Subtypes of MS

Because the course of MS varies with each person, many different terms have been used to describe patterns of the disease. Confusion over these descriptions made it clear that a common language was needed to describe the clinical course of the disease. This was important not only to physicians trying to describe what was happening to their patients, but also to researchers. In clinical trials, the more homogeneous the study population the fewer patients are needed to demonstrate the benefits of a medication. Carefully defining clinical subtypes improves our ability to identify homogeneous groups of patients, which decreases the number of patients needed for a research study and speeds the development of medications for the disease.

Recognizing the need for improved definitions, the National MS Society conducted a survey of physicians who specialized in treating MS (Lublin FD. Neurology 1996;46:907-11). There was a consensus of opinion regarding the definitions of four subtypes of MS: relapsing/remitting, primary progressive, secondary progressive and progressive relapsing. Relapsing/remitting is now called relapsing MS. As a result, these are the only four subtypes of MS that are currently recognized.

There was not a consensus regarding other definitions including chronic progressive, benign and malignant MS. Because the definition of these terms is unclear, their use is discouraged.

It should be emphasized that these terms are used primarily for descriptive purposes. Though patients are often concerned about which type of MS they might have, the use of subtypes in predicting prognosis is limited. The time from diagnosis until impairment of gait is longest for relapsing/remitting MS. This is probably a reflection of relapsing MS being diagnosed earlier because patients present with an acute attack that brings them to medical attention earlier than other forms of MS. In contrast, most patients with primary progressive MS present with slowly worsening spasticity that may take several years to recognize and diagnose. Once patients develop disability however, then the prognosis is the same for the different subtypes of MS. For example, the time that it takes to move from difficulty walking to needing a cane, or needing a wheelchair, is the same for all subtypes. (Confavreux C. N Engl J Med 2000;343:1430-8)

The use of MS subtypes to select a homogeneous population for research studies has led to most medications being tested using relapsing disease. This is because relapsing MS is the most common subtype, and the easiest to study. Research using relapsing MS requires fewer patients, simpler outcome measures, less time, and therefore less money to achieve an answer. Measuring clinical outcomes in studies of primary and secondary progressive forms have been more difficult. Negative results from studies of progressive forms of MS must be interpreted carefully because they may reflect inadequacies in our ability to measure outcomes, technical difficulties in conducting the study, patients entering the study later in the course of the disease, or differences in the biology of MS subtypes. Because of these limitations, the use of MS subtype to select treatments for individual patients is not applied in a uniform manner among MS specialists.
Descriptions and graphs of the four recognized subtypes are shown below.

Relapsing MS is characterized by the abrupt onset of neurological symptoms occurring over several hours or days. This is followed by recovery, which may be complete (left panel), but more commonly is partial so that there is a residual disability (right panel). Relapses must last at least 24 hours, but commonly last days to weeks. Disability that worsens through a series of attacks is still classified as relapsing/remitting MS.

Secondary progressive MS starts as relapsing/remitting disease. After a period of time, the secondary progressive phase begins. This is characterized by slow worsening of baseline symptoms. Attacks may (right panel), or may not (left panel) continue during the progressive phase. Secondary progressive MS differs from relapsing MS in that the baseline slowly worsens between attacks.
Primary progressive MS slowly worsens from the onset. By definition, patients do not have attacks. Progression may be steady (left panel), or may have periods of faster or slower progression (right panel). There may even be periods of slight improvement. It is the complete absence of attacks that identifies this subtype.

Progressive/relapsing MS begins like primary progressive, but relapses then develop later in the disease course. Following these relapses, there may be recovery (left panel) or no recovery (right panel).