cabergoline | (ergot) | 0.5-1 mg/day | 2-6 mg/day | *late* motor symptoms, fluctuations | as in levodopa *ergotism |
| ropinerole | (non ergot) | 0.25 mg/tds | 2-6 mg/tds | *early or late* | as in levodopa somnolence, impulse control disorders |
| entacapone | COMT inhibitor | 200 mg tab with each dose levodopa | max 2000 mg/day | *late* motor symptoms & fluctuations | as in levodopa, dyskinesia, diarrhoea |
| selegiline | MOB inhibitor | 5 mg/bd | 5 mg/bd | *late* motor symptoms & fluctuations | confusion, insomnia |
| benzhexol | anticholinergic | 1-2 mg/bd | 2-5 mg/tds | *early* for tremor (effect modest) | confusion, cognitive impairment, dry mouth, constipation urinary retention |

*\* Ergotism: 3% of patients develop pulmonary or less commonly retroperitoneal fibrosis*

### Non drug treatments

Physiotherapy is helpful to many patients with PD and their quality of life can be helped by the provision of simple aids to the activities of daily living. Surgical treatment is helpful when drug treatment has failed or is intolerable usually in selected younger patients. Surgery usually involves either a thalamotomy or pallidotomy or deep brain stimulation of the globus pallidus or subthalamic nucleus and accounts of these are available in larger textbooks.

### Course

PD progresses slowly over many years. There is no cure and progression is variable with many patients functioning well despite the presence of the disease for years. Drug treatment is necessary for patients with motor disability and can be effective and long-lasting. As the disease progresses immobility, pain, sleep disturbance, depression and dementia (40-50%) are all very common and these may require separate management and treatment. The deterioration is slow and variable with death occurring on average 10-15 years after onset.

## Key points

- early PD does not usually require drug treatment
- Levodopa is the most effective drug treatment for PD
- side effects are  nausea, vomiting , hypotension, confusion, hallucinations & dyskinesia
- drug treatments are started at a lower dosage & slowly increased over weeks
- PD typically progresses slowly over years with death following after 10-15 yrs

# OTHER EXTRAPYRAMIDAL SYNDROMES

## Parkinson plus syndromes

There are other uncommon or rare neurological disorders with features of parkinsonism which are briefly mentioned here. These are all disorders characterized by clinical features of parkinsonism in addition to other neurological findings more typical of the specific underlying neurological disorder. These are **multiple system atrophy (MSA)**, **progressive supranuclear palsy (PSP)**, **corticobasal degeneration (CBD), vascular parkinsonism** and **dementia with Lewy bodies**. MSA is characterized by parkinsonism coupled with cerebellar and/or autonomic dysfunction (hypotension) and partial initial response to L-dopa. PSP is characterized by akinetic rigidity, late onset dementia and a slowing or failure of voluntary vertical and eventually all eye movements. CBD is characterized by asymmetric bradykinesia, rigidity and limb apraxia. Vascular parkinsonism involves mainly the lower half of the body with a prominent gait disorder. Dementia with Lewy bodies is characterized by dementia, rigidity and hallucinations. A characteristic of all these disorders is either a reduced, nonsustained or absent response to levodopa treatment. Management is mostly symptomatic and supportive.

## Key points

- Parkinson plus syndromes are uncommon
- characterized by akinesia & other distinguishing neurological features
- they can be separated clinically from PD
- response to L-dopa treatment is generally poor
- prognosis is determined by the underlying condition

# PARKINSONISM

## Drug induced parkinsonism

The neuroleptic drugs, phenothiazines (e.g. chlorpromazine) and the butyrophenones (e.g. haloperidol) are one of the main causes of drug induced parkinsonism in Africa where they are mostly used in the treatment of schizophrenia and chronic confusional states. This is particularly the case with the use of long acting depot or intramuscular preparations. The long term use of some antiemetics including metoclopramide and prochloperazine may also cause parkinsonism. These drugs cause parkinsonism by blocking the effect of dopamine centrally in the brain. Drug induced parkinsonism is characterized by generalized slowness and rigidity without any tremor.

Management is to lower the dose or stop the offending drug. The parkinsonism usually remits within days or weeks of stopping the drug. However if the preparations have been used long term it may take a year or two to recover or there may be no recovery at all. The anticholinergics benzhexol or benztropine prescribed in adequate doses are the drugs of choice in the treatment of drug induced parkinsonism (Table 14.3).

## Key points

- long-term use of antipsychotic & antiemetics can cause drug induced parkinsonism
- management is to stop the offending drug and use anticholinergic drugs

### Neuroleptic malignant syndrome

This is an important syndrome because of the widespread use of neuroleptics and in particular the use of depot preparations for sedation of confused or aggressive patients. The main causes are phenothiazines and haloperidol. The symptoms usually start within days or weeks or months of starting the offending drug and is commonly misdiagnosed as meningitis because of neck rigidity and fever. It is characterized by generalised rigidity, altered level of consciousness and autonomic instability and high fever. The disorder is life threatening and the patient needs intensive medical care. Management is to stop the neuroleptic and to add a dopaminergic drug e.g. bromocriptine. Anticholinergics and muscle relaxants may also be used.

## Key points

- neuroleptic syndrome is characterized by fever, rigidity & history of recent drug exposure
- Rx: withdraw offending drug, use dopamine agonist & anticholinergic & muscle relaxants

### Akinetic-rigid syndrome

Decreased or absent movement (akinesia) can be the outcome of all causes of parkinsonism. It is characterized by generalised rigidity and immobility with the patient eventually confined to bed. The main causes are summarized in Table 14.4. It is a life threatening condition which frequently requires urgent medical attention. Complications include dehydration, pneumonia and pressure sores. The differential diagnosis in Africa includes other causes of increasing immobility including stroke, subdural haematoma, SOL, dementia and chronic psychosis. Management includes the use of parenteral anticholinergics and muscle relaxants and treating the underlying cause and complications.

**Table 14.4** Causes of akinetic-rigid syndrome

| |
|---|
| **Parkinson's disease**<br>**parkinsonism**<br>**parkinson plus syndromes** |
| **Drugs**<br>neuroleptics<br>antiemetics |
| **Vascular**<br>strokes (multiple lacunar)<br>subdural haematoma (chronic) |

*continues*

| **Trauma** |
| --- |
| traumatic brain injury |
| **Chronic psychosis** |
| schizophrenia |
| **Other causes** |
| dementia |
| post encephalitic/inflammatory |
| toxins, chronic carbon monoxide, manganese |
| Wilson's disease |

## Key points

- akinetic-rigid syndrome is characterized by immobility & rigidity
- management includes anticholinergics & muscle relaxants
- treat the underlying cause & complications

## INVOLUNTARY MOVEMENTS

The main involuntary movement disorders are tremor, dystonia, chorea, athetosis, hemiballismus, myoclonic jerks and tics (Table 14.5 & 6).

### Tremor

Tremor is an involuntary repetitive, rhythmical shaking movement of a part of the body, most commonly seen in the fingers, hands and arms. Tremors are categorized as either fine or coarse and according to the position in which the tremor occurs maximally. In order to demonstrate this, the hands are examined in three main positions: at rest, with the arms and hands outstretched and on action. The common tremors in these positions are outlined in Table 14.5.

### Rest

This is a coarse, regular tremor which mainly affects the limbs, occurs at rest and improves initially on action such as holding a cup or newspaper. It can affect any part of the body including the fingers, toes hands, feet, limbs, chin, tongue, head and trunk. The main causes are Parkinson's disease and parkinsonism.

### Postural

This is a fine regular tremor and is the most common type of tremor. This occurs on posture e.g. when holding the hands outstretched and affects the fingers and hands. It may also affect the lower limbs, head, and trunk. The two most common types are physiological and benign essential tremor.

### Action

This is a regular coarse tremor which occurs on action and mainly affects the limbs but may involve the trunk. It is most evident when testing for finger nose or heel shin co-ordination during neurological examination of the limbs. The main causes are cerebellar disease and benign essential tremor.

**Table 14.5** Common Tremors

| Position | Cause | Clinical features | Treatment |
|----------|-------|-------------------|-----------|
| **Rest** | Parkinson's disease | regular, coarse, slow | anticholinergics<br>levodopa |
| **Postural** | physiological,<br>benign essential tremor,<br>anxiety,<br>hyperthyroidism<br>beta agonists,<br>alcohol, HIV | regular, fine, medium, fast | treat the cause<br>beta-blockers |
| **Action** | cerebellar,<br>essential | regular, coarse, slow | no effective treatment<br>beta-blockers or primidone<br>(essential tremor) |

# BENIGN ESSENTIAL TREMOR

Benign essential tremor (BET) or familial tremor is one of the more common neurological disorders and is a very recognizable tremor. There are few studies on its frequency in Africa but its reported frequency there ranges widely from 5-81/100,000. It is frequently inherited as autosomal dominant, so there is often a positive family history. It occurs in all age groups including teenagers and young adults but with increasing frequency in advancing age, hence is more common in older age groups. The tremor affects the hands and/or the head but usually spares the legs. It is most apparent during posture such as holding a cup or newspaper and may persist throughout the action as evident on finger nose testing. The tremor is usually helped by a small amount of alcohol, made worse by anxiety and worsens slowly but over many years.

Many patients require only reassurance and no further treatment. If treatment is required beta-blockers are the drugs of first choice. Propranolol is prescribed initially in a low dose of 10 mg twice daily increasing slowly over months to a maximum dose of 80 mg twice or three times daily. The dose should be titrated against response or may be taken only on an as required basis at times when the tremor is likely to be very disabling. Adverse effects of beta blockers include fatigue, hypotension and bronchospasm. Primidone may also be used. The initial dose is 25-50 mg daily increasing slowly by 50 mg every 2 weeks to a maximum of 250 mg twice or three times daily. A dose of 100-150 mg three times daily may be effective. Adverse effects are drowsiness, fatigue and occasionally idiosyncratic reaction.

## Key points

- BET is a mainly postural tremor with a strong family history
- occurs in teenagers and young adults but is more common in old age
- worsens slowly over years but usually does not cause disability
- patients may need reassurance because of anxiety & embarrassment
- drug treatment is with propranolol or primidone

## DYSTONIA

Dystonia is a complex disorder of motor control characterized by prolonged muscular contraction that gives rise to abnormal postures and involuntary movements. These are most apparent during voluntary action but may also occur at rest. Dystonia may be focal affecting one part of the body (Fig. 14.3) or generalised affecting more than one part (Fig. 14.4). It may occur at any age and clinical pattern, age of onset, and systemic features may point to the underlying cause. The focal dystonias are fairly common and the main examples in clinical practice are torticollis, blepharospasm and writer's cramp. The generalized dystonias are uncommon and these tend to occur in childhood or in young adults.

The main causes of dystonia are idiopathic, genetic or secondary to a systemic disease such as stroke, drugs or Wilson's disease. In a typical severe generalized dystonia the head may be tilted or retracted, the back rotated or twisted (Fig. 14. 4). and the limbs extended with inverted feet or cramping of the hand. This posture may be maintained or be triggered by movement or a specific action. The main causes of drug induced dystonias are levodopa, chlorpromazine, metoclopramide and haloperidol. A more complex involuntary chewing and grimacing movement, associated with the use of long term neuroleptics is called tardive dyskinesia.

Orofacial dyskinesia & blepharospasm

**Figure 14.3**  Dystonia (Meige syndrome)
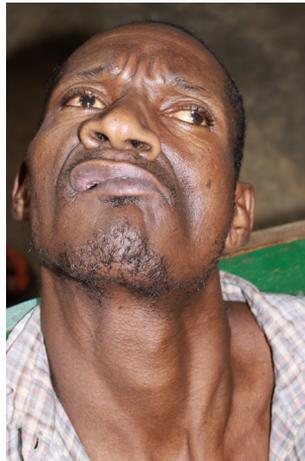
Torticollis & hemifacial dystonia

**Figure 14.4**  Dystonia generalised

Management of drug related dystonia includes the withdrawal of suspected drugs and the use of benzodiazepines. Management of persisting dystonia is generally disappointing but all patients under 40 years should first have a trial of levodopa. Other treatments include high dose anticholinergics (Benzhexol 5-10 mg three to four times daily or tetrabenazine used either alone or  together in combination with a dopamine agonist e.g. bromocriptine). Focal dystonias e.g., torticollis, blepharospasm and laryngospasm respond well but temporarily to local botulinum toxin injections. Deep brain stem stimulation targeting the globus pallidus can be effective in some generalized dystonias.

### Acute dystonic reactions

These occur typically within 24 hours after a single dose of neuroleptics or antiemetics, in particular metoclopramide. These may be focal or generalised and are usually self limiting. They are recognizable by the characteristic writhing movement of the tongue, mouth, face and neck and occasionally limbs and trunk. If the eyes roll up involuntarily, this is called an oculogyric crisis. The treatment of choice is parenteral benztropine 1-2 mgs iv/im and repeated within 30 mins, if the first dose is not effective. Oral anticholinergic therapy should be continued for the next 5-7 days. The patient should be advised to avoid the offending drug in the future.

### Chorea

Chorea is an irregular dance-like, semi-purposeful, non repetitive, movement involving flexion and extension of the limbs and trunk. The movement is unpredictable, jerky, chaotic and fidgeting in nature. The main causes are streptococcal infection in Sydenham's chorea and genetic in the case of Huntington's disease (Chapter 18). It occurs very occasionally in HIV disease secondary to an opportunistic process involving the basal ganglia and as a long-term side effect of dopaminergic drugs. Unilateral chorea can result from a stroke affecting the basal ganglia. Sydenham's chorea is typically self limiting after a few days or weeks or occasionally months and does not require treatment. Huntington's chorea may respond initially to low dose haloperidol, tetrabenazine and also benzodiazepine if there is a disability or anxiety. However over time it usually becomes resistant to symptomatic treatment.

### Athetosis

This is a characteristic slow writhing movement that mainly affects trunk muscles. The main causes are cerebral palsy and basal ganglia disease. It may occur in combination with chorea and dystonia and these can be difficult to distinguish from each other. Treatment is similar to that of chorea.

### Hemiballismus

This is a sudden irregular explosive flinging movement of the limbs on one side. The main cause is vascular or a stroke affecting the contralateral subthalamic nucleus and it may occur after head injury in young persons. Opportunistic processes in HIV disease in particular toxoplasmosis affecting the area of the basal ganglia are also a known cause. Hemiballismus may remit spontaneously or with treatment of the underlying cause. Haloperidol or tetrabenazine may be helpful if it becomes disabling.

### Myoclonus

Myoclonus is a sudden shock movement or jerk that may occur normally in children and in adults on falling asleep. It is only pathological if it persists such as occurs in myoclonic epilepsy, organ failure, dementia and occasionally with the use of the SSRI drugs in the treatment of depression. It arises in the CNS from cortical, sub cortical and spinal cord levels and can be stimulus sensitive or elicited by noise or touch, disappearing in sleep. The management is the treatment of the underlying disease. Myoclonus may respond to benzodiazepines such as clonazepam or to the anticonvulsants sodium valproate or levetiracetam.

## Tics

A tic is a brief stereotyped irresistible repetitive purposeful movement. It differs from chorea in that it can be voluntarily suppressed at will for a short while. Simple tics like blinking, grimacing or shoulder shrugging are common in children and are usually outgrown. A wider range of tics causing vocalizations, noises and sometimes expletives is very suggestive of **Gilles de la Tourette syndrome**. This responds to dopamine antagonists e.g. haloperidol but the drug needs to be continued long term.

## Asterixis

This is a characteristic sudden flapping of the outstretched dorsiflexed hands. It is an important clinical bedside sign suggestive of metabolic encephalopathy. It occurs in association with organ failure characteristically liver, renal and respiratory failure. Treatment is management of the underlying disorder.

## Hiccups

Hiccups are caused by a sudden spontaneous contraction of the diaphragm. They are usually transient and are a normal phenomenon but may be a complication of renal failure. In rare cases hiccups can persist for days or even months. In this case a local source of irritation of the diaphragm, either from above or below, should be excluded. Management of persistent hiccups is not easy. The usual drug of choice is chlorpromazine initially 25 mg twice or three times daily increasing to 50 mg as needed. Baclofen and gabapentin have been used with variable success.

**Table 14.6**  Main characteristics of other involuntary movements

| Type | Clinical features | Causes |
|---|---|---|
| **Dystonia** | | |
| generalized | abnormal posture, involuntary movements | neuroleptics: phenothiazines, haloperidol, levodopa, Wilson's disease, idiopathic |
| focal | localised abnormal posture **(e.g. torticollis, blepharospasm, writer's cramp)** | |
| **Chorea** | irregular, dance-like, non repetitive, semi purposeful | Sydenham's, Huntington's, HIV, stroke |
| **Athetosis** | slow, writhing, purposeless | cerebral palsy |
| **Hemiballismus** | explosive, unilateral | stroke, head injury, HIV |
| **Myoclonus** | sudden jerk | encephalopathy, epilepsy |
| **Tics** | movement, brief, stereotyped, suppressible **(e.g. blinking, sniffing, shrugging)** | psychological |

## Key points

- tremor is a rhythmical alternating movement of part of the body
- dystonia is an abnormal posturing & involuntary movement
- chorea is a brief dance-like semi purposeful non repetitive movement
- myoclonus is a sudden jerk like movement
- a tic is a brief stereotyped irresistible repetitive purposeful movement

# MOTOR NEURONE DISEASE

Motor neurone disease (MND) is a progressive neurodegenerative disease that affects upper and lower motor neurones in the brain and spinal cord. The cause is not known. It is an uncommon worldwide disorder with an incidence rate of 2 per 100,000 reported in high income countries with most cases occurring in >60 year age groups. However MND can affect all age groups and around 5% of reported cases are familial; these occur mostly in a younger age group. The frequency of MND in Africa in not known but may be less frequent there because of the lower overall life expectancy. An association between MND and HIV has been reported in some high income countries.

The pathogenesis of MND is not known but may involve a form of neuroexcitatory cell death mediated by free radicals. MND is exclusively a motor disease without any clinical sensory, bladder or ocular involvement. It is made up of four clinical subtypes; amyotrophic lateral sclerosis, progressive bulbar palsy, progressive muscular atrophy and primary lateral sclerosis.

## CLINICAL SUBTYPES

### Amyotrophic lateral sclerosis (ALS)

ALS is the most common clinical presentation of MND accounting for approximately three quarters of all cases. ALS is an alternative name which is frequently used to describe MND. Patients with ALS present typically with slow but progressive weakness and wasting involving the limbs occurring usually over months. The upper limbs are more commonly involved earlier on than the lower limbs and limb involvement can be asymmetrical early on (Fig. 14.5).

On examination, there is a mixture of upper and lower motor neurone signs in the limbs. Typically there is marked wasting and hyperreflexia in the upper limbs combined with increased tone, hyperreflexia in the legs and extensor plantar reflexes. Fasciculation is frequently widespread involving limbs and trunk muscles and may involve the tongue. There are no sensory signs. Emotional lability is a feature in some patients. All four limbs and the brain stem become involved later on (Fig. 14.6). Clinical presentation in Africa is typically late with most patients at the time of clinical presentation having a mixture of quadriplegia and a bulbar/pseudobulbar palsy. The average survival time from the onset of first symptoms is 2-3 years.



Wasting of the hand muscles & clawing of the hands in advanced MND

**Figure 14.5**  Amyotrophic lateral sclerosis affecting the hands

## Progressive bulbar/pseudobulbarpalsy (PBP/PSP)

PBP/PSP is the main form of clinical presentation of MND in 10-20% of patients. It occurs more commonly in the elderly. Dysarthria and dysphagia progressing over months are the main presenting complaints. Signs of mixed bulbar and pseudobulbar palsy are always present. The main neurological findings are those of a spastic, immobile and fasciculating tongue (Fig 14.6) coupled with either an increased or absent gag reflex. The jaw jerk is usually brisk. Isolated signs of limb involvement including spasticity and hyperreflexia and occasionally fasciculation may already be apparent on neurological examination or more typically develop later on. Survival times are usually shorter than in ALS.

**Spastic & ridged tongue in ALS**



**Spastic immobile tongue & wasted hands in ALS**



**Figure 14.6**  Bulbar/pseudobulbar palsy

## Progressive muscular atrophy (PMA)

PMA accounts for about 5% of cases. PMA presents as progressive lower motor neurone weakness in the limbs (Fig. 14.7). The neurological findings are weakness, wasting, fasciculation and absent reflexes. Bulbar involvement may follow. Survival times are 4-5 years.



**Figure 14.7**  Progressive muscular atrophy. Foot drop (bilateral) in MND

### Primary lateral sclerosis (PLS)

PLS accounts for 1% of cases. PLS presents as a very slowly progressive upper motor neurone type weakness affecting the limbs. There are no lower motor neurone findings and survival times are 15-20 years.

Other rarer clinical presentations of MND include flail arm, man in the barrel syndrome, head drop and dementia. Cognitive & behavioural changes may precede, accompany or follow the development of clinical MND/ALS. Cognitive changes in MND are much commoner than is generally appreciated and although in most patients these are subtle, a minority may develop a frank dementia or aphasia, usually of a frontotemporal dementia type (FTD). In some familial cases the same gene mutation can cause FTD, MND, or both.

### Differential diagnosis

The main differential diagnosis includes cervical spondylosis, syringomyelia, post polio syndrome and lead poisoning. Uncommonly or rarely some genetic or inherited muscle and nerve disorders need to be considered in the differential diagnosis. These include limb girdle muscular dystrophy (LGMD), spinal muscular atrophy (childhood or adolescent onset), affecting mainly the proximal limbs and slowly progressive and may mimic LGMD), and Kennedy's syndrome (twitching movements of chin & tongue fasciculations, tremor hands, proximal weakness, gynecomastia, diabetes and neuropathy, slowly progressive).

### Investigations

Laboratory investigations in MND are usually normal apart from an occasional elevated creatinine phosphokinase and/or infrequently isolated elevation in CSF protein. X-ray of the neck excludes cervical spondylosis and neuroimaging of the brain may occasionally be necessary to exclude other possible causes.

### Diagnosis

The diagnosis in MND is mostly a clinical one and clinical diagnostic criteria for MND have been established by the World Federation of Neurology according to the degree of clinical certainty. The definite diagnosis of MND requires the presence of upper and lower motor signs in at least two spinal regions (cervical, thoracic and lumbosacral) and also involving the bulbar region. The diagnostic criteria are set out in Table 14.7

Table 14.7  El Escorial criteria for diagnosis of MND*

| Diagnostic certainty | Clinical features |
|---|---|
| Definite | upper & lower motor neurone signs in the bulbar and two spinal regions or in three spinal regions |
| Probable | upper & lower motor neurone signs in two or more regions; the regions may differ but some UMN signs must be proximal to LMN signs |
| Possible | upper & lower motor neurone signs in only one region or UMN signs alone in two or more regions or LMN signs proximal to UMN signs |
| Suspected | LMN (not UMN) signs in at least 2 regions |

* criteria of the World Federation of Neurology

### Management

The management of MND involves explaining to the patient and family the nature of the illness. It is important to emphasise the practical approach in caring for the patient. Most drug treatment is symptomatic. The anticholinergic drug benzhexol is used for reducing saliva

secretions and baclofen and diazepam for spasticity and anxiety. Other medications include paracetamol for pain, quinine sulphate for cramps and opiates as required for palliative care. The antiglutamate drug Riluzole 50 mg bd has been shown to increase life expectancy but only by about 3-6 months in some patients.

**Prognosis**

Survival with MND from onset is on average 3-5 years with around 10% surviving 5 years or longer. The cause of death is most frequently respiratory infection.

## Key points

- MND is an uncommon neurodegenerative disease
- characterized by a mixture of upper & lower motor neurone signs
- common presentations are limb weakness & bulbar palsy
- treatment is largely symptomatic & supportive
- survival on average ranges 3-5 years from onset

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