Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

2 Cohen ME, Eichel R, Steiner-Birmanns B, et al. A case of probable Parkinson's disease after SARS-CoV-2 infection. *Lancet Neurol* 2020; **19:** 804–05.

3 Volc D, Poewe W, Kutzelnigg A, et al. Safety and immunogenicity of the α-synuclein active immunotherapeutic PD01A in patients with Parkinson's disease: a randomised, single-blinded, phase 1 trial. *Lancet Neurol* 2020; **19:** 591–600.

4 Mullin S, Smith L, Lee K, et al. Ambroxol for the treatment of patients with Parkinson disease with and without glucocerebrosidase gene mutations: a nonrandomized, noncontrolled trial. *JAMA Neurol* 2020; **77:** 427–34.

5 Olanow CW, Factor SA, Espay AJ, et al. Apomorphine sublingual film for off episodes in Parkinson's disease: a randomised, double-blind, placebo-controlled phase 3 study. *Lancet Neurol* 2020; **19:** 135–44.

6 Pagan FL, Hebron ML, Wilmarth B, et al. Nilotinib effects on safety, tolerability, and potential biomarkers in Parkinson disease: a phase 2 randomized clinical trial. *JAMA Neurol* 2020; **77:** 309–17.

7 Zech M, Jech R, Boesch S, et al. Monogenic variants in dystonia: an exome-wide sequencing study. *Lancet Neurol* 2020; **19:** 908–18.

8 Cortese A, Tozza S, Yau WY, et al. Cerebellar ataxia, neuropathy, vestibular areflexia syndrome due to RFC1 repeat expansion. *Brain* 2020; **143:** 480–90.

9 Wan L, Chen Z, Wan N, et al. Biallelic intronic AAGGG expansion of RFC1 is related to multiple system atrophy. *Ann Neurol* 2020; published online Sept 16. https://doi.org/10.1002/ana.25902.

10 Ma D, Tan YJ, Ng ASL, et al. Association of NOTCH2NLC repeat expansions with Parkinson disease. *JAMA Neurol* 2020; published online Aug 24. https://doi.org/10.1001/jamaneurol.2020.3023.

Multiple sclerosis in 2020: *un bon cru*

The landscape of multiple sclerosis is changing, with new insights on prognosis, the emergence of artificial intelligence in brain imaging, technological advances challenging knowledge on disease pathogenesis, and the identification of novel therapeutic pathways. However, 2020 will certainly be remembered for the spread of the COVID-19 pandemic. In this context, the possibility of an increased susceptibility to severe COVID-19 in patients with multiple sclerosis has rapidly become an important question. Higher age, an Expanded Disability Status Scale score of 6 or more, and obesity were identified as independent risk factors for severe COVID-19 in a French multicentre observational cohort.[1] Whereas in this study, which included 347 patients, there was no significant association between disease-modifying treatment exposure and COVID-19 severity, some evidence is now emerging that therapies targeting CD20 might be linked to an increased risk of severe COVID-19, and several studies aiming to establish whether this is the case are ongoing.

How to manage individuals with radiologically isolated syndrome—people with brain MRI scans compatible with CNS inflammation but without neurological symptoms—remains challenging because the long-term outcome after this diagnosis is unknown. The multicentre Radiologically Isolated Syndrome Consortium study,[2] the largest and longest study to date, included 277 individuals with radiologically isolated syndrome. The cumulative probability of a clinical event at 10 years was 51·2%. Consistent with previous publications, young age and spinal cord lesions were identified as independent predictors of a first clinical event. The novelty here is the identification of two additional risk factors—the presence of oligoclonal bands or elevated IgG index in the CSF and infratentorial lesions—with a stepwise increase of risk associated with the number of factors (probability ranging from 29% for individuals with at least one risk factor to 87% for those with four risk factors). Nevertheless, in the absence of results from ongoing trials of potential disease-modifying drugs (TERIS [NCT03122652] and ARISE [NCT02739542]), there is no recommendation to treat individuals with radiologically isolated syndrome.

Artificial intelligence has opened new avenues for medical imaging in general. In multiple sclerosis, one example is a deep learning approach applying convolutional neural networks,[4] evaluating the possibility of predicting brain lesion activity without the need for contrast injection. In this study, conventional MRI data from 519 patients with a total of 1390 enhancing lesions were used to train and test network performance. Participants with enhancing lesions were classified with 70% accuracy. Similarly, a method proposed by Wei and colleagues[4] could offer an alternative to PET scanning to predict myelin content changes by using multisequence quantitative MRI. Myelin imaging with ^{11}C-PIB PET allows quantification of myelin content changes in vivo, but is invasive, with injection of a radioactive tracer, and is poorly suited to multicentre studies. The deep learning approach used by Wei and colleagues[4] allowed generation of synthetic images predicting myelin content changes in a longitudinal analysis of patients with multiple sclerosis. By providing MRI-based algorithms, deep learning methods are likely to modify, in the near future, the management of patients with multiple sclerosis, as well as the design of therapeutic studies.

With regard to disease pathogenesis, single-cell RNA-sequencing methods have revealed heterogeneity

in oligodendroglia, neurons, and microglia in healthy and multiple sclerosis tissue. In a single-cell genetic and epigenetic study, Wheeler and colleagues[5] investigated the heterogeneity of astrocytes in multiple sclerosis tissue and in experimental autoimmune encephalomyelitis (a rodent model of multiple sclerosis); they identified a subpopulation of astrocytes characterised by decreased expression of the antioxidant transcription factor NRF2 and increased expression of the transcription factor MAFG, leading to repression of anti-oxidant and anti-inflammatory transcriptional programmes. Such pro-inflammatory astrocytes are detected within active white matter lesions in patients with multiple sclerosis. These results, which identify how astrocytes might contribute to inflammation and tissue damage, open perspectives for therapeutic candidates targeting neurotoxic astrocytic activity.

Promoting neuroprotection in multiple sclerosis is a major challenge because irreversible disability is highly correlated with the accumulation of neuronal damage. Several trials of pro-remyelinating candidates are ongoing.[6] In this context, negative results from the AFFINITY trial of the effect of opicinumab on disability in patients with relapsing multiple sclerosis were released, ending the development of the anti-LINGO-1 strategy. Bexarotene to promote remyelination has also been trialled in patients with relapsing multiple sclerosis (EudraCT 2014-003145-99) and, although the primary efficacy outcome was reported to be negative and the drug was poorly tolerated, secondary outcomes suggest that it might promote myelin repair.[7]

With regard to direct neuroprotection, the negative results of the MS-SMART study were disappointing.[8] This phase 2b, multi-arm, parallel-group, double-blind, randomised placebo-controlled trial aimed to evaluate three neuroprotective drugs (amiloride, fluoxetine, and riluzole) selected from searches of research in animal models and clinical trials. In the primary analysis of 393 patients with secondary progressive multiple sclerosis, none of the therapeutic groups showed an improvement in the primary outcome (volumetric MRI percentage brain volume change) from baseline to 96 weeks compared with placebo. However, despite this negative result, the study convincingly showed the value and feasibility of a multi-arm phase 2 trial designed to inform a go or no-go decision for phase 3 trials targeting neuroprotection. Finally, the results of a trial of masitinib (NCT01433497) to target innate immunity suggested a positive effect of the drug versus placebo on disability in patients with progressive multiple sclerosis.[9]

Finally, exciting data on behavioural interventions from animal models are accumulating. In a study published earlier this year,[10] live imaging methods were used to follow oligodendrocytes and individual myelin sheaths in murine demyelinated motor cortex to assess the effect of learning a motor task on remyelination. Training led to increased remyelination by both new and surviving oligodendrocytes—an important result in the debate on the identity of remyelinating cells in the adult CNS. This study not only strengthens the evidence on the role of neuronal activity in myelination, but also provides a convincing demonstration that timely behavioural intervention (after the onset of remyelination) accelerates functional recovery through enhanced remyelination.

EM reports grants and personal fees from Biogen, Novartis, and Roche; and personal fees from Merck-Serono, Teva, Sanofi-Genzyme, and Ad Scientiam outside of the submitted work. CL reports grants and personal fees from Biogen; and personal fees from Merck-Serono, Roche, Rewind, and Ipsen outside of the submitted work.

*Elisabeth Maillart, *Catherine Lubetzki*
catherine.lubetzki@aphp.fr

Assistance Publique des Hôpitaux de Paris, Sorbonne University, Paris Brain Institute, Groupe Hospitalier Pitié-Salpêtrière, Paris 75013, France (EM, CL)

1 Louapre C, Collongues N, Stankoff B, et al. Clinical characteristics and outcomes in patients with coronavirus disease 2019 and multiple sclerosis. *JAMA Neurol* 2020; **77:** 1079–88.
2 Lebrun-Frenay C, Kantarci O, Siva A, et al. Radiologically isolated syndrome: 10-year risk estimate of a clinical event. *Ann Neurol* 2020; **88:** 407–17.
3 Narayana PA, Coronado I, Sujit SJ, Wolinsky JS, Lublin FD, Gabr RE. Deep learning for predicting enhancing lesions in multiple sclerosis from noncontrast MRI. *Radiology* 2020; **294:** 398–404.
4 Wei W, Poirion E, Bodini B, et al. Predicting PET-derived myelin content from multisequence MRI for individual longitudinal analysis in multiple sclerosis. *Neuroimage* 2020; **223:** 117308.
5 Wheeler MA, Clark IC, Tjon EC, et al. MAFG-driven astrocytes promote CNS inflammation. *Nature* 2020; **578:** 593–99.
6 Lubetzki C, Zalc B, Williams A, Stadelmann C, Stankoff B. Remyelination in multiple sclerosis: from basic science to clinical translation. *Lancet Neurol* 2020; **19:** 678–88.
7 Brown W, Cunnife N, Prados F, et al. Phase 2 clinical trial evidence that a retinoid-X receptor agonist promotes remyelination in people with relapsing-remitting multiple sclerosis. MSVirtual2020; virtual; Sept 11–13, 2020 (abstr LB01.02).
8 Chataway J, De Angelis F, Connick P, et al. Efficacy of three neuroprotective drugs in secondary progressive multiple sclerosis (MS-SMART): a phase 2b, multiarm, double-blind, randomised placebo-controlled trial. *Lancet Neurol* 2020; **19:** 214–25.
9 Vermersch P, Hermine O. Masitinib in primary progressive (PPMS) and non-active secondary progressive (nSPMS) multiple sclerosis: results from phase 3 study AB07002. MSVirtual2020; virtual; Sept 11–13, 2020 (abstr FC04.01).
10 Bacmeister CM, Barr HJ, McClain CR, et al. Motor learning promotes remyelination via new and surviving oligodendrocytes. *Nat Neurosci* 2020; **23:** 819–31.