Patient

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Multiple sclerosis

What is multiple sclerosis? [1] [2] [3]

Multiple sclerosis (MS) is an acquired, chronic, immune-mediated, inflammatory condition of the central nervous system that can affect the brain, brainstem, and spinal cord. The inflammatory process causes areas of demyelination, gliosis, and neuronal damage throughout the central nervous system.

The onset of MS is typically in young adulthood. Neurological symptoms and signs vary widely and include visual and sensory disturbances, limb weakness, gait problems, and bladder and bowel symptoms. There are three main patterns of the disease:

- **Relapsing-remitting MS (RRMS)**: the most common pattern of disease (about 85% of people at onset). Exacerbations of symptoms (relapses) are followed by recovery (remissions) and periods of stability.
- **Secondary progressive MS (SPMS)**: occurs when there is a gradual accumulation of disability unrelated to relapses, which become less frequent or stop completely. About two thirds of people with RRMS progress to SPMS.
- **Primary progressive MS (PPMS)**: there is a steady progression and worsening of the disease from the onset, without remissions. Occurs in about 10-15% of people with MS.

A relapse is defined as the onset of new symptoms, or the worsening of pre-existing symptoms, attributable to demyelinating disease lasting for more than 24 hours in the absence of infection or any other cause after a stable period of at least a month.

MS is described as 'advanced' when it has progressed to the point where a person is severely affected by their symptoms and has significant ongoing physical or cognitive impairment (this typically happens in the late stages of primary and secondary progressive MS). People with advanced MS are unable to carry out most of their usual activities of daily living independently and need other people to assist them. The term is used to describe the level of burden rather than the type or duration of the MS.[1]

Clinically isolated syndrome (CIS) corresponds to the typical first MS episode, especially when associated with other asymptomatic demyelinating lesions, without clinical, radiological and immunological sign of any differential diagnosis. After a CIS, the delay before a relapse, which corresponds to the conversion to clinically definite MS, varies from several months to more than 10 years. 10-15% of patients have benign relaxing-remitting MS or 'benign MS'. Benign MS is a variation of relapsing-remitting MS where relapses are very mild, there are very long periods between relapses and/or only a few relapses ever occur.[4]

Radiologically isolated syndrome (RIS)[5] was defined in 2009 for asymptomatic patients who presented incidentally identified white matter anomalies within the central nervous system suggestive of MS. Approximately one third of people with RIS will develop a clinical demyelinating event within five years of the identification of their abnormal MRI scan.[6]

How common is multiple sclerosis? (Epidemiology)[7] [8]

- MS estimated prevalence is 190 cases per 100,000 population.
- MS is more than twice as common in females than males.
  The highest prevalence for MS occurs in the 60 to 69 years age group for both sexes.
- The MS estimated incidence in England is between 8 and 11 new cases per 100,000 population.
- The highest proportion of new female cases occurs in the 30 to 34 years and 40 to 44 years age groups. The highest proportion of new recorded diagnoses in males is in the 45 to 49 years age group.

- It is most prevalent in North America (140 cases per 100,000) and Europe (108 cases per 100,000). The prevalence is lowest in sub-Saharan Africa (2.1 cases per 100,000) and East Asia (2.2 cases per 100,000).

Risk factors [2]

A combination of risk factors may contribute to triggering an autoimmune response and development of MS, including:

- Genetics: over 200 alleles have been identified as contributing small risk effects. The concordance rate in monozygotic twins is about 18-30% compared with about 5% in dizygotic twins. The risk of a first-degree relative of a person with MS developing MS is about 1 in 40 for non-twin siblings, and about 1 in 50 for a child (compared with about 1 in 330 risk for the general population).
- Vitamin D deficiency: vitamin D may have an immuno-modulatory role that helps to prevent MS but the mechanism is not clear.
- Cigarette smoking: risk increases with duration and pack years and is greater in men than in women. Smoking may adversely affect disease course.
- Diet and obesity in early life are associated with two-fold increase in risk. The mechanism is unclear but may be partly due to lower vitamin D levels in obesity.
- Latitude: the prevalence of MS increases the greater the distance north or south of the equator. One theory for this is that lower levels of sunlight exposure result in lower average levels of vitamin D.
- Epstein-Barr virus (EBV): infection with EBV is common in the general population but some studies suggest it is more common in people with MS compared with people without MS, and it may have a disease-triggering role in susceptible people.
- Female gender: MS is 2-3 times more common in women than in men.

Diagnosis[1]

Refer people suspected of having MS for diagnosis by a consultant neurologist or a specialist under their supervision. Contact the consultant neurologist directly if you think a person needs to be seen urgently.

MS should be diagnosed using a combination of history, examination, MRI and laboratory findings, and by following the 2017 revised McDonald criteria. This should include:

- Assessing that symptoms are consistent with an inflammatory demyelinating process; for example, headache is not suggestive of MS.
- Excluding alternative diagnoses (targeted laboratory tests may be indicated if the history, examination or MRI findings are atypical).
- Establishing that lesions on MRI scans have developed at different times and are in different anatomical locations for a diagnosis of relapsing-remitting MS.
- Looking for cerebrospinal fluid-specific oligoclonal bands if there is no clinical or radiological evidence of lesions developing at different times.
- Establishing progressive neurological deterioration over one year or more for a diagnosis of primary progressive MS.

If the McDonald criteria are not met but MS is suspected or the person has confirmed clinically isolated syndrome:

- Plan a review to reassess the possibility of MS. Discuss the timing of this and future reviews with the person (for example, annually).
- Provide information and ensure that the person knows who to contact for advice if they develop further neurological symptoms or if current symptoms worsen.

McDonald criteria[9]

Two or more relapses, and either:

- Objective clinical evidence of two or more lesions; **or**

- Objective clinical evidence of one lesion together with reasonable historical evidence of a previous relapse.

Two or more relapses; objective clinical evidence of one lesion (dissemination in time), plus dissemination in space shown by:

- One or more MRI detected lesions typical of MS; **or**
- A further relapse showing damage to another part of the CNS.

One relapse; objective clinical evidence of two or more lesions (dissemination in space), plus dissemination in time shown by:

- Oligoclonal bands; **or**
- MRI evidence of a new lesion since a previous scan; **or**
- A further relapse.

One attack/relapse; objective clinical evidence of one lesion (clinically isolated syndrome), plus:

- Dissemination in space shown by:
  - One or more MRI detected lesions typical of MS; **or**
  - A further relapse showing activity in another part of the CNS.
- Dissemination in time shown by:
  - Oligoclonal bands; **or**
  - MRI showing new lesions since a previous scan; **or**
  - A further relapse.

Insidious neurological progression suggestive of MS (typical for primary progressive MS), plus any two of:

- One or more MRI detected lesions in the brain typical of MS.
- Two or more MRI detected lesions in the spinal cord.
- Oligoclonal bands in the spinal fluid.

Multiple sclerosis symptoms[1]

People with MS present with neurological symptoms or signs and are often aged under 50, may have a history of previous neurological symptoms, have symptoms that have evolved over more than 24 hours, have symptoms that may persist over several days or weeks and then improve and do not have fever or infection. Possible presentations include a wide range of symptoms affecting different parts of the body. The most common symptoms are:

- Loss or reduction of vision in one eye with painful eye movements.
- Double vision.
- Ascending sensory disturbance and/or weakness.
- Altered sensation or pain travelling down the back and sometimes into the limbs when bending the neck forwards (Lhermitte's sign).
- Progressive difficulties with balance and gait.

Common presenting features include:

- Visual:
    - Very common, usually due to demyelination of the optic nerve.
    - Can cause sight impairment or hemianopia.
    - Optic neuritis is an acute, sometimes painful, reduction or loss of vision in one eye and is a relatively common presenting symptom of MS.
    - If a person has an episode of isolated, optic neuritis, confirmed by an ophthalmologist, they should be referred to a consultant neurologist for further assessment. See also the separate article on Acute Optic Neuritis.

- Eye movements:
    - Very common - may cause double vision.
    - The most frequent sign is symmetrical horizontal jerking nystagmus.
    - Also common is lateral rectus weakness. See the separate Diplopia and III, IV and VI Cranial Nerve Lesions article.
- Facial weakness:
    - Bell's palsy can occur alone or with other indications of brainstem disorder.
    - Other features may include one or more of trigeminal neuralgia, paroxysmal dysarthria and ataxia (with a clumsy arm, disturbed sensation and painful tetanic posturing of the limb, lasting 1-2 minutes).
    - There may be other paroxysmal symptoms, which may include one or more of the following: bursts of pain, bursts of paraesthesia, itching, cough, hiccup, painful spasm and complex gaze palsies.
- Hearing and balance:
    - Deafness can occur and feelings of unsteadiness are common.
    - Acute demyelination in the brainstem causes severe positional vertigo, vomiting, ataxia and headache.
- Cognitive symptoms:
    - Visual and auditory attention may be affected, occasionally in the early stages.
    - Effects on intelligence increase with duration of the disease and onset of the progressive phase, causing loss of memory more than language skills.

- Psychological symptoms:
    - Psychotic symptoms are rare but depression is common.
- Taste and smell:
    - Frequently found if specifically looked for.
- Unpleasant sensations:
    - Tightness, burning, twisting, tearing and pulling sensations may be reported due to damage to the posterior columns in the cervical cord.
    - When the spinothalamic tract is involved this causes loss of thermal and pain sensation.
    - Nonspecific tingling is common.
- Paraesthesiae and numbness:
    - Loss of sensation in the legs ascending to the trunk is caused when spinal nerves of the dorsal or lumbar segments are affected.
    - May be sacral sparing but a characteristic feature in MS is numbness of the perineum and genitalia with altered sphincter function.
- Transverse myelitis:
    - An acute episode of weakness or paralysis of both legs, with sensory loss and loss of control of bowels and bladder; requires urgent hospital admission.

- Autonomic system:
    - Bladder symptoms: loss of inhibition of reflex bladder emptying causes urgency and frequency with incontinence when there is associated immobility. May alternatively be impaired bladder emptying. Faecal incontinence due to impaired rectal sphincter is less common.
    - Sexual problems: impotence is common in men; there may also be problems of spasticity, altered sensation and problems with indwelling catheters.
    - Loss of thermoregulation: excess sweating, pyrexia or hypothermia.
- Other symptoms:
    - These include Horner's syndrome, abnormal cardiac rhythm, abnormal vascular responses (with acute pulmonary oedema), weight loss, and inappropriate antidiuretic hormone (ADH) secretion.

Before referring a person suspected of having MS to a neurologist, confirm that this is a neurological episode by taking a history, undertaking a physical examination and excluding alternative, more common diagnoses. Do not routinely suspect MS if a person's main symptoms are fatigue, depression, dizziness or vague sensory phenomena, unless they have a history or evidence of focal neurological symptoms or signs.

Differential diagnosis

- Hereditary spastic paraplegia: mimics familial MS; other inherited diseases can also appear as MS.
- Cerebral variant of systemic lupus erythematosus (SLE) can present with features of MS without other clinical manifestations of SLE.
- Sarcoidosis.
- In patients of African or Asian origin, alternative diagnoses should be considered - eg, AIDS, tropical spastic paraplegia or neuromyelitis optica.

Investigations

MS should not be diagnosed on the basis of MRI findings alone.[1]

- Before referring to a neurologist, exclude differential diagnoses by checking FBC, inflammatory markers, U&E, LFT, TFT, glucose, HIV serology, calcium and B12 levels.
- Electrophysiology: can detect demyelination in apparently unaffected pathways with characteristic delays. Visual evoked potential studies should be the first choice.
- MRI scan: 95% of patients have periventricular lesions and over 90% show discrete white matter abnormalities. Areas of focal demyelination can also be seen as plaques in the optic nerve, brainstem and spinal cord. By using a contrast agent, active inflammatory plaques can be distinguished from inactive ones. The number and size of lesions do not correlate well with disease activity or progress. It also excludes other lesions producing the symptoms.
- Cerebrospinal fluid: rise in total protein with increase in immunoglobulin concentration with presence of oligoclonal cases.

Multiple sclerosis treatment and management[1] [2]

The care for people with MS should be based on a co-ordinated multidisciplinary approach, including MS nurses, consultant neurologists, physiotherapists and occupational therapists, speech and language therapists, psychologists, dieticians, social care, continence specialists and specialist neuropharmacists or specialist MS pharmacists, consultants in rehabilitation medicine as well as the primary healthcare team.

All people with MS have a comprehensive review of all aspects of their care at least once a year. The comprehensive review should be carried out by healthcare professionals with expertise in MS and its complications. Refer people with MS to palliative care services for symptom control and for end-of-life care when appropriate.

General measures

The management of people with MS should include:

- Good communication with patients and their carers.
- Provision of written information regarding the disease, treatments and available help and support.
- Informing them of their legal obligation to notify the DVLA of their condition.
- Ensuring all available help and support with rehabilitation, employment and mobility.
- Encouraging autonomy/self-management.
- Support to the family and carers, including respite care.
- Close co-operation and communication between all health professionals involved in caring for the person (including their GP, nurse specialists and specialists).
- Address modifiable risk factors for relapse or progression of MS, including encouraging exercise, and smoking cessation.
- Live vaccinations may be contra-indicated in people being treated with disease-modifying therapies. Flu vaccinations should be offered to people with MS in line with national guidance.
- DVLA assessment of fitness to drive:[10]
    - Group 1 Car and motorcycle: must notify DVLA. May continue to drive as long as safe vehicle control is maintained at all times. The licence may specify a restriction to cars with certain controls.
    - Group 2 Bus and lorry: must notify DVLA. May continue to drive as long as safe vehicle control is maintained at all times. A licence will be refused or revoked if the individual's condition is progressive or disabling. If driving is not impaired and the underlying condition is stable, licensing will be considered on an individual basis subject to satisfactory medical reports and annual review.
- Legal rights including social care, employment rights, and benefits.

Pharmacological

Relapse and exacerbation

- Diagnose a relapse of MS if the person develops new symptoms or has worsening of existing symptoms and these last for more than 24 hours in the absence of infection or any other cause after a stable period of at least one month. Do not routinely diagnose a relapse of MS if symptoms are present for more than three months.
- Before diagnosing a relapse of MS, rule out infection, particularly urinary tract and respiratory infections, and discriminate between the relapse and fluctuations in disease or progression.
- Non-specialists should discuss a person's diagnosis of relapse and whether to offer steroids with a healthcare professional with expertise in MS because not all relapses need treating with steroids.
- Offer treatment for relapse of MS with oral methylprednisolone 0.5 g daily for five days (do not prescribe steroids at lower doses). Consider intravenous methylprednisolone 1 g daily for 3-5 days as an alternative if oral steroids have failed or not been tolerated, or if admission to hospital is needed for a severe relapse or monitoring of medical or psychological conditions such as diabetes or depression.
- Do not give people with MS a supply of steroids to self-administer at home for future relapses.
- Ensure that the MS multidisciplinary team is told that the person is having a relapse, because relapse frequency may influence which disease-modifying therapies are chosen and whether they need to be changed.
- Identify whether the person having a relapse of MS or their family members or carers have social care needs and if so refer them to social services for assessment.
- Offer inpatient treatment if their relapse is severe or if it is difficult to meet their medical and social care needs at home.
- Identify whether the person with MS having a relapse or exacerbation needs additional symptom management, rehabilitation or consideration for disease-modifying treatments.

Disease-modifying therapy [11]

NB: any woman receiving disease-modifying therapy (eg, interferon) must stop treatment for at least 12 months before trying to conceive.

- Relapsing-remitting MS:
    - Disease-modifying drugs are the recommended treatment for active relapsing-remitting MS. Interferon beta and glatiramer acetate may be the preferred choice for some patients. Peginterferon beta-1a requires less frequent administration and is an alternative to the non-pegylated interferon beta therapies.
    - Teriflunomide and dimethyl fumarate are treatment options for patients with active disease. They may be preferred due to their oral route of administration. There is insufficient evidence for the use of either drug to treat highly active or rapidly-evolving severe relapsing-remitting MS.
    - More active disease may be treated with natalizumab or alemtuzumab. The MHRA has released restrictions on the use of alemtuzumab due to reports of serious cardiovascular and immune-mediated reactions. Natalizumab may therefore be preferred. Natalizumab is only recommended for rapidly evolving severe relapsing-remitting MS.
    - Fingolimod is the recommended treatment for highly active disease. The NHS England Clinical Commissioning Policy (see References below) advises that fingolimod is a suitable alternative for patients receiving natalizumab who are at high risk of developing progressive multifocal leukoencephalopathy (defined as previously exposed to the John Cunningham (JC) virus or who are receiving immunosuppressants or who have been receiving treatment with natalizumab for more than two years).

- Secondary progressive MS:
    - Interferon beta 1b is licensed for secondary progressive MS. Interferon beta 1b reduces the risk of relapse and of short-term relapse-related disability, but does not prevent the development of permanent physical disability or retard progression once it is established. Therefore its role in secondary progressive disease is limited.
    - Siponimod is recommended by NICE as an option for treating secondary progressive MS with evidence of active disease (relapses or imaging features of inflammatory activity) in adults. [12]
- Primary progressive MS: currently there are no effective disease-modifying treatments licensed for primary progressive MS. Interferon beta has been used, but there is limited evidence to support its use due to the lack of a significant reduction in disability progression.
- Progressive-relapsing MS: there are no specific treatment options for this type of MS. None of the currently licensed disease-modifying drugs are recommended in non-relapsing progressive disease.

Low levels of vitamin D are believed to be a risk factor for developing MS. Patients with diagnosed MS are usually given regular vitamin D after assessment of their serum levels of vitamin D, but there is insufficient evidence to support its use as a treatment for MS. Patients should not be offered vitamin D solely for the purpose of treating MS.

- Interferon beta:[13]

    - This is licensed for use in patients with relacing-remitting MS (characterised by at least two attacks of neurological dysfunction over the previous two or three years, followed by complete or incomplete recovery) who are able to walk 100 m unaided. Not all patients respond and a deterioration in the bouts has been observed in some.
    - Interferon beta-1b is also licensed for use in patients with secondary progressive MS.
    - Interferon beta-1a is recommended by NICE as an option for treating MS, only for relaxing-remitting MS.
    - Interferon beta-1b (Extavia®) is recommended by NICE as an option for treating MS, only for relapsing-remitting MS with two or more relapses within the previous two years, or for secondary progressive MS with continuing relapses.[13]

- Glatiramer:[13]

    - This is licensed for reducing the frequency of relapses in ambulatory patients with relapsing-remitting MS who have had at least two clinical relapses in the previous two years.
    - It is given daily by subcutaneous injection. Injection site reactions are common, as are flu-like symptoms. These decrease over time.
    - Glatiramer acetate is recommended by NICE as an option for treating MS, only for relapsing-remitting MS.[13]

- Dimethyl fumarate:[14]

    - Dimethyl fumarate is recommended by NICE as an option for treating adults with active relapsing-remitting MS (two clinically significant relapses in the previous two years) but only if they do not have highly active or rapidly evolving severe relapsing-remitting MS.

- Diroximel fumarate: [15]
    - Diroximel fumarate is recommended by NICE as an option for treating adults with active relapsing-remitting MS (two clinically significant relapses in the previous two years) but only if they do not have highly active or rapidly evolving severe relapsing-remitting MS.
    - Studies have shown when comparing the two drugs, diroximel fumarate works similarly to dimethyl fumarate and is therefore a comparable alternative option. It has also been shown to have lower gastrointestinal (GI) side-effects than those seen with dimethyl fumarate use.
- Teriflunomide: [16]
    - Teriflunomide is recommended by NICE as an option for treating adults with active relapsing-remitting MS (normally defined as two clinically significant relapses in the previous two years), only if they do not have highly active or rapidly evolving severe relapsing-remitting MS.
- Alemtuzumab: [17]
    - Also recommended by NICE as an option for treating adults with active relapsing-remitting MS.

Second-line therapies

- Natalizumab:
    - This is a recombinant humanised monoclonal antibody, produced in murine myeloma cells. NICE approval was granted in August 2007. It is given monthly by IV infusion. [18]
- Fingolimod:
    - The first oral therapy for MS. Approved by NICE in April 2012. [19]

Ofatumumab for relapsing multiple sclerosis [20]

NICE has recommended ofatumumab as an option for treating relapsing-remitting MS in adults with active disease defined by clinical or imaging features, as long as the company provides ofatumumab according to the commercial arrangement.

NICE has issued a technological appraisal on ozanimod.[21] The committee **does not** recommend ozanimod, within its marketing authorisation, for treatment of relapsing-remitting MS in the patients in the same category as ofatumumab (above). However, they recommend that patients taking ozanimod before publication of the guidance should continue without change to the funding arrangements in place for them before the guidance was published, until they and their NHS clinician consider it appropriate to stop.

Ponesimod for relapsing-remitting MS[22]
NICE has issued guidance recommending ponesimod as an option for treating relapsing-remitting multiple sclerosis with active disease defined by clinical or imaging features in adults, as long as the company provides ponesimod according to the commercial arrangement.

The committee notes that people on ponesimod have fewer relapses than those on teriflunomide, but that its effect on disability progression is unclear and that comparisons with other disease-modifying drugs are uncertain.

Other treatments

- Cannabinoids:
    - There is a great deal of anecdotal evidence for the therapeutic benefits of cannabis for a variety of MS symptoms, including spasticity, tremor, bladder problems and pain.
    - Sativex® oromucosal spray is now licensed in the UK on a named patient basis.
    - NICE recommends that THC:CBD spray (Sativex®) can be offered as a four-week trial to treat moderate to severe spasticity in adults with MS if other pharmacological treatments for spasticity are not effective. After the four-week trial, THC:CBD spray can be continued if the person has had at least a 20% reduction in spasticity-related symptoms on a 0 to 10 patient-reported numeric rating scale.[23]

General problems

Fatigue

- Do not assume that the person's fatigue is always caused by MS. Assess for other causes, which may include sleep problems, symptoms of MS (eg, pain, spasticity and bladder dysfunction), side-effects of medicines, illnesses (eg, infections, anaemia and thyroid dysfunction), or anxiety and depression.
- Provide advice on conserving energy, and review lifestyle factors such as diet and exercise.
- Consider vestibular rehabilitation for fatigue associated with limited standing balance.
- Help the person continue to exercise - eg, by referring to a physiotherapist or to exercise referral schemes:
    - Use stress management and well-being approaches such as mindfulness and cognitive behavioural techniques to help with day-to-day activities.
    - Consider supervised exercise programmes involving moderate progressive resistance training and aerobic exercise.
    - Aerobic, resistance and balance exercises, including yoga and Pilates, may be helpful in treating MS-related fatigue.

- There is no evidence that a specific diet will improve fatigue in people with MS, but that a healthy diet will benefit general health.
- For people with MS with moderately impaired mobility, consider a programme of supervised aerobic and moderate progressive resistance activity and cognitive behavioural techniques.
- Do not use vitamin B12 injections or hyperbaric oxygen to treat fatigue in people with MS.
- If medication to treat fatigue might be an option, refer to a specialist to discuss the treatment options in full, which may include amantadine, modafinil (except in people who are pregnant or planning pregnancy), or an SSRI.

Mobility problems

- Functional electrical stimulation for drop foot - see the NICE interventional procedures guidance on functional electrical stimulation for drop foot of central neurological origin.
- Assessment usually involves rehabilitation specialists and physiotherapists with expertise in MS.
- Consider vestibular rehabilitation for people with mobility problems associated with limited standing balance.
- Consider supervised exercise programmes involving moderate progressive resistance training and aerobic exercise.
- Help the person with MS continue to exercise - eg, by referring them to a physiotherapist or to exercise referral schemes.
- Do not offer fampridine to treat mobility problems. Fampridine is a clinically effective treatment for some people, but NICE recommends that it is not currently cost-effective. People who have already started treatment with fampridine in the NHS, should be able to continue treatment until appropriate to stop.

Pain

- Musculoskeletal pain is common and is usually secondary to problems with immobility, spasticity and posture.
- Assess and investigate the cause of pain.

- Consider the impact of pain on mental well-being, and provide advice and support.
- Treatment options include analgesia, and cognitive behavioural therapy.
- Treat neuropathic pain and refer to pain services as required.

Visual and communication

Visual problems

- Difficulty in reading or seeing television is not uncommon and the usual reason (other than the lack of glasses) is that the control over eye movement is poor.
- Actual loss of visual function due to optic neuritis is rare.
- Visual disturbance associated with MS requires an ophthalmological opinion.
- The patient should be assessed for glasses by an optometrist and, if necessary, at a specialist ophthalmology clinic.
- If nystagmus is causing reduced visual acuity or other visual symptoms, offer a trial of treatment with oral gabapentin (initiated and monitored in a specialist clinic).
- May need low-vision equipment and adaptive technology and require to be registered as sight impaired.
- Oscillopsia (visual disturbance in which objects in the visual field appear to oscillate):
    - Consider gabapentin as a first-line drug, and memantine as the second-line treatment.
    - Refer for specialist advice if there is no improvement in oscillopsia after treatment with gabapentin and memantine or if side-effects prevent continued use.

Speech difficulties

- Dysarthria may cause great difficulty. This should be assessed and advice given by a specialist speech and language therapist.

- May need alternative non-verbal means of assisting with or replacing speech.

Motor problems

- Weakness and cardiorespiratory fitness:

    - Exercises and techniques to maximise strength and endurance appropriate to their circumstances, including aerobic training.
    - Motor weakness may require equipment - eg, orthoses or specialist supportive equipment for postural difficulties.

- Spasticity and spasms:
    - Suspect spasticity when a person with MS presents with any of the following:
        - Involuntary muscle movements (spasms).
        - Muscle stiffness.
        - Pain and restriction with certain movements or positions causing difficulty in performing various activities.
        - A change in their mobility or upper limb function.
    - Assess for factors that might worsen spasticity - eg, pressure ulcers, bladder and bowel dysfunction and infections, poor posture or positioning, and pain.
    - Advise on physical techniques - eg, passive stretching, to reduce spasticity and avoid the development of contractures.
    - Consider oral baclofen as a first-line drug treatment. If oral baclofen is not tolerated or does not provide adequate relief, consider gabapentin as a second-line option.
    - When using oral baclofen or gabapentin to treat spasticity, increase the dose gradually in at least two-week increments to optimise symptom improvement or until reaching the maximum tolerated dose.
    - Consider a combination of oral baclofen and gabapentin if individual medicines do not provide adequate relief, or if side-effects from individual medicines prevent the dose being increased.
    - If spasticity is causing significant impairments in mobility, posture or function and initial treatments are unsuccessful, refer to a multidisciplinary team experienced in the management of spasticity for assessment and treatment planning.
    - THC:CBD spray (Sativex®) can be offered as a four-week trial to treat moderate to severe spasticity in adults with MS if other pharmacological treatments for spasticity are not effective.[23]

    - Contractures at joints: specific treatments include prolonged stretching - eg, with serial plaster casts.
- Ataxia and tremor:
    - Should be assessed by a specialist rehabilitation team.
    - If problems remain severe and intractable, the person should also be assessed by a neurosurgical team for suitability for operative intervention.
    - Deep brain stimulation may be considered for tremor and dystonia.[24]
- Pressure ulcers:
    - Many people with MS are at high risk of developing pressure ulcers because of, for example, limited mobility, impairment of sensory functioning and reduced cognitive function.
    - Most pressure ulcers can be avoided.

Urological

- Bladder symptoms: check for underlying urinary tract infection and assess postmicturition residual bladder volume by ultrasound.

- Urgency or urge incontinence:

    - Offer convene drain (for men) or pads (for women); consider toilet arrangements (eg, a commode downstairs) and intermittent self-catheterisation if there is a high residual volume.
    - Consider anticholinergics (eg, oxybutynin, tolterodine).
    - Desmopressin may be used for night problems or to control urinary frequency during the day but should never be used more than once in 24 hours.
    - Continued incontinence, despite treatment, can be treated by a course of pelvic floor exercises preceded by a course of electrical stimulation of the pelvic floor muscles.
    - Continued bladder symptoms may require intermittent self-catheterisation or longer-term urethral catheterisation. Suprapubic catheterisation is useful if active sexual function is wanted.

Gastroenterological

- Urgency, pain, constipation or incontinence may occur.
- Faecal incontinence may be due to constipation with overflow, possibly exacerbated by laxative use.
- Constipation may require the routine use of suppositories or enemas.

- Swallowing difficulties:
    - Dysphagia may lead to choking and aspiration of food or liquid, leading to chest infections.
    - Assessment is advised if there are any symptoms or chest infections.
    - Should be assessed by a specialist speech and language therapist and given advice on specific swallowing techniques and on adapting food consistencies and dietary intake.
    - May need further assessment (eg, by videofluoroscopy), possibly short-term nutritional support via nasogastric tube or percutaneous endoscopic gastrostomy (PEG) tubes.

Higher functions

- Cognitive losses:
    - Symptoms of MS can include cognitive problems, including memory problems, that the person may not immediately recognise or associate with MS.
    - Anxiety, depression, difficulty sleeping, fatigue and medication can affect cognition.
    - For persisting cognitive impairments, consider referring to an occupational therapist and/or a neuropsychologist to assess and manage these symptoms according to the person's needs.
- Emotionalism:
    - May cry or laugh with minimal provocation and with little control.
    - A full assessment of their emotional state may be required and antidepressant medication and/or advice on behavioural management strategies may be beneficial.
    - Consider amitriptyline to treat emotional lability (involuntary laughing and crying related to a frontal lobe lesion).

- Depression:
    - Assessment should include all contributory factors (eg, chronic pain or social isolation) and consideration of interventions to ameliorate these.
    - Antidepressant medication or CBT should be considered as part of an overall programme.
- Anxiety: may require psychologically based treatment or medication such as antidepressants or very short-term benzodiazepines.

Sexual dysfunction

- May disturb the normal sexual physiology and it may result in other impairments (such as spasms) that make normal sexual behaviour difficult.
- If sexual dysfunction is persistent, specific treatments (eg, sildenafil) should be offered and discussed.
- Male sexual dysfunction: erectile dysfunction needs full assessment of possible causes such as anxiety and, possibly, medication.
- Female sexual dysfunction: full assessment of general and specific underlying factors that might cause or worsen sexual dysfunction and that are amenable to treatment.

Other considerations

- Infections may be associated with a worsening of disability and may trigger a relapse. People with MS should be offered immunisation against influenza. People with relapsing-remitting MS should be warned that vaccination may trigger a relapse.
- Complementary therapies: there is some evidence to suggest possible benefit from some complementary therapies - eg, reflexology and massage.
- People with MS should be advised that linoleic acid 17-23 g/day may reduce progression of disability.
- Fish oils may also be beneficial.

Multiple sclerosis prognosis[2]

There is currently no cure for MS. Prognosis varies widely, but neurological disability gradually increases over time for most people with MS. Prompt diagnosis is important as early intervention with disease-modifying drugs may reduce risk of relapse and may delay disability progression.

- Relapsing-remitting MS RRMS: (85-90% of people with MS):
    - Severity and frequency of relapses and the time it takes to progress to the secondary progressive phase of the disease and to significant permanent disability are very variable.
    - Treatment of a relapse with steroids may shorten the length and severity of the relapse, but does not alter the overall course or prognosis of the disease.
    - In pregnancy, relapse frequency typically reduces but some MS symptoms (eg, fatigue, balance, and bladder symptoms) may worsen, particularly in later pregnancy. Around a quarter of women will experience a relapse during the first three months postpartum.
    - 10-20 years after onset of relapsing-remitting MS, over half of people develop progressive disease (secondary progressive MS).
- Primary-progressive MS PPMS (10-15% of people with MS): progression to disability is generally more rapid with PPMS than with RRMS.

Clinical factors that have been associated with poorer prognosis include:

- Male sex.
- Older age at onset.
- Multifocal presentation.
- Involvement of pyramidal and cerebellar systems.
- Partial recovery from relapses.
- High relapse rate during the first two years following onset.

- Higher lesion burden on MRI.

Further reading

- Multiple Sclerosis Society
- Multiple sclerosis; NICE Quality Standard (January 2016)
- Filippini G, Del Giovane C, Clerico M, et al; Treatment with disease-modifying drugs for people with a first clinical attack suggestive of multiple sclerosis. Cochrane Database Syst Rev. 2017 Apr 25;4:CD012200. doi: 10.1002/14651858.CD012200.pub2.
- Reich DS, Lucchinetti CF, Calabresi PA; Multiple Sclerosis. N Engl J Med. 2018 Jan 11;378(2):169-180. doi: 10.1056/NEJMra1401483.

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