

Secondary progressive multiple sclerosis



‘How do you know if you have developed secondary progressive MS?’
‘How should secondary progressive MS be managed?’

Here, the MS Society’s Medical Adviser, Professor Alan Thompson of The National Hospital for Neurology and Neurosurgery in London, addresses some of the frequently asked questions about secondary progressive multiple sclerosis.

The term secondary progressive multiple sclerosis has been in use for almost 20 years. It is a phase of MS which is secondary to – or comes after – relapsing remitting MS. In other words, secondary progressive MS only occurs in people who have already had relapsing remitting MS.

Most neurologists do not use the term secondary progressive MS unless they are sure there is clear evidence of sustained deterioration, completely independent of relapses, which continues for a minimum of six months – or longer.

In MS, a build up of disability can result from two mechanisms:

- › One mechanism is the failure to recover (or incomplete recovery) from relapses.
- › The other is slow progression.

In relapsing remitting MS, disability results from the former, while in secondary progressive MS, it can result from both.

To diagnose secondary progressive MS, the neurologist must be sure that disability is occurring as a result of slow progression and this can be difficult to establish, especially when some people with secondary progressive MS continue to have relapses while others do not.

Because secondary progressive MS follows relapsing remitting MS, it can be distinguished from primary progressive MS. Primary progressive MS is progressive from the beginning and does not have an initial relapsing remitting phase.

There needs to be clear evidence of sustained deterioration, completely independent of relapses, which continues for a minimum of six months – or longer

How do you know when you have become secondary progressive?

This is not an easy question and the answer is based entirely on the judgement of the neurologist. Essentially, when someone with relapsing remitting MS becomes aware of a definite deterioration in their level of function that continues for at least six months to one year, which

is not in any way related to a relapse, then it is likely that they now have secondary progressive MS. This usually happens in people who already have some problems or disability as a result of previous MS relapses that have not recovered completely.

Remember, some people with secondary progressive MS will continue to experience relapses while others do not. For people who are no longer having relapses, the diagnosis of secondary progressive MS can be more straightforward. For those who are continuing to have attacks, however, diagnosis can be quite difficult. For instance, although many people recover from relapses within three months, in some cases it can take up to six months, or even longer, before full recovery takes place.

A second problem of diagnosis is trying to establish that this deterioration relates to a worsening in the underlying neurological condition and not some other cause. For example, people with MS may notice a reduction in their level of function because they are depressed, becoming unfit, or they have stopped their exercise regime, or they have more stiffness. Other problems completely separate from MS, such as menopausal symptoms, a fracture or joint pain, may also make evaluation difficult.

A neurologist will need to have a clear history of worsening and will also need to find there has been some change in movement or sensation when they carry out the neurological examination. There may be a change in co-ordination of legs or hands, balance, speech, reflexes, or perhaps new signs of weakness.

Does everyone with relapsing remitting MS develop secondary progressive MS?

Most people with relapsing remitting MS will eventually develop secondary progressive MS, though the time it takes for this to occur from the beginning of the condition varies from person to person – in keeping with the unpredictable and variable nature of MS. On average, by 15 years, approximately 65 per cent of people with relapsing remitting MS will have developed secondary progressive MS. The longer you have the condition, the higher the percentage becomes.

Some people with relapsing remitting MS never seem to develop secondary progression, even after many decades. These people are sometimes described as having ‘benign’

MS. This does not mean their MS is free of problems – it means simply that they have not developed major disability, despite having MS for a long time. If we could establish why some people do not seem to enter the secondary progressive phase – this could, for example, be influenced by genetic make up – then it would be a major breakthrough in our understanding of MS and may provide a potential target for treatment.

Once the damage to axons reaches a certain level – a kind of threshold – it does have an effect on function

What are the implications of secondary progressive MS?

There are two aspects to this question:

- 1 What are the changes in the nervous tissues (pathology) in secondary progressive MS, and are the changes any different from relapsing remitting MS?
- 2 What are the clinical changes (features) in someone who has secondary progressive MS?

Changes in the nervous tissues:

It is now well established that there are three key processes going on in the nervous tissues of someone with MS. These are: inflammation (invasion by lots of ‘activated’ white blood cells); damage to the myelin sheath (that protects the nerve fibre); and in some situations there is damage or even death of the nerve fibre itself (called the axon).

When people with MS have a relapse, the main process going on is inflammation and it is often possible to see the inflammation on a person’s MRI scan. However, it is likely that during most relapses some damage also occurs to myelin and to the axons. If the axon dies then repair cannot occur.

Fortunately, each of us can afford to lose quite a lot of axons (perhaps up to 40 per cent) without getting into trouble. However once the damage to axons reaches a certain level – a kind of threshold – it does have an effect on function. From then on, each time more axons are lost, a worsening in the level of function occurs.

This theory of a ‘threshold effect’ has been suggested only recently but it does provide a possible explanation for what happens in secondary progressive MS. People have a number

of relapses (and the number can vary hugely), during which they lose a number of axons. While that is not a problem in the initial attacks, at a certain stage (again, hugely variable), they reach a level where any further loss of axons will cause a worsening in their level of function. From that time, there is a gradual loss of axons, and that in turn results in a gradual deterioration in their level of function – a ‘progression’.

If this theory is true, then it has implications for our approach to treatment of this stage of the condition.

Clinical changes:

Usually, deterioration associated with secondary progressive MS tends to relate to mobility and people often notice an increasing reliance on mobility aids.

There may also be progressive worsening in other symptoms, like co-ordination, tremor, bladder and bowel dysfunction, visual and cognitive function.

It is important to appreciate, however, that the rate of deterioration can be quite variable, and at times things can almost seem to stand still.

How do you manage secondary progressive MS?

Acute attacks:

If and when people have clear-cut acute relapses, then these can be treated with steroids – either by oral or intravenous route. If the individual has not benefited from steroids previously, it does not necessarily mean that they will not benefit from further treatment, particularly if the attack is affecting a different part of the nervous system. Steroid treatment may need to be followed by further therapy or multi-disciplinary rehabilitation.

Influencing the underlying neurological deterioration:

The obvious thing would be to try to prevent or at least delay the onset of secondary progressive MS.

In relapsing remitting MS, the disease modifying drugs – the beta interferons and glatiramer acetate – reduce both the frequency and severity of relapses for some people. It might seem logical to conclude this would delay the onset of the more disabling secondary progressive phase. However, the pathology of MS is highly complex and one ought to be cautious before drawing conclusions about long-term benefits in this way. We need further studies of longer duration to address this important issue.

Studies have shown that rehabilitation can be of considerable benefit to people with secondary progressive MS

Another possibility is to try to identify drug treatment that will have a beneficial effect during secondary progressive MS. However, this is not an easy task, either.

For instance, during secondary progressive MS, it may be helpful if treatment suppressed inflammation.

(Suppressing inflammation may be the main effect of disease modifying drugs such as the beta interferons and glatiramer acetate, for example.) In secondary progressive MS, studies of beta interferon 1b gave conflicting results. There were positive results in the trial that included people who were having frequent relapses (indicating inflammation). In contrast, trials where the majority of people with secondary progressive MS were no longer having attacks showed no beneficial effect on the rate of progression.

At present, beta interferon 1b – Betaferon – is the only disease modifying drug licensed in the UK to treat people with secondary progressive MS. The guidelines produced by the Association of British Neurologists say that Betaferon should be prescribed for people with secondary progressive MS if they are still having attacks and if it is clear that their deterioration results from these attacks.

Other drugs that may be beneficial, such as mitoxantrone (Mx) and intravenous immunoglobulin (IVIg) have not yet been licensed for treating MS and more information is required about them, including further trials.

It may prove to be more important to focus on drugs that protect axons and to work on the approaches that encourage axon repair or regeneration. Research continues to identify protective agents that can be tested in randomised controlled trials, and develop the strategies which may enhance repair – such as the use of stem cells.

Treatment of MS symptoms – rehabilitation:

There needs to be an active programme to tackle and improve the range of symptoms that people frequently experience. Often these symptoms – such as spasticity, ataxia (poor co-ordination) and fatigue – interact in a way that increases their impact on disability. For this reason, it is very important to have access to a multi-disciplinary rehabilitation team.

Studies have shown that rehabilitation and its components such as physiotherapy can be of considerable benefit to people with secondary progressive MS. However, it is often very difficult to access such expertise.

The Royal College of Physicians and the Chartered Society of Physiotherapy, under the auspices of NICE, are currently producing new guidelines for MS management. It is hoped that these guidelines, together with the National Services Framework for neurological and other long-term conditions, will result in a marked improvement in access to rehabilitation throughout the UK. The MS Society is contributing to this work.



Multiple Sclerosis Society